REVERSE-TURN MIMETICS AND METHOD RELATING THERETO

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is a continuation-in-part of co-pending U.S. patent application serial No. 10/826,972, filed April 16, 2004, which is a continuation-in-part of co-pending U.S. patent application serial No. 10/803,179 filed March 17, 2004, which is a continuation-in-part of U.S. patent application serial No. 10/411,877 filed April 9, 2003 (now abandoned), which is a continuation-in-part of U.S. patent application serial No. 10/087,443 filed March 01, 2002 (now abandoned), which is a continuation-in-part of U.S. patent application serial No. 09/976,470 filed October 12, 2001 (now abandoned). This application also claims priority to PCT application serial No. PCT/KR02/01901 filed October 11, 2002. The disclosures of these applications are incorporated herein by reference in their entireties.

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates generally to reverse-turn mimetic structures and to a chemical library relating thereto. The invention also relates to applications in the treatment of medical conditions, *e.g.,* cancer diseases, and pharmaceutical compositions comprising the mimetics.

Description of the Related Art

Random screening of molecules for possible activity as therapeutic agents has occurred for many years and resulted in a number of important drug discoveries. While advances in molecular biology and computational chemistry have led to increased interest in what has been termed "rational drug design", such techniques have not proven as fast or reliable as initially predicted. Thus, in recent years there has been a renewed

interest and return to random drug screening. To this end, particular strides having been made in new technologies based on the development of combinatorial chemistry libraries, and the screening of such libraries in search for biologically active members.

In general, combinatorial chemistry libraries are simply a collection of molecules. Such libraries vary by the chemical species within the library, as well as the methods employed to both generate the library members and identify which members interact with biological targets of interest. While this field is still young, methods for generating and screening libraries have already become quite diverse and sophisticated. For example, a recent review of various combinatorial chemical libraries has identified a number of such techniques (Dolle, *J. Com. Chem.*, 2(3): 383-433, 2000), including the use of both tagged and untagged library members (Janda, *Proc. Natl. Acad. Sci. USA* 91:10779-10785, 1994).

Initially, combinatorial chemistry libraries were generally limited to members of peptide or nucleotide origin. To this end, the techniques of Houghten et al. illustrate an example of what is termed a "dual-defined iterative" method to assemble soluble combinatorial peptide libraries via split synthesis techniques (*Nature* (London) 354:84-86, 1991; *Biotechniques* 13:412-421, 1992; Bioorg. *Med. Chem. Lett.* 3:405-412, 1993). By this technique, soluble peptide libraries containing tens of millions of members have been obtained. Such libraries have been shown to be effective in the identification of opioid peptides, such as methionine- and leucine-enkephalin (Dooley and Houghten, *Life Sci.* 52, 1509-1517, 1993), and a N-acylated peptide library has been used to identify acetalins, which are potent opioid antagonists (Dooley et al., *Proc. Natl. Acad. Sci. USA* 90:10811-10815, 1993. More recently, an all D-amino acid opioid peptide library has been constructed and screened for analgesic activity against the mu ("μ") opioid receptor (Dooley et al, *Science* 266:2019-2022, 1994).

While combinatorial libraries containing members of peptide and nucleotide origin are of significant value, there is still a need in the art for libraries containing members of different origin. For example, traditional peptide libraries to a large extent merely vary the amino acid sequence to generate library members. While it is well recognized that the secondary structures of peptides are important to biological activity, such peptide libraries do not impart a constrained secondary structure to its library members.

To this end, some researchers have cyclized peptides with disulfide bridges in an attempt to provide a more constrained secondary structure (Tumelty et al., *J. Chem. Soc.* 1067-68, 1994; Eichler et al., *Peptide Res.* 7:300-306, 1994). However, such cyclized peptides are generally still quite flexible and are poorly bioavailable, and thus have met with only limited success.

More recently, non-peptide compounds have been developed which more closely mimic the secondary structure of reverse-turns found in biologically active proteins or peptides. For example, U.S. Pat. No. 5,440,013 to Kahn and published PCT applications nos. WO94/03494, WO01/00210A1, and WO01/16135A2 to Kahn each disclose conformationally constrained, non-peptidic compounds, which mimic the three-dimensional structure of reverse-turns. In addition, U.S. Pat. No. 5,929,237 and its continuation-in-part U.S. Pat. No. 6,013,458, both to Kahn, disclose conformationally constrained compounds which mimic the secondary structure of reverse-turn regions of biologically active peptides and proteins. The synthesis and identification of conformationally constrained, reverse-turn mimetics and their application to diseases were well reviewed by Obrecht (Advances in Med. Chem., 4, 1-68, 1999).

While significant advances have been made in the synthesis and identification of conformationally constrained, reverse-turn mimetics, there remains a need in the art for small molecules which mimic the secondary structure of peptides. There is also a need in the art for libraries containing

such members, as well as techniques for synthesizing and screening the library members against targets of interest, particularly biological targets, to identify bioactive library members.

The present invention also fulfills these needs, and provides further related advantages by providing confomationally constrained compounds which mimic the secondary structure of reverse-turn regions of biologically active peptides and proteins.

Wnt signaling pathway regulates a variety of processes including cell growth, oncogenesis, and development (Moon et al., 1997, Trends Genet. 13, 157-162; Miller et al., 1999, Oncogene 18, 7860-7872; Nusse and Varmus, 1992, Cell 69, 1073-1087; Cadigan and Nusse, 1997, Genes Dev. 11, 3286-3305; Peifer and Polakis, 2000 Science 287, 1606-1609; Polakis 2000, Genes Dev. 14, 1837-1851). Wnt signaling pathway has been intensely studied in a variety of organisms. The activation of TCF4/β-catenin mediated transcription by Wnt signal transduction has been found to play a key role in its biological functions (Molenaar et al., 1996, Cell 86:391-399; Gat et al., 1998 Cell 95:605-614; Orford et al., 1999 J. Cell. Biol. 146:855-868; Bienz and Clevers, 2000, Cell 103:311-20).

In the absence of Wnt signals, tumor suppressor gene adenomatous polyposis coli (APC) simultaneously interacts with the serine kinase glycogen synthase kinase (GSK)-3β and β-catenin (Su et al., 1993, Science 262, 1734-1737: Yost et al., 1996 Genes Dev. 10, 1443-1454: Hayashi et al., 1997, Proc. Natl. Acad. Sci. USA, 94, 242-247: Sakanaka et al., 1998, Proc. Natl. Acad. Sci. USA, 95, 3020-3023: Sakanaka and William, 1999, J. Biol. Chem 274, 14090-14093). Phosphorylation of APC by GSK-3β regulates the interaction of APC with β-catenin, which in turn may regulate the signaling function of β-catenin (B. Rubinfeld et al., Science 272, 1023, 1996). Wnt signaling stabilizes β-catenin allowing its translocation to the nucleus where it interacts with members of the lymphoid enhancer factor (LEF1)/T-cell factor (TCF4) family of transcription factors (Behrens et al., 1996 Nature 382,

638-642 : Hsu et al., 1998, Mol. Cell. Biol. 18, 4807-4818 : Roose et all., 1999 Science 285, 1923-1926).

Recently c-myc, a known oncogene, was shown to be a target gene for β-catenin/TCF4-mediated transcription (He et al., 1998 Science 281 1509-1512: Kolligs et al., 1999 Mol. Cell. Biol. 19, 5696-5706). Many other important genes, including cyclin D1, and metalloproteinase, which are also involved in oncogenesis, have been identified to be regulated by TCF4/bata-catenin transcriptional pathway (Crawford et al., 1999, Oncogene 18, 2883-2891: Shtutman et al., 1999, Proc. Natl. Acad. Sci. USA., 11, 5522-5527 : Tetsu and McCormick, 1999 Nature, 398, 422-426).

Moreover, overexpression of several downstream mediators of Wnt signaling has been found to regulate apoptosis (Moris et al., 1996, Proc. Natl. Acad. Sci. USA, 93, 7950-7954 : He et al., 1999, Cell 99, 335-345 : Orford et al, 1999 J. Cell. Biol., 146, 855-868: Strovel and Sussman, 1999, Exp. Cell. Res., 253, 637-648). Overexpression of APC in human colorectal cancer cells induced apoptosis (Moris et al., 1996, Proc. Natl. Acad. Sci. USA.,93, 7950-7954), ectopic expression of β-catenin inhibited apoptosis associated with loss of attachment to extracellular matrix (Orford et al, 1999, J. Cell Biol.146, 855-868). Inhibition of TCF4/β-catenin transcription by expression of dominant-negative mutant of TCF4 blocked Wnt-1-mediated cell survival and rendered cells sensitive to apoptotic stimuli such as anti-cancer agent (Shaoqiong Chen et al., 2001, J. Cell. Biol., 152, 1, 87-96) and APC mutation inhibits apoptosis by allowing constitutive survivin expression, a well-known anti-apoptotic protein (Tao Zhang et al., 2001, Cancer Research, 62, 8664-8667).

Although mutations in the Wnt gene have not been found in human cancer, a mutation in APC or β-catenin, as is the case in the majority of colorectal tumors, results in inappropriate activation of TCF4, overexpression of c-myc and production of neoplastic growth (Bubinfeld et al, 1997, Science, 275, 1790-1792 : Morin et al, 1997, Science, 275, 1787-1790 : Casa et al,

1999, Cell. Growth. Differ. 10, 369-376). The tumor suppressor gene (APC) is lost or inactivated in 85% of colorectal cancers and in a variety of other cancers as well (Kinzler and Vogelstein, 1996, Cell 87, 159-170). APC's principal role is that of a negative regulator of the Wnt signal transduction cascade. A center feature of this pathway involves the modulation of the stability and localization of a cytosolic pool of β-catenin by interaction with a large Axin-based complex that includes APC. This interaction results in phosphorylation of β-catenin thereby targeting it for degradation.

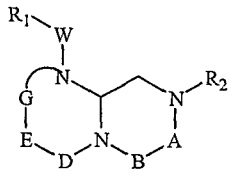
CREB binding proteins (CBP)/p300 were identified initially in protein interaction assays, first through its association with the transcription factor CREB (Chrivia et al, 1993, Nature, 365, 855-859) and later through its interaction with the adenoviral-transforming protein E1A (Stein et al., 1990, J. Viol., 64, 4421-4427 : Eckner et al., 1994, Genes. Dev., 8, 869-884). CBP had a potential to participate in variety of cellular functions including transcriptional coactivator function (Shikama et al., 1997, Trends. Cell. Biol., 7, 230-236 : Janknecht and Hunter, 1996, Nature, 383, 22-23). CBP/p300 potentiates β-catenin-mediated activation of the siamois promoter, a known Wnt target (Hecht et al, 2000, EMBO J. 19, 8, 1839-1850). β-catenin interacts directly with the CREB-binding domain of CBP and β-catenin synergizes with CBP to stimulate the transcriptional activation of TCF4/β-catenin (Ken-Ichi Takemaru and Randall T. Moon, 2000 J. Cell. Biol., 149, 2, 249-254).

BRIEF SUMMARY OF THE INVENTION

From this background, it is seen that TCF4/β-catenin and CBP complex of Wnt pathway can be taken as target molecules for the regulation of cell growth, oncogenesis and apoptosis of cells, etc. Accordingly, the present invention addresses a need for compounds that block TCF4/β-catenin transcriptional pathway by inhibiting CBP, and therefore can be used for treatment of cancer, especially colorectal cancer.

In brief, the present invention is directed to a new type of conformationally constrained compounds, which mimic the secondary structure of reverse-turn regions of biologically active peptides and proteins. This invention also discloses libraries containing such compounds, as well as the synthesis and screening thereof.

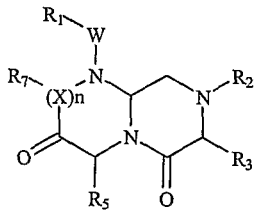
The compounds of the present invention have the following general formula (I):



(I)

wherein A is -(CHR_3)- or -(C=O)-, B is -(CHR_4)- or -(C=O)-, D is –(CHR_5)- or -(C=O)-, E is –(ZR_6)- or -(C=O)-, G is –(XR_7)$_n$-, -(CHR_7)-(NR_8)-, -(C=O)-(XR_9)-, or -(C=O)-, W is –Y(C=O)-, -(C=O)NH-, -(SO_2)- or is absent, Y is oxygen, sulfur, or -NH-, X and Z is independently nitrogen or CH, n=0 or 1; and R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are the same or different and independently selected from an amino acid side chain moiety or derivative thereof, the remainder of the molecule, a linker and a solid support, and stereoisomers thereof.

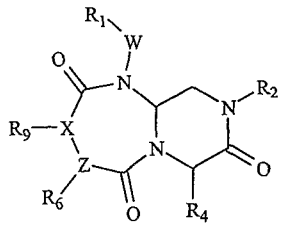
In an embodiment wherein A is –(CHR_3)-, B is –(C=O)-, D is -(CHR_5)-, E is –(C=O)-, and G is –(XR_7)$_n$-, the compounds of this invention have the following formula (II):



(II)

wherein W, X, Y and n are as defined above, and R_1, R_2, R_3, R_5 and R_7 are as defined in the following detailed description.

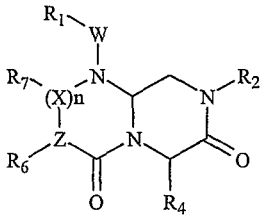
In an embodiment wherein A is –(C=O)-, B is -(CHR$_4$)-, D is -(C=O)-, E is –(ZR$_6$)-, and G is –(C=O)-(XR$_9$)-, the compounds of this invention have the following formula (III):



(III)

wherein W, X and Y are as defined above, Z is nitrogen or CH (with the proviso that when Z is CH, then X is nitrogen), and R$_1$, R$_2$, R$_4$, R$_6$ and R$_9$ are as defined in the following detailed description.

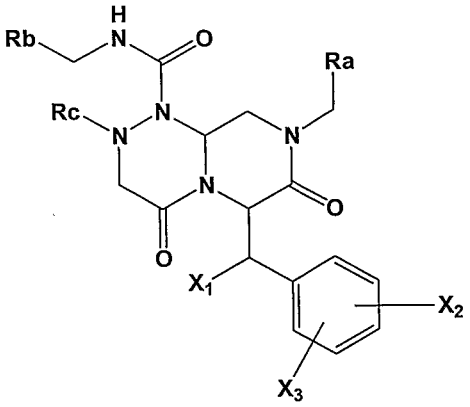
In an embodiment wherein A is –(C=O)-, B is –(CHR$_4$)-, D is -(C=O)-, E is –(ZR$_6$)-, and G is (XR$_7$)$_n$-, the compounds of this invention have the following general formula (IV):



(IV)

wherein W, Y and n are as defined above, Z is nitrogen or CH (when Z is nitrogen, then n is zero, and when Z is CH, then X is nitrogen and n is not zero), and R$_1$, R$_2$, R$_4$, R$_6$ and R$_7$, are as defined in the following detailed description.

In certain embodiments, the compounds of this invention have the following general formula (VI):



(VI)

wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a bicyclic aryl group having 8 to 11 ring members, which may have 1 to 3 heteroatoms selected from nitrogen, oxygen or sulfur; R_b is a monocyclic aryl group having 5 to 7 ring members, which may have 1 to 2 heteroatoms selected from nitrogen, oxygen or sulfur, and aryl ring in the compound may have one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups; R_c is a saturated or unsaturated C_{1-6}alkyl, C_{1-6}alkoxy, perfluoro C_{1-6}alkyl group; and X_1, X_2, and X_3 may be the same or different and independently selected from hydrogen, hydroxyl, and halide.

The present invention is also related to prodrugs using the libraries containing one or more compounds of formula (I). A prodrug is typically designed to release the active drug in the body during or after absorption by enzymatic and/or chemical hydrolysis. The prodrug approach is

an effective means of improving the oral bioavailability or i.v. administration of poorly water-soluble drugs by chemical derivatization to more water-soluble compounds. The most commonly used prodrug approach for increasing aqueous solubility of drugs containing a hydroxyl group is to produce esters containing an ionizable group; *e.g.*, phosphate group, carboxylate group, alkylamino group (Fleisher *et al.*, *Advanced Drug Delivery Reviews*, 115-130, 1996; Davis *et al.*, *Cancer Res.*, 7247-7253, 2002, Golik *et al.*, *Bioorg. Med. Chem. Lett.*, 1837-1842, 1996).

In certain embodiments, the prodrugs of the present invention have the following general formula (VII):

$$(VI)\text{-}Y\text{-}R_{10}$$

wherein (VI) is general formula (VI) as described above; Y is oxygen, sulfur, or nitrogen of a group selected from R_a, R_b, R_c, X_1, X_2 and X_3;

R_{10} is phosphate, hemisuccinate, hemimalate, phosphoryloxymethyloxycarbonyl, dimethylaminoacetate, dimethylaminoalkylcarbamates, hydroxyalkyls, amino acid, glycosyl,substituted or unsubstituted piperidine oxycarbonyl, or a salt thereof; and wherein the prodrugs are capable of serving as a substrate for a phosphatase or a carboxylase and are thereby converted to compounds having general formula (VI).

In some embodiments, R_{10} of the general formula (VII) is not an amino acid group or a phospho-amino acid group.

The present invention is also directed to libraries containing one or more compounds of formula (I) above, as well as methods for synthesizing such libraries and methods for screening the same to identify biologically active compounds. Compositions containing a compound of this invention in combination with a pharmaceutically acceptable carrier or diluent are also disclosed.

The present invention is also related to methods for identifying a biologically active compound using the libraries containing one or more

compound of formula (I). In a related aspect, the present invention provides a method for performing a binding assay, comprising (a) providing a composition comprising a first co-activator and an interacting protein, said first co-activator comprising a binding motif of LXXLL, LXXLI or FXXFF wherein X is any amino acid; (b) combining the first co-activator and the interacting protein with a test compound; and (c) detecting alteration in binding between the first co-activator and the interacting protein in the presence of the compound having general formula (I).

The present invention also provides methods for preventing or treating disorders associated with Wnt signaling pathway. Disorders that may be treated or prevented using a compound or composition of the present invention include tumor or cancer (*e.g.*, KSHV-associated tumor), restenosis associated with angioplasty, polycystic kidney disease, aberrant angiogenesis disease, rheumatoid arthritis disease, ulcerative colitis, tuberous sclerosis complex, hair loss, and Alzheimer's disease. Such methods comprise administering to a subject in need thereof a compound or composition of the present invention in an amount effective to achieve the desired outcome.

In a related aspect, the present invention further provides methods for promoting neurite outgrowth, differentiation of a neural stem cell, and apoptosis in cancer cells. Such methods comprise administering to appropriate cells a compound or composition of the present invention in an amount effective to achieve the desired outcome.

These and other aspects of this invention will be apparent upon reference to the attached figure and following detailed description. To this end, various references are set forth herein, which describe in more detail certain procedures, compounds and/or compositions, and are incorporated by reference in their entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 provides a general synthetic scheme for preparing reverse-turn mimetics of the present invention.

Figure 2 provides a general synthetic scheme for preparing reverse-turn mimetics of the present invention.

Figure 3 shows a graph based on the measurement of IC_{50} for Compound A of the present invention using SW480 cells, wherein cell growth inhibition on SW480 cells was measured at various concentrations of Compound A prepared in Example 4 to obtain the IC_{50} value. Specifically, the degree of inhibition in firefly and renilla luciferase activities by Compound A was determined. As a result, the IC_{50} of Compound A against SW480 cell growth was found as disclosed in Table 4. Detailed procedures are the same as disclosed in Example 6.

Figure 4. PC-12 cells were cultured on coated dishes, and differentiated for 10 days in 50 ng/ml nerve growth factor (NGF) (as described in Example 7). (A, B) Vector-transfected PC-12 cells (A) and PC-12 cells overexpressing wt PS-1 (B) exhibit extensive neurite outgrowth after 10 days in NGF. (C) PC-12 cells expressing mutant PS-1/ L286V do not display significant neurites under the same culture conditions. (D,E) Immunofluorescence analysis of GAP-43 (as described in Example 7), a molecular marker of neurite outgrowth, demonstrates intense staining for GAP-43 in the neurites (D) of vector-transfected and overexpressing PS-1/WT in PC-12 cells (E). (F) Lack of neurite outgrowth corresponds to weak GAP-43 immunostaining in the mutant cells. Data represent at least two independent experiments. (G) Differentiated cells were transfected with, Topflash, a TCF/ß-catenin reporter construct. Cells were lysed, and luciferase activity measured 6 hours post-transfection (as described in Example 7). Data represent the mean of three independent experiments (±SD). Asterisk indicate $P < 0.05$.

Fig. 5. Compound D phenotypically corrects deficient neuronal differentiation in PC-12 overexpressing mutant PS-1/L286V cells. Mutant cells

were exposed to 10 μM Compound D, in addition to NGF, during the differentiation period (Misner *et al.*, *Proc. Natl. Acad. Sci. U S A* **98,** 11714 (2001)). (A) Neurite elongation and extension are observed in PC-12 cells overexpressing PS-1/L286V upon treatment with Compound D. (B) GAP-43 (green) is significantly elevated in the mutant cells, and is seen in the neurites. (C) Quantitation of neurite outgrowth in PC-12 cells. Number of mutant cells with neurite lengths greater than two cell diameters was less than 10% that of the vector-transfected and overexpressing PS-1/WT in PC-12 cells. Number of mutant PS-1/L286V cells that had the defined neurite lengths was significantly increased, after treatment with 10 μM Compound D. The results are the average (± SD) of three independent determinations. Asterisk indicate $P < 0.05$.

Fig. 6. Ephrin B2 (EphB2) receptor expression.

Immunofluorescence analysis and RT-PCR were performed to detect EphB2 receptor expression (as described in Example 7). (A, B) EphB2 receptors are clearly demonstrated in neurites of vector-transfected and overexpressing PS-1/WT cells. The intensity of staining correlates with the high expression level. (C) In contrast, PS-1/L286V PC-12 cells have markedly reduced EphB2 receptor expression. (D) Treatment of mutant cells with Compound D leads to increased EphB2 receptor expression, which is focused at points of neurite outgrowth. (E) Expression of EphB2 receptor has previously been shown to be transcriptionally regulated (Guo *et al.*, *J. Neurosci.* **17,** 4212 (1997).). Lane 1, vector-transfected PC-12 cells, lane 2, overexpressing PS-1/WT cells, lane 3, overexpressing mutant PS-1/L286V cells, lane 4, mutant cells treated with Compound D. RT-PCR analysis indicates message for EphB2 receptor in cells overexpressing mutant PS-1/L286V is decreased compared to those in both the vector-transfected and overexpressing wt PS-1 PC-12 cells. Treatment with 10 μM Compound D upregulates EphB2 message. GAPDH is used an internal control.

Figure 7. A. Compound D arrests cells in G_1. FACS analysis was performed on SW480 (lower panel) and HCT116 (upper panel) cells treated for 24 hours with either Compound D (25 μM) (right) or control (0.5% DMSO (left). 5.5 X 10^6 cells were fixed and stained with propidium iodide (PI). B. Compound D selectively activates caspases in colon carcinoma cell lines. SW480 and HCT116 (left graph) cells (10^5) along with the normal colonocytes CCD18Co (right graph) were treated with either control (0.5% DMSO) or Compound D (25 μM). 24 hours post treatment, cells were lysed and the caspase-3/7 enzymatic activities were measured. Relative fluorescence units (RFU) were calculated by subtracting the unit values of the blank (control, without cells) from the treated samples (Compound D or control) and plotted.

Figure 8. Compound D reduces colony growth in soft agar in a dose dependent manner. Increasing concentrations of 5-fluorouracil (5-FU) (0.5-32 μM) and Compound D (0.25-5 μM) were added to SW480 (5000 cells/well) of triplicate wells. Cells were washed and suspended in soft agar growth medium. The number of colonies after 8 days (colonies over 60 μM diameter) were counted and plotted against the compound concentration. Mean ± SE of three determinations is indicated. The colony number of control in the absence of the compound was 1,637 ± 71.

Figure 9. A. Compound C reduces tumor growth in nude mouse model. B. Compound C slightly reduces body weight in nude mouse model.

Figure 10. The survivin transcriptional activity is upregulated by Wnt1, but knout-down by Compound D. Percent luciferase activities were measured in wildtype, CBP+/-, and p300+/- 3T3 cells in the absence of Wnt1 and Compound D, or in the presence of Wnt1, Compound D or both.

Figure 11. Compound A (right graph) and Compound D (left graph) inhibit the activity of a survivin luciferase reporter in SW480 cells. The luciferase activities under the control of the survivin promoter were measured in SW480 cells treated with compound A or Compound D at various concentrations.

Figure 12. RT-PCR analsis indicates that Compound D treatment decreases the expression level of the survivin gene.

Figure 13. Compound D decreases the association of various proteins with the survivin promoter. ChIP assays on SW480 cells treated with either Compound D (25 μM) or control (0.5% DMSO) for 18 hours were performed.

Figure 14. Compound D decreases survivin expression at the translational level. A. Western blot analysis of extracts of cells treated with vehicle (0.5% DMSO) alone, 10 μM or 25 μM Compound D, or 5 μM 5-FU was performed using survivin 6E4 monoclonal antibody (Cell Signaling Technolgy). B. Survivin immunofluorescence microscopy. Cultured cancer cells were fixed and stained with anti-survivin green. C. Survivin immunofluorescence microscopy. SW480 cells treated with Compound D were fixed and stained with anti-survivin green.

Figure 15. Compound D activates the caspase 3 activity (but not the caspase 2 activity) via suppression of the survivin expression. Cultured cells with or without transfection of a construct containing the survivin gene were treated with stausporine (0.5 μM), Compound D (2.5 μM or 5.0 μM), or both. The caspase 2 and caspase 3 activities in these cells were measured.

Figure 16. Compound D promotes cell death via suppression of the survivin expression. Cultured cancer cells with or without transfection of a construct containing the survivin gene were treated with stausporine (0.5 μM), Compound D (5.0 μM), or both. The cell death of these cells was measured.

Figure 17. Compound D increases the number of cells in G_0. Cultured cancer cells with or without transfection of a construct containing the survivin gene were treated with stausporine (0.5 μM), Compound D (5 μM), or both. FACS analysis was performed on these cells and the percentages of cells in G_0 are indicated.

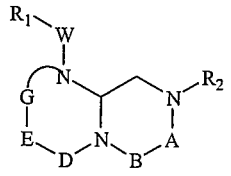
Figure 18 shows the changes of concentrations of prodrug A and its parent compound in mouse plasma with the increase of time after i.v. bolus injection of prodrug A. Square: parent compound; Diamond: prodrug A.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to conformationally constrained compounds that mimic the secondary structure of reverse-turn regions of biological peptide and proteins (also referred to herein as "reverse-turn mimetics", and is also directed to chemical libraries relating thereto.

The reverse-turn mimetic structures of the present invention are useful as bioactive agents, including (but not limited to) use as diagnostic, prophylactic and/or therapeutic agents. The reverse-turn mimetic structure libraries of this invention are useful in the identification of bioactive agents having such uses. In the practice of the present invention, the libraries may contain from tens to hundreds to thousands (or greater) of individual reverse-turn structures (also referred to herein as "members").

In one aspect of the present invention, a reverse-turn mimetic structure is disclosed having the following formula (I):



(I)

wherein A is -(CHR_3)- or -(C=O)-, B is -(CHR_4)- or -(C=O)-, D is –(CHR_5)- or –(C=O)-, E is –(ZR_6)- or -(C=O)-, G is –(XR_7)$_n$-, -(CHR_7)-(NR_8)-, -(C=O)-(XR_9)-, or -(C=O)-, W is –Y(C=O)-, -(C=O)NH-, -(SO_2)- or nothing, Y is oxygen, sulfur, or -NH-, X and Z is independently nitrogen or CH, n=0 or 1; and R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are the same or different and independently selected from an amino acid side chain moiety or derivative thereof, the remainder of the molecule, a linker and a solid support, and stereoisomers thereof.

In one embodiment, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are independently selected from the group consisting of aminoC_{2-5}alkyl, guanidineC_{2-5}alkyl, C_{1-4}alkylguanidinoC_{2-5}alkyl, diC_{1-4}alkylguanidino-C_{2-5}alkyl, amidinoC_{2-5}alkyl, C_{1-4}alkylamidinoC_{2-5}alkyl, diC_{1-4}alkylamidinoC_{2-5}alkyl, C_{1-3}alkoxy, phenyl, substituted phenyl (where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), benzyl, substituted benzyl (where the substituents on the benzyl are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), naphthyl, substituted naphthyl (where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), bis-phenyl methyl, substituted bis-phenyl methyl (where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyridyl, substituted pyridyl, (where the substituents are independently selected from one or more of amino amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyridylC_{1-4}alkyl, substituted pyridylC_{1-4}alkyl (where the pyridine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyrimidylC_{1-4}alkyl, substituted pyrimidylC_{1-4}alkyl (where the pyrimidine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino,

halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), triazin-2-yl-C_{1-4}alkyl, substituted triazin-2-yl-C_{1-4}alkyl (where the triazine substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), imidazoC_{1-4}alkyl, substituted imidazol C_{1-4}alkl (where the imidazole sustituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), imidazolinylC_{1-4}alkyl, N-amidinopiperazinyl-N-C_{0-4}alkyl, hydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, hydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, C_{1-5}dialkylaminoC_{2-5}alkyl, N-amidinopiperidinylC_{1-4}alkyl and 4-aminocyclohexylC_{0-2}alkyl.

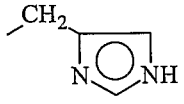
In one embodiment, R_1, R_2, R_6 of E, and R_7, R_8 and R_9 of G are the same or different and represent the remainder of the compound, and R_3 of A, R_4 of B or R_5 of D is selected from an amino acid side chain moiety or derivative thereof. As used herein, the term "remainder of the compound" means any moiety, agent, compound, support, molecule, linker, amino acid, peptide or protein covalently attached to the reverse-turn mimetic structure at R_1, R_2, R_5, R_6, R_7, R_8 and/or R_9 positions. This term also includes amino acid side chain moieties and derivatives thereof.

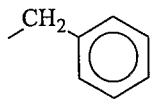
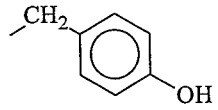
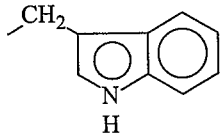
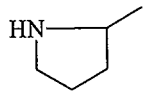
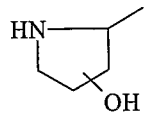
In another embodiment R_3 of A, R_5 of D, R_6 of E, and R_7, R_8, and R_9 of G are the same or different and represent the remainder of the compound, while one or more of, and in one aspect all of, R_1, R_2 and R_4 of B represent an amino acid sidechain. In this case, the term "remainder of the compound" means any moiety, agent, compound, support, molecule, linker, amino acid, peptide or protein covalently attached to the reverse-turn mimetic structure at R_3, R_5, R_6, R_7, R_8 and/or R_9 positions. This term also includes amino acid side chain moieties and derivatives thereof.

As used herein, the term "remainder of the compound" means any moiety, agent, compound, support, molecule, atom, linker, amino acid, peptide or protein covalently attached to the reverse-turn mimetic structure. This term also includes amino acid side chain moieties and derivatives thereof. In one aspect of the invention, any one or more of the R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and/or R_9 positions may represent the remainder of the compound. In one aspect of the invention, one or more of R_1, R_2 and R_4 represents an amino acid side chain moiety or a derivative thereof.

As used herein, the term "amino acid side chain moiety" represents any amino acid side chain moiety present in naturally occurring proteins including (but not limited to) the naturally occurring amino acid side chain moieties identified in Table 1. Other naturally occurring amino acid side chain moieties of this invention include (but are not limited to) the side chain moieties of 3,5-dibromotyrosine, 3,5-diiodotyrosine, hydroxylysine, γ-carboxyglutamate, phosphotyrosine and phosphoserine. In addition, glycosylated amino acid side chains may also be used in the practice of this invention, including (but not limited to) glycosylated threonine, serine and asparagine.

TABLE 1

Amino Acid Side Chain Moiety	Amino Acid
–H	Glycine
$-CH_3$	Alanine
$-CH(CH_3)_2$	Valine
$-CH_2\ CH(CH_3)_2$	Leucine
$-CH(CH_3)CH_2\ CH_3$	Isoleucine
$-(CH_2)_4NH_3^+$	Lysine
$-(CH_2)_3NHC(NH_2)NH_2^+$	Arginine
	Histidine
$-CH_2COO^-$	Aspartic acid
$-CH_2CH_2COO^-$	Glutamic acid
$-CH_2CONH_2$	Asparagine
$-CH_2CH_2CONH_2$	Glutamine

	Phenylalanine
	Tyrosine
	Tryptophan
$-CH_2SH$	Cysteine
$-CH_2CH_2SCH_3$	Methionine
$-CH_2OH$	Serine
$-CH(OH)CH_3$	Threonine
	Proline
	Hydroxyproline

In addition to naturally occurring amino acid side chain moieties, the amino acid side chain moieties of the present invention also include various derivatives thereof. As used herein, a "derivative" of an amino acid side chain moiety includes modifications and/or variations to naturally occurring amino acid side chain moieties. For example, the amino acid side chain moieties of alanine, valine, leucine, isoleucine and phenylalanine may generally be classified as lower chain alkyl, aryl, or arylalkyl moieties. Derivatives of amino acid side chain moieties include other straight chain or branched, cyclic or noncyclic, substituted or unsubstituted, saturated or unsaturated lower chain alkyl, aryl or arylalkyl moieties.

As used herein, "lower chain alkyl moieties" contain from 1-12 carbon atoms, "lower chain aryl moieties" contain from 6-12 carbon atoms and "lower chain aralkyl moieties" contain from 7-12 carbon atoms. Thus, in one

embodiment, the amino acid side chain derivative is selected from a C_{1-12} alkyl, a C_{6-12} aryl and a C_{7-12} arylalkyl, and in a more preferred embodiment, from a C_{1-7} alkyl, a C_{6-10} aryl and a C_{7-11} arylalkyl.

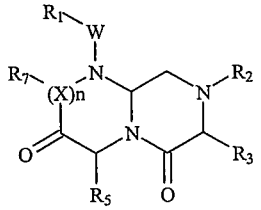
Amino side chain derivatives of this invention further include substituted derivatives of lower chain alkyl, aryl, and arylalkyl moieties, wherein the substituent is selected from (but is not limited to) one or more of the following chemical moieties: -OH, -OR, -COOH, -COOR, -$CONH_2$, -NH_2, -NHR, -NRR, -SH, -SR, -SO_2R, -SO_2H, -SOR and halogen (including F, Cl, Br and I), wherein each occurrence of R is independently selected from straight chain or branched, cyclic or noncyclic, substituted or unsubstituted, saturated or unsaturated lower chain alkyl, aryl and aralkyl moieties. Moreover, cyclic lower chain alkyl, aryl and arylalkyl moieties of this invention include naphthalene, as well as heterocyclic compounds such as thiophene, pyrrole, furan, imidazole, oxazole, thiazole, pyrazole, 3-pyrroline, pyrrolidine, pyridine, pyrimidine, purine, quinoline, isoquinoline and carbazole. Amino acid side chain derivatives further include heteroalkyl derivatives of the alkyl portion of the lower chain alkyl and aralkyl moieties, including (but not limited to) alkyl and aralkyl phosphonates and silanes.

Representative R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 moieties specifically include (but are not limited to) -OH, -OR, -COR, -COOR, -$CONH_2$, -CONR, -CONRR, -NH_2, -NHR, -NRR, -SO_2R and -COSR, wherein each occurrence of R is as defined above.

In a further embodiment, and in addition to being an amino acid side chain moiety or derivative thereof (or the remainder of the compound in the case of R_1, R_2, R_3, R_5, R_6, R_7, R_8 and R_9), R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 may be a linker facilitating the linkage of the compound to another moiety or compound. For example, the compounds of this invention may be linked to one or more known compounds, such as biotin, for use in diagnostic or screening assay. Furthermore, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 may be a linker joining the compound to a solid support (such as a support used in solid

phase peptide synthesis) or alternatively, may be the support itself. In this embodiment, linkage to another moiety or compound, or to a solid support, is preferable at the R_1, R_2, R_7 or R_8, or R_9 position, and more preferably at the R_1 or R_2 position.

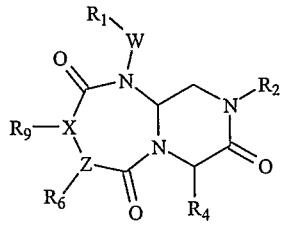
In the embodiment wherein A is $-(CHR_3)-$, B is $-(C=O)-$, D is $-(CHR_5)-$, E is $-(C=O)-$, and G is $-(XR_7)_n-$, the reverse turn mimetic compound of this invention has the following formula (II):



(II)

wherein R_1, R_2, R_3, R_5, R_7, W, X and n are as defined above. In a preferred embodiment, R_1, R_2 and R_7 represent the remainder of the compound, and R_3 or R_5 is selected from an amino acid side chain moiety.

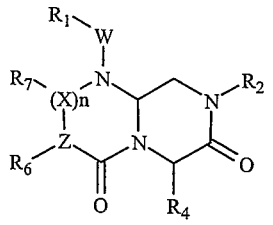
In the embodiment wherein A is $-(C=O)-$, B is $-(CHR_4)-$, D is $-(C=O)-$, E is $-(ZR_6)-$, G is $-(C=O)-(XR_9)-$, the reverse turn mimetic compound of this invention has the following general formula (III):



(III)

wherein R_1, R_2, R_4, R_6, R_9, W and X are as defined above, Z is nitrogen or CH (when Z is CH, then X is nitrogen). In a preferred embodiment, R_1, R_2, R_6 and R_9 represent the remainder of the compound, and R_4 is selected from an amino acid side chain moiety.

In a more specific embodiment wherein A is $-(C=O)-$, B is $-(CHR_4)-$, D is $-(C=O)-$, E is $-(ZR_6)-$, and G is $(XR_7)_n-$, the reverse turn mimetic compound of this invention has the following formula (IV):

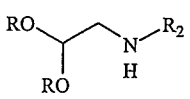


(IV)

wherein R_1, R_2, R_4, R_6, R_7, W, X and n are as defined above, and Z is nitrogen or CH (when Z is nitrogen, then n is zero, and when Z is CH, then X is nitrogen and n is not zero). In a preferred embodiment, R_1, R_2, R_6 and R_7 represent the remainder of the compound, and R_4 is selected from an amino acid side chain moiety. In one aspect, R_6 or R_7 is selected from an amino acid side chain moiety when Z and X are both CH.

These compounds may be prepared by utilizing appropriate starting component molecules (hereinafter referred to as "component pieces"). Briefly, in the synthesis of reverse-turn mimetic structures having formula (I), first and second component pieces are coupled to form a combined first-second intermediate, if necessary, third and/or fourth component pieces are coupled to form a combined third-fourth intermediate (or, if commercially available, a single third intermediate may be used), the combined first-second intermediate and third-fourth intermediate (or third intermediate) are then coupled to provide a first-second-third-fourth intermediate (or first-second-third intermediate) which is cyclized to yield the reverse-turn mimetic structures of this invention. Alternatively, the reverse-turn mimetic structures of formula (I) may be prepared by sequential coupling of the individual component pieces either stepwise in solution or by solid phase synthesis as commonly practiced in solid phase peptide synthesis.

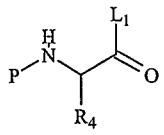
Specific component pieces and the assembly thereof to prepare compounds of the present invention are illustrated in Figure 1. For example, a "first component piece" may have the following formula S1:



(S1)

wherein R_2 is as defined above, and R is a protective group suitable for use in peptide synthesis, where this protection group may be joined to a polymeric support to enable solid-phase synthesis. Suitable R groups include alkyl groups and, in a preferred embodiment, R is a methyl group. In Figure 1, one of the R groups is a polymeric (solid) support, indicated by "Pol" in the Figure. Such first component pieces may be readily synthesized by reductive amination of H_2N-R_2 with $CH(OR)_2$-CHO, or by a displacement reaction between H_2N-R_2 and $CH(OR)_2$-CH_2-LG (wherein LG refers to a leaving group, *e.g.,* a halogen (Hal) group).

A "second component piece" may have the following formula S2:



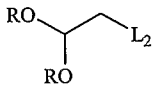
(S2)

where P is an amino protection group suitable for use in peptide synthesis, L_1 is hydroxyl or a carboxyl-activation group, and R_4 is as defined above. Preferred protection groups include t-butyl dimethylsilyl (TBDMS), t-butyloxycarbonyl (BOC), methyloxycarbonyl (MOC), 9H-fluorenylmethyloxycarbonyl (FMOC), and allyloxycarbonyl (Alloc). N-Protected amino acids are commercially available; for example, FMOC amino acids are available from a variety of sources. In order for the second component piece to be reactive with the first component piece, L_1 is a carboxyl-activation group, and the conversion of carboxyl groups to activated carboxyl groups may be readily achieved by methods known in the art for the activation of carboxyl groups. Suitable activated carboxylic acid groups include acid halides where L_1 is a halide such as chloride or bromide, acid anhydrides where L_1 is an acyl group such as acetyl, reactive esters such as an N-hydroxysuccinimide esters and pentafluorophenyl esters, and other activated intermediates such as the active intermediate formed in a coupling reaction using a carbodiimide such as dicyclohexylcarbodiimide (DCC).

Accordingly, commercially available N-protected amino acids may be converted to carboxylic activated forms by means known to one of skill in the art.

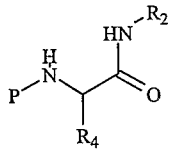
In the case of the azido derivative of an amino acid serving as the second component piece, such compounds may be prepared from the corresponding amino acid by the reaction disclosed by Zaloom et al. (*J. Org. Chem.* 46:5173-76, 1981).

Alternatively, the first component piece of the invention may have the following formula S1':



(S1')

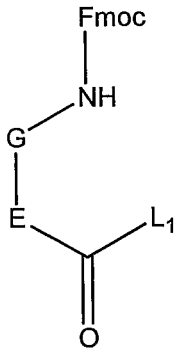
wherein R is as defined above and L_2 is a leaving group such as halogen atom or tosyl group, and the second component piece of the invention may have the following formula S2':



(S2')

wherein R_2, R_4 and P are as defined above,

A "third component piece" of this invention may have the following formula S3:



(S3)

where G, E, L_1 and L_2 are as defined above. Suitable third component pieces are commercially available from a variety of sources or can be prepared by methods well known in organic chemistry.

In Figure 1, the compound of formula (1) has –(C=O)- for A, -(CHR_4)- for B, -(C=O)- for D, and –(CR_6)- for E. Compounds of formula (1) wherein a carbonyl group is at position B and an R group is at position B, *i.e.,* compounds wherein A is –(CHR_3)- and B is –(C=O)-, may be prepared in a manner analogous to that shown in Figure 1, as illustrated in Figure 2. Figure 2 also illustrates adding a fourth component piece to the first-second-third component intermediate, rather than attaching the fourth component piece to the third component piece prior to reaction with the first-second intermediate piece. In addition, Figure 2 illustrates the prepartion of compounds of the present invention wherein D is -(CHR_5)- (rather than –(C=O)- as in Figure 1), and E is –(C=O)- (rather than -(CHR_6)- as in Figure 1). Finally, Figure 2 illustrates the preparation of compounds wherein G is NR_7.

Thus, as illustrated above, the reverse-turn mimetic compounds of formula (I) may be synthesized by reacting a first component piece with a second component piece to yield a combined first-second intermediate, followed by reacting the combined first-second intermediate with third component pieces sequentially to provide a combined first-second-third-fourth intermediate, and then cyclizing this intermediate to yield the reverse-turn mimetic structure.

The syntheses of representative component pieces of this invention are described in Preparation Examples and working Examples.

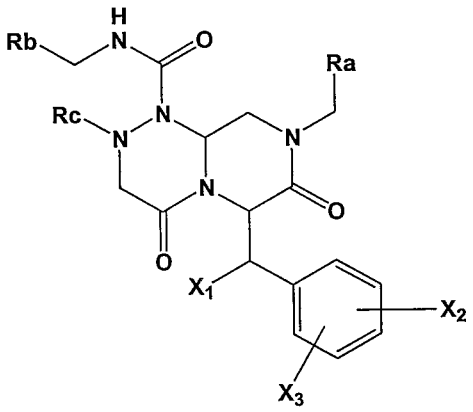
The reverse-turn mimetic structures of formula (III) and (IV) may be made by techniques analogous to the modular component synthesis disclosed above, but with appropriate modifications to the component pieces.

The reverse-turn mimetic structures of the present invention are useful as bioactive agents, such as diagnostic, prophylactic, and therapeutic agents. For example, the reverse-turn mimetic structures of the present

invention may be used for modulating a cell signaling transcription factor related peptides in a warm-blooded animal, by a method comprising administering to the animal an effective amount of the compound of formula (I).

Further, the reverse-turn mimetic structures of the present invention may also be effective for inhibiting peptide binding to PTB domains in a warm-blooded animal; for modulating G protein coupled receptor (GPCR) and ion channel in a warm-blooded animal; for modulating cytokines in a warm-blooded animal.

Meanwhile, it has been found that the compounds of the formula (I), especially compounds of formula (VI) are effective for inhibiting or treating disorders modulated by Wnt-signaling pathway, such as cancer, especially colorectal cancer.



(VI)

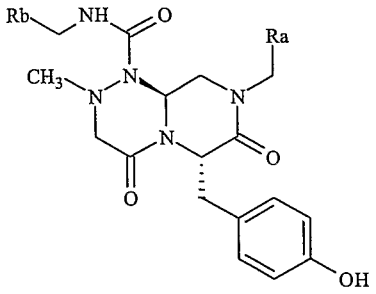
wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a bicyclic aryl group having 8 to 11 ring members, which may have 1

to 3 heteroatoms selected from nitrogen, oxygen or sulfur; R_b is a monocyclic aryl group having 5 to 7 ring members, which may have 1 to 2 heteroatoms selected from nitrogen, oxygen or sulfur, and aryl ring in the compound may have one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups; Rc is a saturated or unsaturated C_{1-6}alkyl, C_{1-6}alkoxy, perfluoro C_{1-6}alkyl group; and X_1, X_2, and X_3 may be the same or different and independently selected from hydrogen, hydroxyl, and halide.

In another aspect, it is an object of the present invention to provide a pharmaceutical composition comprising a safe and effective amount of the compound having general formula (VI) and pharmaceutically acceptable carrier, which can be used for treatment of disorders modulated by Wnt signaling pathway, especially by TCF4-β-catenin-CBP complex.

Further, the present invention is to provide a method for inhibiting the growth of tumor cells by using the above-described composition of the present invention; a method for inducing apoptosis of tumor cells by using the above-described composition of the present invention; a method for treating a disorder modulated by TCF4-β catenin-CBP complex by using the above-described composition of the present invention; and a method of treating cancer such as colorectal cancer by administering the composition of the present invention together with other anti-cancer agent such as 5-fluorouracil (5-FU), taxol, cisplatin, mitomycin C, tegafur, raltitrexed, capecitabine, and irinotecan, etc.

In a preferred embodiment of the present invention, the compound of the present invention has a (6S,10R)-configuration as follows:



(VIa)

wherein R_a and R_b have the same meanings as defined above.

In another aspect of this invention, prodrugs derived from compounds having general formula (I) are disclosed. The prodrugs generally increase aqueous solubility and thus bioavailability of compounds having general formula (I). In certain embodiments, the prodrugs of the present invention have the following general formula (VII):

$$(VI)\text{-}Y\text{-}R_{10}$$

wherein (VI) is general formula (VI) as described above; Y is oxygen, sulfur, or nitrogen of a group selected from R_a, R_b, R_c, X_1, X_2 and X_3; R_{10} is phosphate, hemisuccinate, hemimalate, phosphoryloxymethyloxycarbonyl, dimethylaminoacetate, dimethylaminoalkylcarbamate, hydroxyalkyl, amino acid, glycosyl, substituted or unsubstituted piperidine oxycarbonyl, or a salt thereof; and wherein the prodrugs are capable of serving as a substrate for a phosphatase or a carboxylase and are thereby converted to compounds having general formula (VI). In some embodiments, R_{10} of the general formula (VII) is not an amino acid group or a phospho-amino acid group.

In another aspect of this invention, libraries containing reverse-turn mimetic structures of the present invention are disclosed. Once assembled, the libraries of the present invention may be screened to identify individual members having bioactivity. Such screening of the libraries for bioactive members may involve; for example, evaluating the binding activity of the members of the library or evaluating the effect the library members have on a functional assay. Screening is normally accomplished by contacting the

library members (or a subset of library members) with a target of interest, such as, for example, an antibody, enzyme, receptor or cell line. Library members which are capable of interacting with the target of interest, are referred to herein as "bioactive library members" or "bioactive mimetics". For example, a bioactive mimetic may be a library member which is capable of binding to an antibody or receptor, or which is capable of inhibiting an enzyme, or which is capable of eliciting or antagonizing a functional response associated, for example, with a cell line. In other words, the screening of the libraries of the present invention determines which library members are capable of interacting with one or more biological targets of interest. Furthermore, when interaction does occur, the bioactive mimetic (or mimetics) may then be identified from the library members. The identification of a single (or limited number) of bioactive mimetic(s) from the library yields reverse-turn mimetic structures which are themselves biologically active, and thus are useful as diagnostic, prophylactic or therapeutic agents, and may further be used to significantly advance identification of lead compounds in these fields.

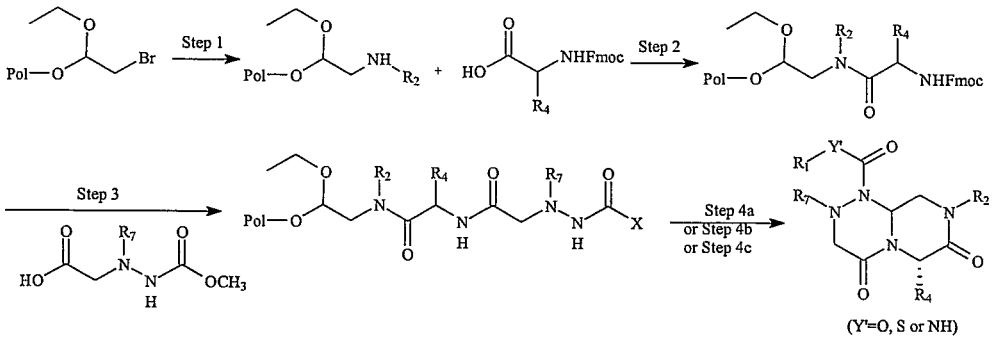
Synthesis of the peptide mimetics of the library of the present invention may be accomplished using known peptide synthesis techniques, in combination with the first, second and third component pieces of this invention. More specifically, any amino acid sequence may be added to the N-terminal and/or C-terminal of the conformationally constrained reverse-turn mimetic. To this end, the mimetics may be synthesized on a solid support (such as PAM resin) by known techniques (see, *e.g.*, John M. Stewart and Janis D. Young, Solid Phase Peptide Synthesis, 1984, Pierce Chemical Comp., Rockford, Ill.) or on a silyl-linked resin by alcohol attachment (see Randolph et al., *J. Am Chem. Soc.* 117:5712-14, 1995).

In addition, a combination of both solution and solid phase synthesis techniques may be utilized to synthesize the peptide mimetics of this invention. For example, a solid support may be utilized to synthesize the linear peptide sequence up to the point that the conformationally constrained

reverse-turn is added to the sequence. A suitable conformationally constrained reverse-turn mimetic structure which has been previously synthesized by solution synthesis techniques may then be added as the next "amino acid" to the solid phase synthesis (*i.e.*, the conformationally constrained reverse-turn mimetic, which has both an N-terminus and a C-terminus, may be utilized as the next amino acid to be added to the linear peptide). Upon incorporation of the conformationally constrained reverse-turn mimetic structures into the sequence, additional amino acids may then be added to complete the peptide bound to the solid support. Alternatively, the linear N-terminus and C-terminus protected peptide sequences may be synthesized on a solid support, removed from the support, and then coupled to the conformationally constrained reverse-turn mimetic structures in solution using known solution coupling techniques.

In another aspect of this invention, methods for constructing the libraries are disclosed. Traditional combinatorial chemistry techniques (see, *e.g.*, Gallop et al., *J. Med. Chem.* 37:1233-1251, 1994) permit a vast number of compounds to be rapidly prepared by the sequential combination of reagents to a basic molecular scaffold. Combinatorial techniques have been used to construct peptide libraries derived from the naturally occurring amino acids. For example, by taking 20 mixtures of 20 suitably protected and different amino acids and coupling each with one of the 20 amino acids, a library of 400 (*i.e.*, 20^2) dipeptides is created. Repeating the procedure seven times results in the preparation of a peptide library comprised of about 26 billion (*i.e.*, 20^8) octapeptides.

Specifically, synthesis of the peptide mimetics of the library of the present invention may be accomplished using known peptide synthesis techniques, for example, the General Scheme of [4,4,0] Reverse-Turn Mimetic Library as follows:



Synthesis of the peptide mimetics of the libraries of the present invention was accomplished using a FlexChem Reactor Block which has 96 well plates by known techniques. In the above scheme 'Pol' represents a bromoacetal resin (Advanced ChemTech) and detailed procedure is illustrated below.

Step 1

A bromoacetal resin (37mg, 0.98 mmol/g) and a solution of R_2-amine in DMSO (1.4mL) were placed in a Robbins block (FlexChem) having 96 well plates. The reaction mixture was shaken at 60°C using a rotating oven [Robbins Scientific] for 12 hours. The resin was washed with DMF, MeOH, and then DCM

Step 2

A solution of commercial available FmocAmino Acids (4 equiv.), PyBob (4 equiv.), HOAt (4 equiv.), and DIEA (12 equiv.) in DMF was added to the resin. After the reaction mixture was shaken for 12 hours at room temperature, the resin was washed with DMF, MeOH, and then DCM.

Step 3

To the resin swollen by DMF before reaction was added 25% piperidine in DMF and the reaction mixture was shaken for 30 min at room temperature. This deprotection step was repeated again and the resin was

washed with DMF, Methanol, and then DCM. A solution of hydrazine acid (4 equiv.), HOBt (4 equiv.), and DIC (4 equiv.) in DMF was added to the resin and the reaction mixture was shaken for 12 hours at room temperature. The resin was washed with DMF, MeOH, and then DCM.

Step 4a (Where hydrazine acid is MOC carbamate)

The resin obtained in Step 3 was treated with formic acid (1.2 mL each well) for 18 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under a reduced pressure using SpeedVac [SAVANT] to give the product as oil. The product was diluted with 50% water/acetonitrile and then lyophilized after freezing.

Step 4b (Where Fmoc hydrazine acid is used to make Urea through isocynate)

To the resin swollen by DMF before reaction was added 25% piperidine in DMF and the reaction mixture was shaken for 30 min at room temperature. This deprotection step was repeated again and the resin was washed with DMF, Methanol, then DCM. To the resin swollen by DCM before reaction was added isocynate (5 equiv.) in DCM. After the reaction mixture was shaken for 12 hours at room temperature the resin was washed with DMF, MeOH, then DCM. The resin was treated with formic acid (1.2 mL each well) for 18 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under a reduced pressure using SpeedVac [SAVANT] to give the product as oil. The product was diluted with 50% water/acetonitrile and then lyophilized after freezing.

Step 4c (Where Fmoc-hydrazine acid is used to make Urea through active carbamate)

To the resin swollen by DMF before reaction was added 25% piperidine in DMF and the reaction mixture was shaken for 30 min at room temperature. This deprotection step was repeated again and the resin was

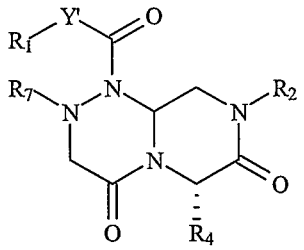
washed with DMF, MeOH, and then DCM. To the resin swollen by DCM before reaction was added p-nitrophenyl chloroformate (5 equiv.) and diisopropyl ethylamine (5 equiv.) in DCM. After the reaction mixture was shaken for 12 hours at room temperature, the resin was washed with DMF, MeOH, and then DCM. To the resin was added primary amines in DCM for 12 hours at room temperature and the resin was washed with DMF, MeOH, and then DCM. After reaction the resin was treated with formic acid (1.2 mL each well) for 18 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under a reduced pressure using SpeedVac [SAVANT] to give the product as oil. The product was diluted with 50% water/acetonitrile and then lyophilized after freezing.

To generate these block libraries the key intermediate hydrazine acids were synthesized according to the procedure illustrated in Preparation Examples.

Tables 2A and 2B show a [4,4,0] Reverse turn mimetics library which can be prepared according to the present invention, of which representative preparation is given in Example 4.

TABLE 2A

THE [4,4,0]REVERSE TURN MIMETICS LIBRARY



No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
1	2,4-Cl_2-benzyl	4-HO-benzyl	Allyl	OCH_3	533	534
2	2,4-Cl_2-benzyl	4-NO_2-benzyl	Allyl	OCH_3	562	563
3	2,4-Cl_2-benzyl	2,4-F_2-benzyl	Allyl	OCH_3	553	554
4	2,4-Cl_2-benzyl	4-Cl-benzyl	Allyl	OCH_3	552	553
5	2,4-Cl_2-benzyl	2,2-bisphenylethyl	Allyl	OCH_3	594	595
6	2,4-Cl_2-benzyl	3-t-Bu-4-HO-benzyl	Allyl	OCH_3	590	591
7	2,4-Cl_2-benzyl	4-Me-benzyl	Allyl	OCH_3	531	532
8	2,4-Cl_2-benzyl	Cyclohexylmethyl	Allyl	OCH_3	523	524
9	2,4-Cl_2-benzyl	4-F-benzyl	Allyl	OCH_3	535	536

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
10	2,4-Cl_2-benzyl	2-Cl-benzyl	Allyl	OCH_3	552	553
11	2,4-Cl_2-benzyl	2,4-Cl_2-benzyl	Allyl	OCH_3	586	587
12	2,4-Cl_2-benzyl	Naphth-2-ylmethyl	Allyl	OCH_3	567	568
13	2,4-Cl_2-benzyl	4-HO-benzyl	Benzyl	OCH_3	583	584
14	2,4-Cl_2-benzyl	4-NO_2-benzyl	Benzyl	OCH_3	612	613
15	2,4-Cl_2-benzyl	2,4-F_2-benzyl	Benzyl	OCH_3	603	604
16	2,4-Cl_2-benzyl	4-Cl-benzyl	Benzyl	OCH_3	602	603
17	2,4-Cl_2-benzyl	2,2-bisphenylethyl	Benzyl	OCH_3	644	645
18	2,4-Cl_2-benzyl	3-t-Bu-4-HO-benzyl	Benzyl	OCH_3	640	641
19	2,4-Cl_2-benzyl	4-Me-benzyl	Benzyl	OCH_3	582	583
20	2,4-Cl_2-benzyl	Cyclohexylmethyl	Benzyl	OCH_3	574	575
21	2,4-Cl_2-benzyl	4-F-benzyl	Benzyl	OCH_3	585	586
22	2,4-Cl_2-benzyl	2-Cl-benzyl	Benzyl	OCH_3	602	603
23	2,4-Cl_2-benzyl	2,4-Cl_2-benzyl	Benzyl	OCH_3	636	637
24	2,4-Cl_2-benzyl	Naphth-2-ylmethyl	Benzyl	OCH_3	618	619
25	2,4-Cl_2-benzyl	4-HO-benzyl	Allyl	OCH_3	479	480
26	2,4-Cl_2-benzyl	4-NO_2-benzyl	Allyl	OCH_3	508	509
27	2,4-Cl_2-benzyl	2,4-F_2-benzyl	Allyl	OCH_3	499	500
28	2,4-Cl_2-benzyl	4-Cl-benzyl	Allyl	OCH_3	497	498
29	Phenethyl	2,2-bisphenylethyl	Allyl	OCH_3	539	540
30	Phenethyl	3-t-Bu-4-HO-benzyl	Allyl	OCH_3	535	536
31	Phenethyl	4-Me-benzyl	Allyl	OCH_3	477	478
32	Phenethyl	Cyclohexylmethyl	Allyl	OCH_3	469	470
33	Phenethyl	4-F-benzyl	Allyl	OCH_3	481	482
34	Phenethyl	2-Cl-benzyl	Allyl	OCH_3	497	498
35	Phenethyl	2,4-Cl_2-benzyl	Allyl	OCH_3	531	532
36	Phenethyl	Naphth-2-ylmethyl	Allyl	OCH_3	513	514
37	Phenethyl	4-HO-benzyl	Benzyl	OCH_3	529	530
38	Phenethyl	4-NO_2-benzyl	Benzyl	OCH_3	558	559
39	Phenethyl	2,4-F_2-benzyl	Benzyl	OCH_3	549	550
40	Phenethyl	4-Cl-benzyl	Benzyl	OCH_3	547	548
41	Phenethyl	2,2-bisphenylethyl	Benzyl	OCH_3	589	590
42	Phenethyl	3-t-Bu-4-HO-benzyl	Benzyl	OCH_3	585	586
43	Phenethyl	4-Me-benzyl	Benzyl	OCH_3	527	528
44	Phenethyl	Cyclohexyl-methyl	Benzyl	OCH_3	519	520
45	Phenethyl	4-F-benzyl	Benzyl	OCH_3	531	532
46	Phenethyl	2-Cl-benzyl	Benzyl	OCH_3	547	548
47	Phenethyl	2,4-Cl_2-benzyl	Benzyl	OCH_3	582	583
48	Phenethyl	Naphth-2-ylmethyl	Benzyl	OCH_3	563	564
49	Phenethyl	4-HO-benzyl	Allyl	OCH_3	497	498
50	Phenethyl	4-NO_2-benzyl	Allyl	OCH_3	526	527
51	Phenethyl	2,4-F_2-benzyl	Allyl	OCH_3	517	518
52	Phenethyl	4-Cl-benzyl	Allyl	OCH_3	515	516
53	4-F-phenylethyl	2,2-bisphenylethyl	Allyl	OCH_3	557	558
54	4-F-phenylethyl	3-t-Bu-4-HO-benzyl	Allyl	OCH_3	553	554
55	4-F-phenylethyl	4-Me-benzyl	Allyl	OCH_3	495	496
56	4-F-phenylethyl	Cyclohexyl-methyl	Allyl	OCH_3	487	488
57	4-F-phenylethyl	4-F-benzyl	Allyl	OCH_3	499	500
58	4-F-phenylethyl	2-Cl-benzyl	Allyl	OCH_3	515	516

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
59	4-F-phenylethyl	2,4-Cl_2-benzyl	Allyl	OCH_3	549	550
60	4-F-phenylethyl	Naphth-2-ylmethyl	Allyl	OCH_3	531	532
61	4-F-phenylethyl	4-HO-benzyl	Benzyl	OCH_3	547	548
62	4-F-phenylethyl	4-NO_2-benzyl	Benzyl	OCH_3	576	577
63	4-F-phenylethyl	2,4-F_2-benzyl	Benzyl	OCH_3	567	568
64	4-F-phenylethyl	4-Cl-benzyl	Benzyl	OCH_3	565	566
65	4-F-phenylethyl	2,2-bisphenylethyl	Benzyl	OCH_3	607	608
66	4-F-phenylethyl	3-t-Bu-4-HO-benzyl	Benzyl	OCH_3	603	604
67	4-F-phenylethyl	4-Me-benzyl	Benzyl	OCH_3	545	546
68	4-F-phenylethyl	Cyclohexyl-methyl	Benzyl	OCH_3	537	538
69	4-F-phenylethyl	4-F-benzyl	Benzyl	OCH_3	549	550
70	4-F-phenylethyl	2-Cl-benzyl	Benzyl	OCH_3	565	566
71	4-F-phenylethyl	2,4-Cl_2-benzyl	Benzyl	OCH_3	599	600
72	4-F-phenylethyl	Naphth-2-ylmethyl	Benzyl	OCH_3	581	582
73	4-F-phenylethyl	4-HO-benzyl	Allyl	OCH_3	509	510
74	4-F-phenylethyl	4-NO_2-benzyl	Allyl	OCH_3	538	539
75	4-F-phenylethyl	2,4-F_2-benzyl	Allyl	OCH_3	529	530
76	4-F-phenylethyl	4-Cl-benzyl	Allyl	OCH_3	527	528
77	4-MeO-phenylethyl	2,2-bisphenylethyl	Allyl	OCH_3	569	570
78	4-MeO-phenylethyl	3-t-Bu-4-HO-benzyl	Allyl	OCH_3	565	566
79	4-MeO-phenylethyl	4-Me-benzyl	Allyl	OCH_3	507	508
80	4-MeO-phenylethyl	Cyclohexyl-methyl	Allyl	OCH_3	499	500
81	4-MeO-phenylethyl	4-F-benzyl	Allyl	OCH_3	511	512
82	4-MeO-phenylethyl	2-Cl-benzyl	Allyl	OCH_3	527	528
83	4-MeO-phenylethyl	2,4-Cl_2-benzyl	Allyl	OCH_3	561	562
84	4-MeO-phenylethyl	Naphth-2-ylmethyl	Allyl	OCH_3	543	544
85	4-MeO-phenylethyl	4-HO-benzyl	Benzyl	OCH_3	559	560
86	4-MeO-phenylethyl	4-NO_2-benzyl	Benzyl	OCH_3	588	589
87	4-MeO-phenylethyl	2,4-F_2-benzyl	Benzyl	OCH_3	579	580
88	4-MeO-phenylethyl	4-Cl-benzyl	Benzyl	OCH_3	577	578
89	4-MeO-phenylethyl	2,2-bisphenylethyl	Benzyl	OCH_3	619	620
90	4-MeO-phenylethyl	3-t-Bu-4-HO-benzyl	Benzyl	OCH_3	615	616
91	4-MeO-phenylethyl	4-Me-benzyl	Benzyl	OCH_3	557	558
92	4-MeO-phenylethyl	Cyclohexylmethyl	Benzyl	OCH_3	549	550
93	4-MeO-phenylethyl	4-F-benzyl	Benzyl	OCH_3	561	562
94	4-MeO-phenylethyl	2-Cl-benzyl	Benzyl	OCH_3	577	578
95	4-MeO-phenylethyl	2,4-Cl_2-benzyl	Benzyl	OCH_3	612	613
96	4-MeO-phenylethyl	Naphth-2-ylmethyl	Benzyl	OCH_3	593	594
97	Isoamyl	4-HO-benzyl	Styrylmethyl	OCH_3	521	522
98	Isoamyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	550	551
99	Isoamyl	2,4-F_2-benzyl	Styrylmethyl	OCH_3	541	542
100	Isoamyl	4-Cl-benzyl	Styrylmethyl	OCH_3	539	540
101	Isoamyl	2,2-bisphenylethyl	Styrylmethyl	OCH_3	581	582
102	Isoamyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	497	498

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
103	Isoamyl	4-Me-benzyl	Styrylmethyl	OCH_3	519	520
104	Isoamyl	Cyclohexylmethyl	Styrylmethyl	OCH_3	511	512
105	Isoamyl	4-F-benzyl	Styrylmethyl	OCH_3	523	524
106	Isoamyl	2-Cl-benzyl	Styrylmethyl	OCH_3	539	540
107	Isoamyl	2,4-Cl_2-benzyl	Styrylmethyl	OCH_3	574	575
108	Isoamyl	Naphth-2-ylmethyl	Styrylmethyl	OCH_3	555	556
109	Isoamyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	563	564
110	Isoamyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	592	593
111	Isoamyl	2,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	583	584
112	Isoamyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	582	583
113	Isoamyl	2,2-bisphenylethyl	2,6-Cl_2-benzyl	OCH_3	624	625
114	Isoamyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	540	541
115	Isoamyl	4-Me-benzyl	2,6-Cl_2-benzyl	OCH_3	562	563
116	Isoamyl	Cyclohexylmethyl	2,6-Cl_2-benzyl	OCH_3	554	555
117	Isoamyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	565	566
118	Isoamyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	582	583
119	Isoamyl	2,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	616	617
120	Isoamyl	Naphth-2-ylmethyl	2,6-Cl_2-benzyl	OCH_3	598	599
121	3-MeO-propyl	4-HO-benzyl	Styrylmethyl	OCH_3	523	524
122	3-MeO-propyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	552	553
123	3-MeO-propyl	2,4-F_2-benzyl	Styrylmethyl	OCH_3	543	544
124	3-MeO-propyl	4-Cl-benzyl	Styrylmethyl	OCH_3	541	542
125	3-MeO-propyl	2,2-bisphenylethyl	Styrylmethyl	OCH_3	583	584
126	3-MeO-propyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	499	500
127	3-MeO-propyl	4-Me-benzyl	Styrylmethyl	OCH_3	521	522
128	3-MeO-propyl	Cyclohexyl-methyl	Styrylmethyl	OCH_3	513	514
129	3-MeO-propyl	4-F-benzyl	Styrylmethyl	OCH_3	525	526

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
130	3-MeO-propyl	2-Cl-benzyl	Styrylmethyl	OCH_3	541	542
131	3-MeO-propyl	2,4-Cl_2-benzyl	Styrylmethyl	OCH_3	575	576
132	3-MeO-propyl	Naphth-2-ylmethyl	Styrylmethyl	OCH_3	557	558
133	3-MeO-propyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	565	566
134	3-MeO-propyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	594	595
135	3-MeO-propyl	2,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	585	586
136	3-MeO-propyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	584	585
137	3-MeO-propyl	2,2-bisphenylethyl	2,6-Cl_2-benzyl	OCH_3	626	627
138	3-MeO-propyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	541	542
139	3-MeO-propyl	4-Me-benzyl	2,6-Cl_2-benzyl	OCH_3	563	564
140	3-MeO-propyl	Cyclohexyl-methyl	2,6-Cl_2-benzyl	OCH_3	556	557
141	3-MeO-propyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	567	568
142	3-MeO-propyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	584	585
143	3-MeO-propyl	2,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	618	619
144	3-MeO-propyl	Naphth-2-ylmethyl	2,6-Cl_2-benzyl	OCH_3	600	601
145	4-MeO-phenylethyl	4-HO-benzyl	Styrylmethyl	OCH_3	585	586
146	4-MeO-phenylethyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	614	615
147	4-MeO-phenylethyl	2,4-F_2-benzyl	Styrylmethyl	OCH_3	605	606
148	4-MeO-phenylethyl	4-Cl-benzyl	Styrylmethyl	OCH_3	603	604
149	4-MeO-phenylethyl	2,2-bisphenylethyl	Styrylmethyl	OCH_3	645	646
150	4-MeO-phenylethyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	561	562
151	4-MeO-phenylethyl	4-Me-benzyl	Styrylmethyl	OCH_3	583	584
152	4-MeO-phenylethyl	Cyclohexyl-methyl	Styrylmethyl	OCH_3	575	576
153	4-MeO-phenylethyl	4-F-benzyl	Styrylmethyl	OCH_3	587	588
154	4-MeO-phenylethyl	2-Cl-benzyl	Styrylmethyl	OCH_3	603	604
155	4-MeO-phenylethyl	2,4-Cl_2-benzyl	Styrylmethyl	OCH_3	638	639
156	4-MeO-phenylethyl	Naphth-2-ylmethyl	Styrylmethyl	OCH_3	619	620

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
157	4-MeO-phenylethyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	628	629
158	4-MeO-phenylethyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	657	658
159	4-MeO-phenylethyl	2,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	648	649
160	4-MeO-phenylethyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	646	647
161	4-MeO-phenylethyl	2,2-bisphenylethyl	2,6-Cl_2-benzyl	OCH_3	688	689
162	4-MeO-phenylethyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	604	605
163	4-MeO-phenylethyl	4-Me-benzyl	2,6-Cl_2-benzyl	OCH_3	626	627
164	4-MeO-phenylethyl	Cyclohexylmethyl	2,6-Cl_2-benzyl	OCH_3	618	619
165	4-MeO-phenylethyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	630	631
166	4-MeO-phenylethyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	646	647
167	4-MeO-phenylethyl	2,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	680	681
168	4-MeO-phenylethyl	Naphth-2-ylmethyl	2,6-Cl_2-benzyl	OCH_3	662	663
169	Tetrahydrofuran-2-ylmethyl	4-HO-benzyl	Styrylmethyl	OCH_3	535	536
170	Tetrahydrofuran-2-ylmethyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	564	565
171	Tetrahydrofuran-2-ylmethyl	2,4-F_2-benzyl	Styrylmethyl	OCH_3	555	556
172	Tetrahydrofuran-2-ylmethyl	4-Cl-benzyl	Styrylmethyl	OCH_3	553	554
173	Tetrahydrofuran-2-ylmethyl	2,2-bisphenylethyl	Styrylmethyl	OCH_3	595	596
174	Tetrahydrofuran-2-ylmethyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	511	512
175	Tetrahydrofuran-2-ylmethyl	4-Me-benzyl	Styrylmethyl	OCH_3	533	534
176	Tetrahydrofuran-2-ylmethyl	Cyclohexyl-methyl	Styrylmethyl	OCH_3	525	526
177	Tetrahydrofuran-2-ylmethyl	4-F-benzyl	Styrylmethyl	OCH_3	537	538
178	Tetrahydrofuran-2-ylmethyl	2-Cl-benzyl	Styrylmethyl	OCH_3	553	554
179	Tetrahydrofuran-2-ylmethyl	2,4-Cl_2-benzyl	Styrylmethyl	OCH_3	588	589
180	Tetrahydrofuran-2-ylmethyl	Naphth-2-ylmethyl	Styrylmethyl	OCH_3	569	570
181	Tetrahydrofuran-2-ylmethyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	577	578
182	Tetrahydrofuran-2-ylmethyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	606	607
183	Tetrahydrofuran-2-ylmethyl	2,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	597	598

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
184	Tetrahydrofuran-2-ylmethyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	596	597
185	Tetrahydrofuran-2-ylmethyl	2,2-bisphenylethyl	2,6-Cl_2-benzyl	OCH_3	638	639
186	Tetrahydrofuran-2-ylmethyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	553	554
187	Tetrahydrofuran-2-ylmethyl	4-Me-benzyl	2,6-Cl_2-benzyl	OCH_3	575	576
188	Tetrahydrofuran-2-ylmethyl	Cyclohexyl-methyl	2,6-Cl_2-benzyl	OCH_3	568	569
189	Tetrahydrofuran-2-ylmethyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	579	580
190	Tetrahydrofuran-2-ylmethyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	596	597
191	Tetrahydrofuran-2-ylmethyl	2,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	630	631
192	Tetrahydrofuran-2-ylmethyl	Naphth-2-ylmethyl	2,6-Cl_2-benzyl	OCH_3	612	613
193	Phenethyl	4-HO-benzyl	Methyl	(4-Me-phenyl)amino	528	529
194	Phenethyl	4-HO-benzyl	Methyl	(4-Cl-phenyl)amino	548	549
195	Phenethyl	4-HO-benzyl	Methyl	Phenylamino	514	515
196	Phenethyl	4-HO-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	542	543
197	Phenethyl	4-HO-benzyl	Methyl	Benzylamino	528	529
198	Phenethyl	4-HO-benzyl	Methyl	(4-MeO-phenyl)amino	544	545
199	Phenethyl	4-HO-benzyl	Methyl	(4-Br-phenyl)amino	592	593
200	Phenethyl	4-HO-benzyl	Methyl	(4-CF_3-phenyl)amino	582	583
201	Phenethyl	4-HO-benzyl	Methyl	Pentylamino	508	509
202	Phenethyl	4-HO-benzyl	Methyl	(2-Phenylethyl) amino	542	543
203	Phenethyl	4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	558	559
204	Phenethyl	4-HO-benzyl	Methyl	Cyclohexyl amino	520	521
205	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-Me-phenyl)amino	604	605
206	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-Cl-phenyl)amino	624	625

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
207	2,2-bisphenylethyl	4-HO-benzyl	Methyl	Phenylamino	590	591
208	2,2-bisphenylethyl	4-HO-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	618	619
209	2,2-bisphenylethyl	4-HO-benzyl	Methyl	Benzylamino	604	605
210	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-MeO-phenyl)amino	620	621
211	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-Br-phenyl)amino	669	670
212	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-CF_3-phenyl)amino	658	659
213	2,2-bisphenylethyl	4-HO-benzyl	Methyl	Pentylamino	584	585
214	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(2-Phenylethyl) amino	618	619
215	2,2-bisphenylethyl	4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	634	635
216	2,2-bisphenylethyl	4-HO-benzyl	Methyl	Cyclohexyl amino	596	597
217	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-Me-phenyl)amino	581	582
218	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-Cl-phenyl)amino	601	602
219	Phenethyl	3,4-Cl_2-benzyl	Methyl	Phenylamino	566	567
220	Phenethyl	3,4-Cl_2-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	595	596
221	Phenethyl	3,4-Cl_2-benzyl	Methyl	Benzylamino	581	582
222	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-phenyl)amino	597	598
223	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-Br-phenyl)amino	645	646
224	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-CF_3-phenyl)amino	634	635
225	Phenethyl	3,4-Cl_2-benzyl	Methyl	Pentylamino	561	562
226	Phenethyl	3,4-Cl_2-benzyl	Methyl	(2-Phenylethyl) amino	595	596
227	Phenethyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-benzyl)amino	611	612

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
228	Phenethyl	3,4-Cl_2-benzyl	Methyl	Cyclohexyl amino	573	574
229	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-Me-phenyl)amino	657	658
230	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-Cl-phenyl)amino	677	678
231	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	Phenylamino	643	644
232	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	671	672
233	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	Benzylamino	657	658
234	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-phenyl)amino	673	674
235	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-Br-phenyl)amino	721	722
236	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-CF_3-phenyl)amino	711	712
237	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	Pentylamino	637	638
238	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(2-Phenylethyl) amino	671	672
239	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-benzyl)amino	687	688
240	2,2-bisphenylethyl	3,4-Cl_2-benzyl	Methyl	Cyclohexyl amino	649	650
241	Isoamyl	4-HO-benzyl	Methyl	(4-Me-phenyl)amino	478	479
242	Isoamyl	4-HO-benzyl	Methyl	(4-Cl-phenyl)amino	498	499
243	Isoamyl	4-HO-benzyl	Methyl	Phenylamino	464	465
244	Isoamyl	4-HO-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	492	493
245	Isoamyl	4-HO-benzyl	Methyl	Benzylamino	478	479
246	Isoamyl	4-HO-benzyl	Methyl	(4-MeO-phenyl)amino	494	495
247	Isoamyl	4-HO-benzyl	Methyl	(4-Br-phenyl)amino	542	543
248	Isoamyl	4-HO-benzyl	Methyl	(4-CF_3-phenyl)amino	532	533

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
249	Isoamyl	4-HO-benzyl	Methyl	Pentylamino	458	459
250	Isoamyl	4-HO-benzyl	Methyl	(2-Phenylethyl) amino	492	493
251	Isoamyl	4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	508	509
252	Isoamyl	4-HO-benzyl	Methyl	Cyclohexyl amino	470	471
253	Isoamyl	4-HO-benzyl	Methyl	(4-Me-phenyl)amino	554	555
254	Isoamyl	4-HO-benzyl	Methyl	(4-Cl-phenyl)amino	574	575
255	Isoamyl	4-HO-benzyl	Methyl	Phenylamino	540	541
256	Isoamyl	4-HO-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	568	569
257	Isoamyl	4-HO-benzyl	Methyl	Benzylamino	554	555
258	Isoamyl	4-HO-benzyl	Methyl	(4-MeO-phenyl)amino	570	571
259	Isoamyl	4-HO-benzyl	Methyl	(4-Br-phenyl)amino	619	620
260	Isoamyl	4-HO-benzyl	Methyl	(4-CF_3-phenyl)amino	608	609
261	Isoamyl	4-HO-benzyl	Methyl	Pentylamino	534	535
262	Isoamyl	4-HO-benzyl	Methyl	(2-Phenylethyl) amino	568	569
263	Isoamyl	4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	584	585
264	Isoamyl	4-HO-benzyl	Methyl	Cyclohexyl amino	546	547
265	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Me-phenyl)amino	526	527
266	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Cl-phenyl)amino	546	547
267	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Phenylamino	512	513
268	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	540	541
269	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Benzylamino	526	527

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
270	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-phenyl)amino	542	543
271	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Br-phenyl)amino	591	592
272	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-CF_3-phenyl)amino	580	581
273	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Pentylamino	506	507
274	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(2-Phenylethyl) amino	540	541
275	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-benzyl)amino	556	557
276	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Cyclohexylamino	518	519
277	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Me-phenyl)amino	602	603
278	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Cl-phenyl)amino	622	623
279	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Phenylamino	588	589
280	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	((*R*)-α-methylbenzyl)amino	616	617
281	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Benzylamino	602	603
282	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-phenyl)amino	618	619
283	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-Br-phenyl)amino	667	668
284	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-CF_3-phenyl)amino	656	657
285	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Pentylamino	582	583
286	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(2-Phenylethyl)amino	616	617
287	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	(4-MeO-benzyl)amino	632	633
288	4-methylbenzyl	3,4-Cl_2-benzyl	Methyl	Cyclohexylamino	594	595
289	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(N-Cbz-3-Indoleethyl) amino	751	752
290	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(Naphth-2-ylmethyl)amino	614	615

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
291	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(2-Phenylethyl)amino	578	579
292	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	[2-(4-MeO-phenyl)ethyl]amino	608	609
293	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(3-CF_3-benzyl)amino	632	633
294	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	594	595
295	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(4-F-phenylethyl)amino	596	597
296	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(3,4-Cl_2-benzyl)amino	633	634
297	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(2-HO-ethyl)amino	518	519
298	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(3-MeO-propyl)amino	546	547
299	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(Tetrahydrofuran-2-ylmethyl)amino	558	559
300	Naphth-1-ylmethyl	4-HO-benzyl	Methyl	(cyclohexylmethyl)amino	570	571
301	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(N-Cbz-3-Indoleethyl)amino	779	780
302	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(Naphth-2-ylmethyl)amino	642	643
303	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(2-Phenylethyl)amino	606	607
304	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	[2-(4-MeO-phenyl)ethyl]amino	636	637
305	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(3-CF_3-benzyl)amino	660	661
306	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(4-MeO-benzyl)amino	622	623
307	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(4-F-phenylethyl)amino	624	625
308	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(3,4-Cl_2-benzyl)amino	661	662
309	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(2-HO-ethyl)amino	546	547

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
310	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(3-MeO-propyl)amino	574	575
311	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(Tetrahydrofuran-2-ylmethyl)amino	586	587
312	Naphth-1-ylmethyl	4-HO-benzyl	Propyl	(cyclohexylmethyl)amino	598	599
313	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(N-Cbz-3-Indoleethyl)amino	771	772
314	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(Naphth-2-ylmethyl)amino	634	635
315	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(2-Phenylethyl)amino	598	599
316	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	[2-(4-MeO-phenyl)ethyl]amino	628	629
317	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(3-CF_3-benzyl)amino	652	653
318	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(4-MeO-benzyl)amino	614	615
319	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(4-F-phenylethyl)amino	616	617
320	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(3,4-Cl_2-benzyl)amino	653	654
321	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(2-HO-ethyl)amino	538	539
322	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(3-MeO-propyl)amino	566	567
323	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(Tetrahydrofuran-2-ylmethyl)amino	578	579
324	Naphth-1-ylmethyl	3,4-F_2-benzyl	Methyl	(cyclohexylmethyl)amino	590	591
325	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(N-Cbz-3-Indoleethyl)amino	799	800
326	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(Naphth-2-ylmethyl)amino	662	663
327	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(2-Phenylethyl)amino	626	627

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
328	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	[2-(4-MeO-phenyl)ethyl]amino	656	657
329	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(3-CF_3-benzyl)amino	680	681
330	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(4-MeO-benzyl)amino	642	643
331	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(4-F-phenylethyl)amino	644	645
332	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(3,4-Cl_2-benzyl)amino	681	682
333	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(2-HO-ethyl)amino	566	567
334	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(3-MeO-propyl)amino	594	595
335	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(Tetrahydrofuran-2-ylmethyl)amino	606	607
336	Naphth-1-ylmethyl	3,4-F_2-benzyl	Propyl	(cyclohexylmethyl)amino	618	619
337	Naphth-1-ylmethyl	4-biphenylyl-methyl	Methyl	(N-Cbz-3-Indoleethyl)amino	811	812
338	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(Naphth-2-ylmethyl)amino	674	675
339	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(2-Phenylethyl)amino	638	639
340	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	[2-(4-MeO-phenyl)ethyl]amino	668	669
341	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(3-CF_3-benzyl)amino	692	693
342	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(4-MeO-benzyl)amino	654	655
343	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(4-F-phenylethyl)amino	656	657
344	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(3,4-Cl_2-benzyl)amino	693	694
345	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(2-HO-ethyl)amino	578	579
346	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(3-MeO-propyl)amino	606	607

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
347	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(Tetrahydrofuran-2-ylmethyl)amino	618	619
348	Naphth-1-ylmethyl	4-biphenylylmethyl	Methyl	(cyclohexylmethyl)amino	630	631
349	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(N-Cbz-3-Indoleethyl)amino	839	840
350	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(Naphth-2-ylmethyl)amino	702	703
351	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(2-Phenylethyl)amino	666	667
352	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	[2-(4-MeO-phenyl)ethyl]amino	696	697
353	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(3-CF_3-benzyl)amino	720	721
354	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(4-MeO-benzyl)amino	682	683
355	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(4-F-phenylethyl)amino	684	685
356	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(3,4-Cl_2-benzyl)amino	721	722
357	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(2-HO-ethyl)amino	606	607
358	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(3-MeO-propyl)amino	634	635
359	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(Tetrahydrofuran-2-ylmethyl)amino	646	647
360	Naphth-1-ylmethyl	4-biphenylylmethyl	Propyl	(cyclohexylmethyl)amino	658	659
361	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(N-Cbz-3-Indoleethyl)amino	807	808
362	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(Naphth-2-ylmethyl)amino	670	671
363	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(2-Phenylethyl)amino	634	635
364	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	[2-(4-MeO-phenyl)ethyl]amino	664	665

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
365	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(3-CF_3-benzyl)amino	688	689
366	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(4-MeO-benzyl)amino	650	651
367	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(4-F-phenylethyl)amino	652	653
368	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(3,4-Cl_2-benzyl)amino	689	690
369	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(2-HO-ethyl)amino	574	575
370	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(3-MeO-propyl)amino	602	603
371	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(Tetrahydrofuran-2-ylmethyl)amino	614	615
372	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	(cyclohexylmethyl)amino	626	627
373	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(N-Cbz-3-Indoleethyl)amino	835	836
374	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(Naphth-2-ylmethyl)amino	698	699
375	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(2-Phenylethyl)amino	662	663
376	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	[2-(4-MeO-phenyl)ethyl]amino	692	693
377	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(3-CF_3-benzyl)amino	716	717
378	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(4-MeO-benzyl)amino	678	679
379	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(4-F-phenylethyl)amino	680	681
380	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(3,4-Cl_2-benzyl)amino	717	718
381	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(2-HO-ethyl)amino	602	603
382	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(3-MeO-propyl)amino	630	631
383	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(Tetrahydrofuran-2-ylmethyl)amino	642	643

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
384	Naphth-1-ylmethyl	3-t-Bu-4-HO-benzyl	Propyl	(cyclohexylmethyl)amino	654	655
385	4-Methoxybenzyl	OCH_3	5-F-benzyl	OCH_3	470	471
386	Naphthyl-1-ylmethyl	4-HO-benzyl	Styrylmethyl	OCH_3	591	592
387	Naphthyl-1-ylmethyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	620	621
388	Naphthyl-1-ylmethyl	3,4-F_2-benzyl	Styrylmethyl	OCH_3	611	612
389	Naphthyl-1-ylmethyl	4-Cl-benzyl	Styrylmethyl	OCH_3	609	610
390	Naphthyl-1-ylmethyl	4-Phenyl-benzyl	Styrylmethyl	OCH_3	651	652
391	Naphthyl-1-ylmethyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	647	648
392	Naphthyl-1-ylmethyl	4-Methyl-benzyl	Styrylmethyl	OCH_3	589	590
393	Naphthyl-1-ylmethyl	Cyclohexylmethyl	Styrylmethyl	OCH_3	581	582
394	Naphthyl-1-ylmethyl	4-F-benzyl	Styrylmethyl	OCH_3	593	594
395	Naphthyl-1-ylmethyl	2-Cl-benzyl	Styrylmethyl	OCH_3	609	610
396	Naphthyl-1-ylmethyl	3,4-Cl_2-benzyl	Styrylmethyl	OCH_3	644	645
397	Naphthyl-1-ylmethyl	Naphthyl-1-ylmethyl	Styrylmethyl	OCH_3	625	626
398	3,4-Cl_2-benzyl	4-HO-benzyl	Styrylmethyl	OCH_3	610	611
399	3,4-Cl_2-benzyl	4-NO_2-benzyl	Styrylmethyl	OCH_3	639	640
400	3,4-Cl_2-benzyl	3,4-F_2-benzyl	Styrylmethyl	OCH_3	629	630
401	3,4-Cl_2-benzyl	4-Cl-benzyl	Styrylmethyl	OCH_3	628	629
402	3,4-Cl_2-benzyl	4-Phenyl-benzyl	Styrylmethyl	OCH_3	670	671
403	3,4-Cl_2-benzyl	3-t-Bu-4-HO-benzyl	Styrylmethyl	OCH_3	666	667
404	3,4-Cl_2-benzyl	4-Methyl-benzyl	Styrylmethyl	OCH_3	608	609
405	3,4-Cl_2-benzyl	Cyclohexylmethyl	Styrylmethyl	OCH_3	600	601
406	3,4-Cl_2-benzyl	4-F-benzyl	Styrylmethyl	OCH_3	611	612
407	3,4-Cl_2-benzyl	2-Cl-benzyl	Styrylmethyl	OCH_3	628	629
408	3,4-Cl_2-benzyl	3,4-Cl_2-benzyl	Styrylmethyl	OCH_3	662	663
409	3,4-Cl_2-benzyl	Naphthyl-1-ylmethyl	Styrylmethyl	OCH_3	644	645
410	Naphthyl-1-ylmethyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	634	635

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
411	Naphthyl-1-ylmethyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	663	664
412	Naphthyl-1-ylmethyl	3,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	654	655
413	Naphthyl-1-ylmethyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	652	653
414	Naphthyl-1-ylmethyl	4-Phenyl-benzyl	2,6-Cl_2-benzyl	OCH_3	694	695
415	Naphthyl-1-ylmethyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	690	691
416	Naphthyl-1-ylmethyl	4-Methyl-benzyl	2,6-Cl_2-benzyl	OCH_3	632	633
417	Naphthyl-1-ylmethyl	Cyclohexylmethyl	2,6-Cl_2-benzyl	OCH_3	624	625
418	Naphthyl-1-ylmethyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	636	637
419	Naphthyl-1-ylmethyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	652	653
420	Naphthyl-1-ylmethyl	3,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	686	687
421	Naphthyl-1-ylmethyl	Naphthyl-1-ylmethyl	2,6-Cl_2-benzyl	OCH_3	668	669
422	3,4-Cl_2-benzyl	4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	652	653
423	3,4-Cl_2-benzyl	4-NO_2-benzyl	2,6-Cl_2-benzyl	OCH_3	681	682
424	3,4-Cl_2-benzyl	3,4-F_2-benzyl	2,6-Cl_2-benzyl	OCH_3	672	673
425	3,4-Cl_2-benzyl	4-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	671	672
426	3,4-Cl_2-benzyl	4-Phenyl-benzyl	2,6-Cl_2-benzyl	OCH_3	712	713
427	3,4-Cl_2-benzyl	3-t-Bu-4-HO-benzyl	2,6-Cl_2-benzyl	OCH_3	708	709
428	3,4-Cl_2-benzyl	4-Methyl-benzyl	2,6-Cl_2-benzyl	OCH_3	650	651
429	3,4-Cl_2-benzyl	Cyclohexylmethyl	2,6-Cl_2-benzyl	OCH_3	642	643
430	3,4-Cl_2-benzyl	4-F-benzyl	2,6-Cl_2-benzyl	OCH_3	654	655
431	3,4-Cl_2-benzyl	2-Cl-benzyl	2,6-Cl_2-benzyl	OCH_3	671	672
432	3,4-Cl_2-benzyl	3,4-Cl_2-benzyl	2,6-Cl_2-benzyl	OCH_3	705	706
433	3,4-Cl_2-benzyl	Naphthyl-1-ylmethyl	2,6-Cl_2-benzyl	OCH_3	686	687
434	2-Piperidin-1-yl-ethyl	(S)-4-HO-benzyl	Methyl	Benzylamino	535	536
435	3,4-Cl_2-benzyl	(S)-4-HO-benzyl	Methyl	2-Piperidin-1-yl-ethylamino	604	605
436	3,4-Cl_2-benzyl	(S)-4-HO-benzyl	Methyl	2-(1-Methyl-pyrrolidin-2-yl)-ethylamino	604	605

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
437	3-Pyridylmethyl	(S)-4-HO-benzyl	Methyl	3,4-Cl_2-benzylamino	583	584
438	2-Morpholin-4-yl-ethyl	(S)-4-HO-benzyl	Methyl	3,4-Cl_2-benzylamino	606	607
439	3,4-Cl_2-benzyl	(S)-4-HO-benzyl	Methyl	3-Pyridylmethylamino	583	584
440	3,4-Cl_2-benzyl	(S)-4-HO-benzyl	Methyl	2-Morpholin-4-yl-ethylamino	606	607
441	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	3-Imidazol-1-yl-propylamino	582	583
442	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-Aminophenethylamino	593	594
443	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	3-Pyridylmethylamino	565	566
444	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	2-(3-Pyridylethyl)amino	579	580
445	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-Pyridylmethylamino	565	566
446	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzyloxycarbonylamino	622	623
447	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-F-benzylamino	582	583
448	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-CO_2H-benzylamino	608	609
449	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-CF_3-benzylamino	632	633
450	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	(S)-alpha-methylbenzylamino	578	579
451	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	(R)-alpha-methylbenzylamino	578	579
452	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	2-F-benzylamino	582	583
453	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	2,3-Dimethoxybenzylamino	624	625
454	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Cyanomethylamino	513	514
455	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Phenylhydrazino	565	566

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
456	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-Aminobenzylamino	579	580
457	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	(S,S) {2-[(2-hydroxy-1-methyl-2-phenyl-ethyl)-methyl-carbamoyl]-ethyl}-amino	693	694
458	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	[4-(1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-cyclohexyl]-methylamino	715	716
459	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Indan-1-ylamino	590	591
460	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	PhenylGlycine	622	623
461	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	2,6-F_2-benzylamino	600	601
462	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	3-F-benzylamino	582	583
463	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzimidazol-2-yl-amino	604	605
464	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Diphenylmethylamino	640	641
465	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Furan-2-yl-methylamino	554	555
466	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-Dimethylamino-benzylamino	607	608
467	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Thiofuran-2-yl-methylamino	584	585
468	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-NO_2-benzylamino	609	610
469	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	BnO	565	566
470	4-Methoxy-naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	594	595
471	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Phenethyl	563	564
472	Naphthyl-1-ylmethyl	4-Methoxy-benzyl	Methyl	Benzylamino	578	579

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
473	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	4-CF_3-phenylamino	618	619
474	Naphthyl-1-ylmethyl	4-NO_2-benzyl	Methyl	4-CF_3-phenylamino	647	648
475	Naphthyl-1-ylmethyl	4-NO_2-benzyl	Methyl	Benzylamino	593	594
476	Benzyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	574	575
477	Thiofuran-2-yl-methyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	594	595
478	4-Dimethylamino-benzyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	617	618
479	Phenethyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	588	589
480	8-Quinoline-1yl-methyl	4-HO-benzyl	Methyl	Benzylamino	565	566
481	4-Pyridylmethyl	Naphthyl-1-ylmethyl	Benzyl	OCH_3	550	551
482	3,4-Dimethoxybenzyl	Naphthyl-1-ylmethyl	Benzyl	OCH_3	609	610
483	3,4-Dimethoxy-phenethyl	Naphthyl-1-ylmethyl	Benzyl	OCH_3	623	624
484	Thiofuran-2-yl-methyl	Naphthyl-1-ylmethyl	Benzyl	OCH_3	569	570
485	Naphthyl-1-ylmethyl	3-Pyridylmethyl	Methyl	Benzylamino	549	550
486	Naphthyl-1-ylmethyl	Pentafluorobenzyl	Methyl	Benzylamino	638	639
487	Naphthyl-1-ylmethyl	3-F-4-HO-benzyl	Methyl	Benzylamino	582	583
488	4-F-phenethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	598	599
489	4-Methoxyphenethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	610	611
490	3,4-Dimethoxy-phenethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	640	641
491	Naphthyl-1-ylmethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	616	617
492	3,4-Dimethoxybenzyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	634	635
493	3,4-Dimethoxy-phenethyl	Naphthyl-1-ylmethyl	4-CN-benzyl	OCH_3	648	649
494	4-Quinoline-1yl-methyl	4-HO-benzyl	Methyl	Benzylamino	565	566
495	2-Pyridylmethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	567	568
496	3-Pyridylmethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	567	568

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
497	3,4-Dimethoxybenzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	626	627
498	4-Methyl-benzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	580	581
499	Thiofuran-2-yl-methyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	572	573
500	4-CF_3-benzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	634	635
501	2,6-F_2-benzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	602	603
502	4-F-benzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	584	585
503	Thiofuran-2-yl-ethyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	586	587
504	3,4-Cl_2-benzyl	4-Methyl-benzyl	Methyl	4-CF_3-phenylamino	634	635
505	4-CO2H-Benzyl	4-HO-benzyl	Methyl	Benzylamino	558	559
506	Naphthyl-1-ylmethyl	3-t-Bu-4-HO-benzyl	Methyl	Benzylamino	620	621
507	Naphthyl-1-ylmethyl	3,4-(OH)2-benzyl	Methyl	Benzylamino	580	581
508	2-F-benzyl	4-HO-benzyl	Methyl	Benzylamino	532	533
509	3-F-benzyl	4-HO-benzyl	Methyl	Benzylamino	532	533
510	4-F-benzyl	4-HO-benzyl	Methyl	Benzylamino	532	533
511	2,4-F_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	550	551
512	2,6-F_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	550	551
513	2,5-F_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	550	551
514	3-CF_3-benyl	4-HO-benzyl	Methyl	Benzylamino	582	583
515	4-CF_3-benyl	4-HO-benzyl	Methyl	Benzylamino	582	583
516	3,4,5-F_3-benyl	4-HO-benzyl	Methyl	Benzylamino	568	569
517	2-Cl-benzyl	4-HO-benzyl	Methyl	Benzylamino	548	549
518	3-Cl-benzyl	4-HO-benzyl	Methyl	Benzylamino	548	549
519	2,4-Cl_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	582	583
520	(S)-Methylphenyl	4-HO-benzyl	Methyl	Benzylamino	528	529

No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
521	(R)-Methylphenyl	4-HO-benzyl	Methyl	Benzylamino	528	529
522	4-Methyl-benzyl	4-HO-benzyl	Methyl	Benzylamino	528	529
523	4-Methoxybenzyl	4-HO-benzyl	Methyl	Benzylamino	544	545
524	3,4-Dimethoxybenzyl	4-HO-benzyl	Methyl	Benzylamino	574	575
525	Furan-2-yl-methylamino	4-HO-benzyl	Methyl	Benzylamino	504	505
526	(R)-Methylnaphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	578	579
527	(S)-Methylnaphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	578	579
528	Naphthyl-1-ylmethyl	3-Oxy-pyridin-1-ylmethyl	Methyl	Benzylamino	565	566
529	(R)-alpha-methylbenzyl	4-HO-benzyl	Methyl	Benzylamino	578	579
530	Naphthyl-2-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	564	565
531	4-F-naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	582	583
532	2-Methoxybenzyl	4-HO-benzyl	Methyl	Benzylamino	544	545
533	4-Cl-benzyl	4-HO-benzyl	Methyl	Benzylamino	548	549
534	3,4-Cl_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	582	583
535	2-CF_3Obenzyl	4-HO-benzyl	Methyl	Benzylamino	598	599
536	2-CF_3Sbenzyl	4-HO-benzyl	Methyl	Benzylamino	614	615
537	2-CF_3benzyl	4-HO-benzyl	Methyl	Benzylamino	582	583
538	5-Quinoline-1yl-methyl	4-HO-benzyl	Methyl	Benzylamino	565	566
539	8-Quinoline-1yl-methyl	3-t-Bu-4-HO-benzyl	Methyl	Benzylamino	621	622
540	8-Quinoline-1yl-methyl	4-NO_2-benzyl	Methyl	Benzylamino	594	595
541	8-Quinoline-1yl-methyl	(1H-Pyrrol-2-yl)-methyl	Methyl	Benzylamino	538	539
542	Naphthyl-1-ylmethyl	4-Benzyloxy-carbonylaminobenzyl	Methyl	Benzylamino	697	698
543	2,3-Cl_2-benzyl	4-HO-benzyl	Methyl	Benzylamino	582	583
544	Pentafluorobenzyl	4-HO-benzyl	Methyl	Benzylamino	604	605
545	Benzyl	4-HO-benzyl	Methyl	Benzylamino	514	515
546	Quinoxaline-5yl-methyl	4-HO-benzyl	Methyl	Benzylamino	566	567
547	8-Quinoline-1yl-methyl	3-Pyridylmethyl	Methyl	Benzylamino	550	551

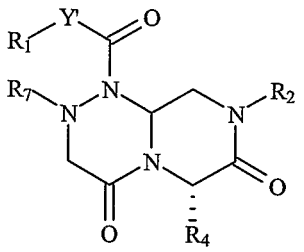
No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
548	8-Quinoline-1yl-methyl	Pentafluorobenzyl	Methyl	Benzylamino	639	640
549	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	Benzylamino(thiourea)	580	581
550	Naphthyl-1-ylmethyl	4-Amino-benzyl	Methyl	Benzylamino	563	564
551	3,4,5-tri-Methoxybenzyl	4-Amino-benzyl	Methyl	Benzylamino	603	604
552	Naphthyl-1-ylmethyl	4-Pyridylmethyl	Methyl	Benzylamino	549	550
553	Naphthyl-1-ylmethyl	(R) 4-HO-phenyl	Methyl	Benzylamino	550	551
554	2-HO-3-Methoxy-benzyl	4-HO-benzyl	Methyl	Benzylamino	560	561
555	Naphthyl-1-ylmethyl	3-Nitro-4-HO-benzyl	Methyl	Benzylamino	609	610
556	Naphthyl-1-ylmethyl	4-CO_2H-CH_2O-benzyl	Methyl	Benzylamino	622	623
557	Naphthyl-1-ylmethyl	1-Naphtoylamino-methyl	Methyl	Benzylamino	641	642
558	Naphthyl-1-ylmethyl	4-Oxy-pyridylmethyl	Methyl	Benzylamino	565	566
559	4-F-alpha-methylbenzyl	4-HO-benzyl	Methyl	Benzylamino	546	547
560	Naphthyl-1-ylmethyl	Benzoylaminoethyl	Methyl	Benzylamino	605	606
561	8-Quinoline-1yl-methyl	3,4-$(OH)_2$-benzyl	Methyl	Benzylamino	581	582
562	4-N,N-Dimethylamino-benzyl	4-HO-benzyl	Methyl	Benzylamino	557	558
563	Naphthyl-1-ylmethyl	(R) 4-F-benzyl	Methyl	Benzylamino	609	610
564	Naphthyl-1-ylmethyl	4-HO-benzyl	Methyl	2-Chloroethyl amino	536	537
565	Naphthyl-1-ylmethyl	4-HO-phenethyl	Methyl	Benzylamino	578	579
566	4-F-benzyl	3-F,4-HO-benzyl	Methyl	Benzylamino	550	551
567	2,4-F_2-benzyl	3-F,4-HO-benzyl	Methyl	Benzylamino	568	569
568	3-CF_3benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	568	569
569	(S)-Methylnaphthyl-1-ylmethyl	(R) 4-HO-phenyl	Methyl	Benzylamino	514	515
570	(R)-Methylnaphthyl-1-ylmethyl	(R) 4-HO-phenyl	Methyl	Benzylamino	514	515
571	2,3,6-F_3-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	554	555
572	3-F-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	518	519
573	4-Cl-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	534	535
574	3-Cl-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	534	535

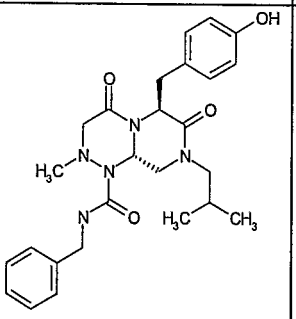
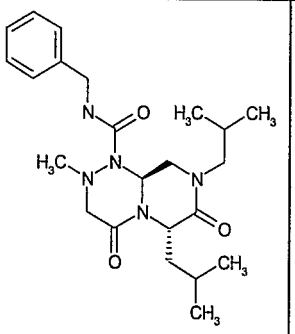
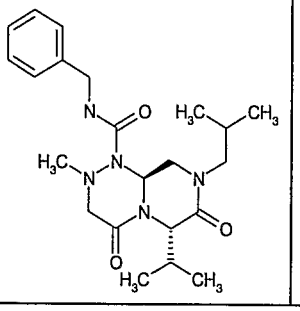
No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
575	2-Cl-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	534	535
576	3,4-Cl_2-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	568	569
577	3-CF_3O-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	584	585
578	4-F-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	518	519
579	2,4-F_2-benzyl	(R) 4-HO-phenyl	Methyl	Benzylamino	536	537
580	3-(2-Chloro-ethyl)-ureido]-benzyl	4-HO-benzyl	Methyl	Benzylamino	634	635
581	3-Aminobenzyl	4-HO-benzyl	Methyl	Benzylamino	529	530
582	3-*N*-Methylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	543	544
583	3-*N,N*-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	557	558
584	1H-Benzoimidazol-4-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	554	555
585	2-HO-benzyl	4-HO-benzyl	Methyl	Benzylamino	530	531
586	2-Pyridylmethyl	4-HO-benzyl	Methyl	Benzylamino	515	516
587	4-Pyridylmethyl	4-HO-benzyl	Methyl	Benzylamino	515	516
588	8-quinolin-2-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	565	566
589	8-Benzofuran-4-ylmethyl	4-HO-benzyl	Methyl	Benzylamino	554	555
590	Naphthyl-1-ylmethyl	4-HO-phenyl	Methyl	Benzylamino	550	551
591	4-F-benzyl	4-HO-phenyl	Methyl	Benzylamino	518	519
592	2,4-F_2-benzyl	4-HO-phenyl	Methyl	Benzylamino	536	537
593	(R)-Toluylmethyl	4-HO-benzyl	Methyl	Benzylamino	542	543
594	(S)-Toluylmethyl	4-HO-benzyl	Methyl	Benzylamino	542	543
595	1,2,3,4-tetrahydro-naphthalen-2-yl	4-HO-benzyl	Methyl	Benzylamino	554	555
596	Naphthyl-1-ylmethyl	3,4-Dimethoxybenzyl	Methyl	Benzylamino	608	609
597	2-Dimethylamino-6-F-benzyl	4-HO-benzyl	Methyl	Benzylamino	575	576
598	2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	557	558
599	Naphthyl-1-ylmethyl	4-CN-benzyl	Methyl	Benzylamino	573	574
600	4-F-2-CF_3-benzyl	4-HO-benzyl	Methyl	Benzylamino	599	600

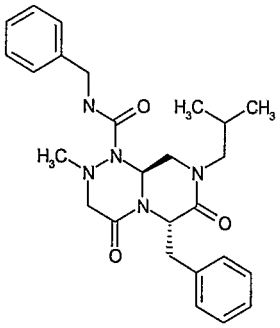
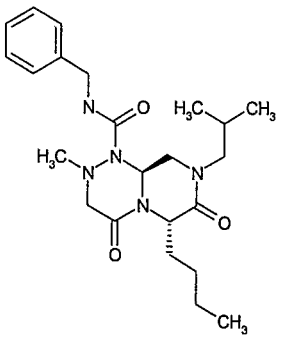
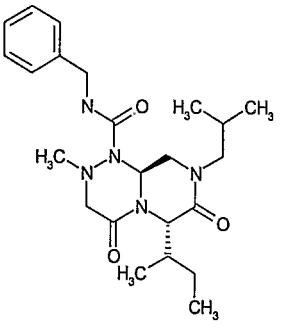
No	R_2	R_4	R_7	R_1-Y'	Mol. Weight	M+H
601	4-Cl-2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	591	592
602	3-*N,N*-Ethylmethyllamino-benzyl	4-HO-benzyl	Methyl	Benzylamino	571	572
603	3-Diethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	585	586
604	4-Cl-3-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	591	592
605	4-F-2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	575	576
606	3,5-$(CH_3)_2$-2-Dimethylamino-benzyl	4-HO-benzyl	Methyl	Benzylamino	585	586
607	3-(CH_3)-2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	571	572
608	6-(CH_3)-2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	571	572
609	3,4-F_2-2-Dimethylaminobenzyl	4-HO-benzyl	Methyl	Benzylamino	593	594

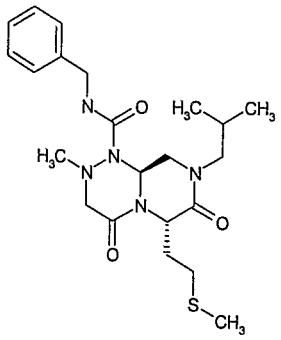
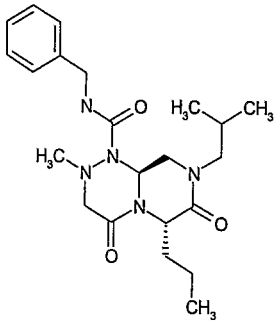
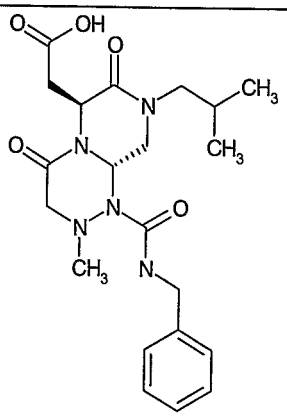
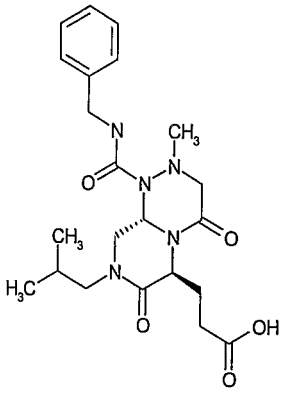
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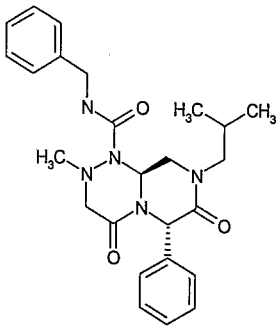
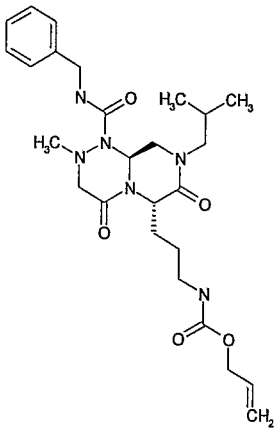
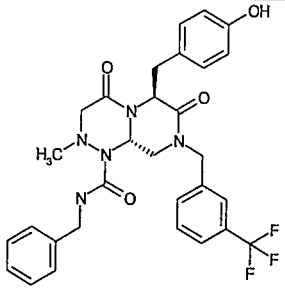
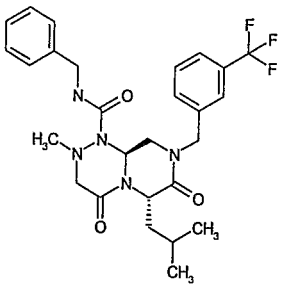
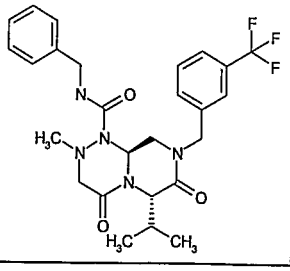
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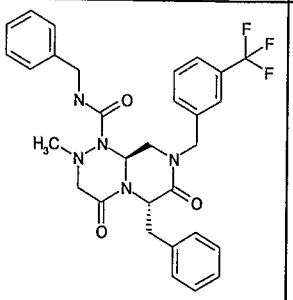
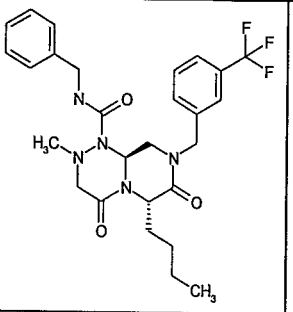
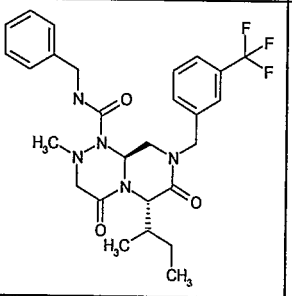
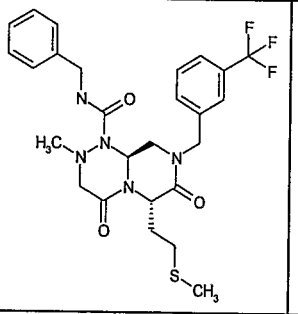
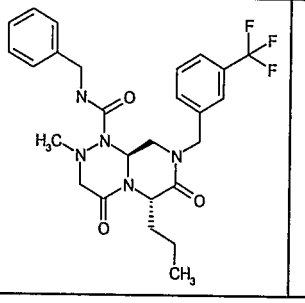


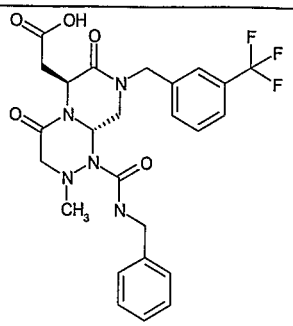
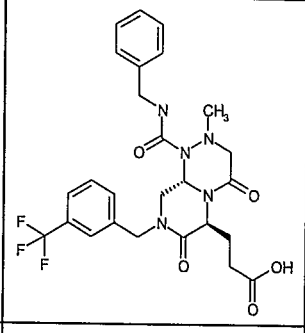
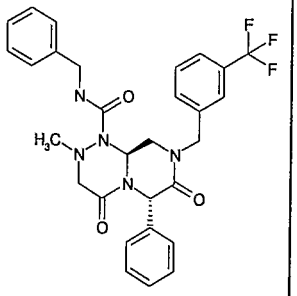
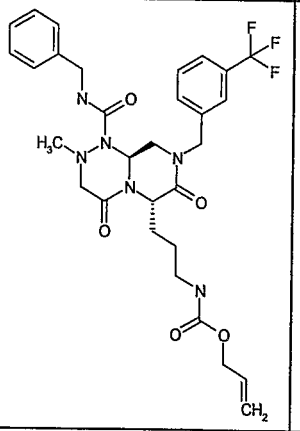
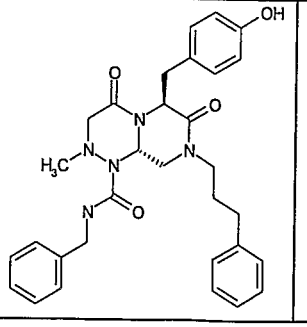
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803		430	431
804		416	417

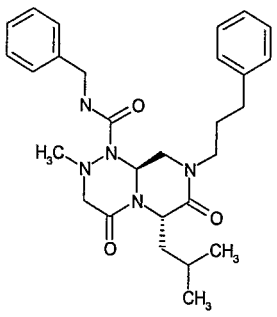
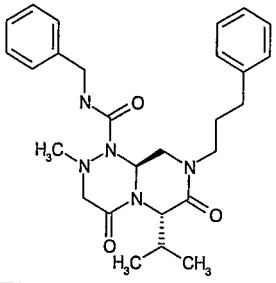
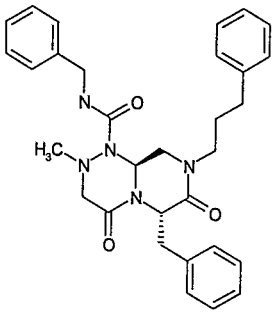
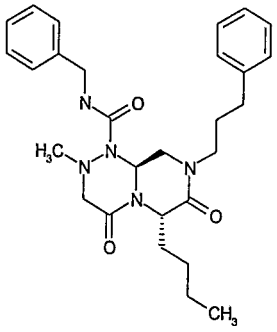
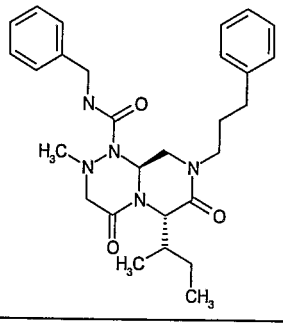
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806		430	431
807		430	431

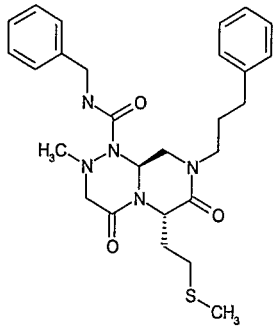
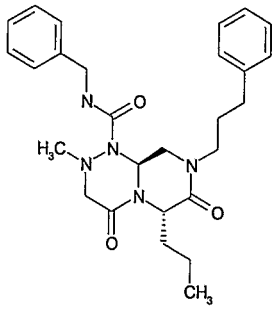
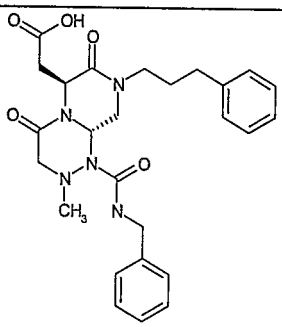
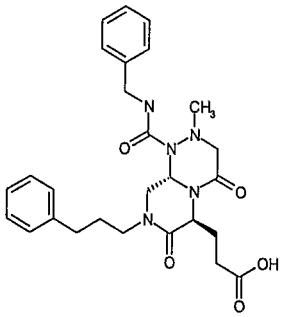
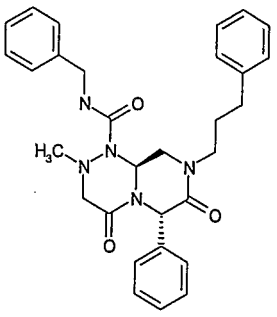
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809		416	417
810		431	432
811		446	447

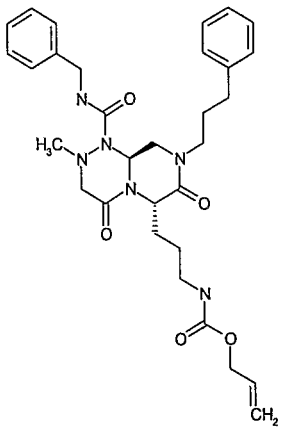
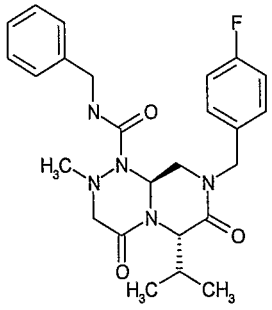
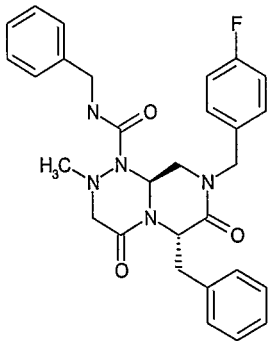
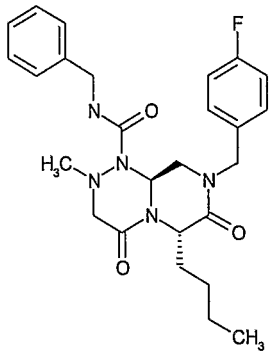
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814		582	583
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816		518	519

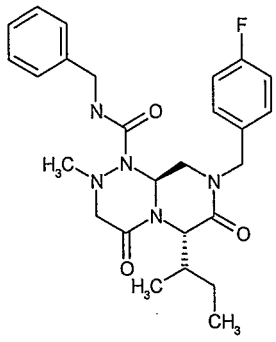
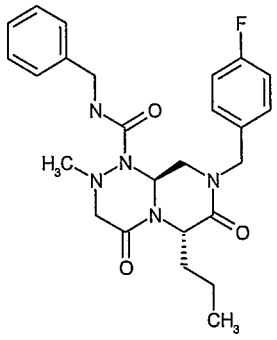
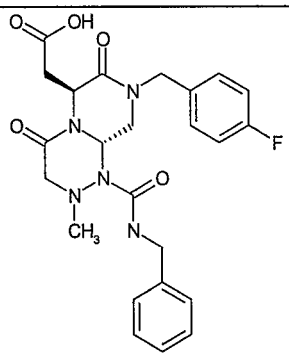
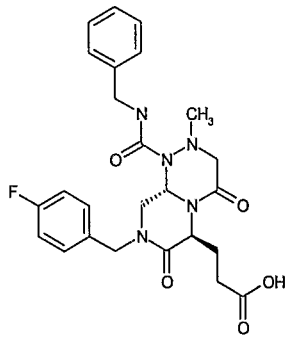
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820		550	551
821		518	519

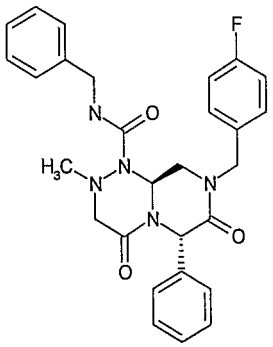
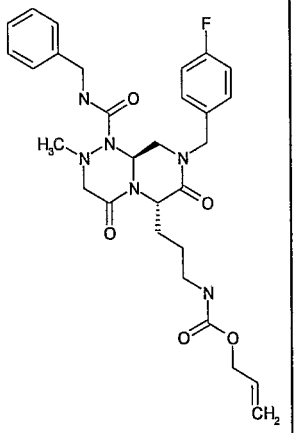
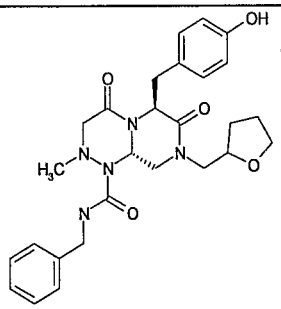
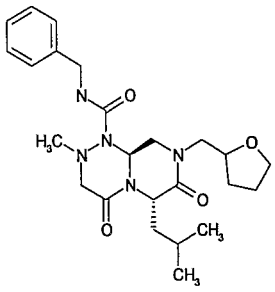
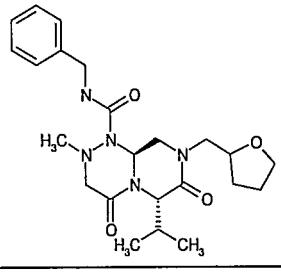
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825		617	618
826		542	543

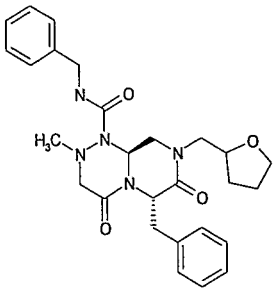
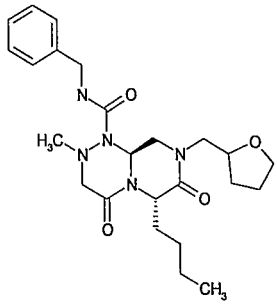
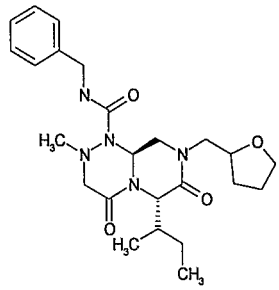
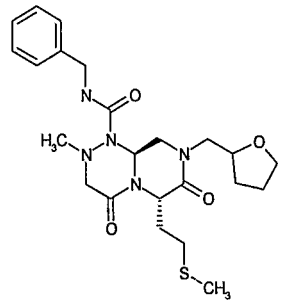
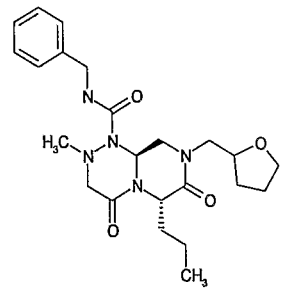
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828		478	479
829		526	527
830		492	493
831		492	493

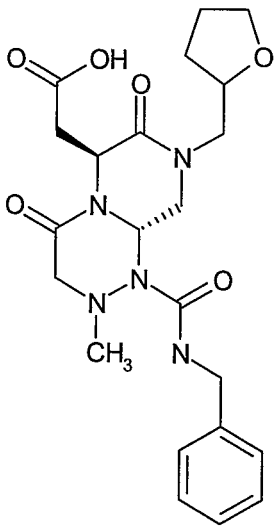
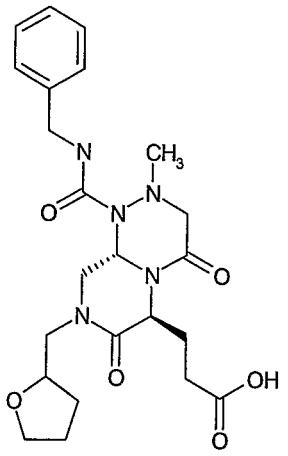
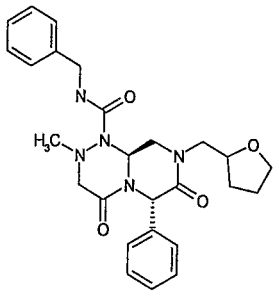
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835		508	509
836		512	513

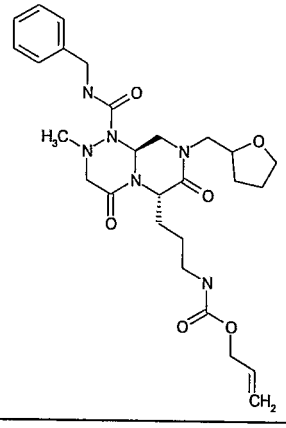
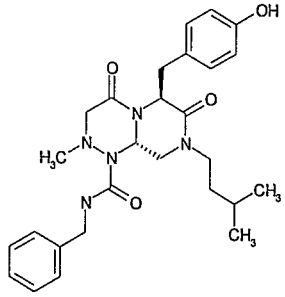
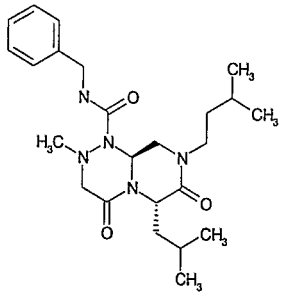
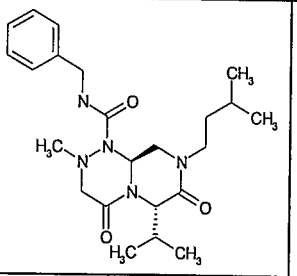
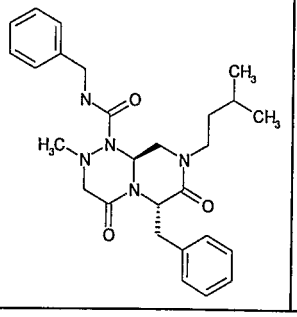
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838		468	469
839		516	517
840		482	483

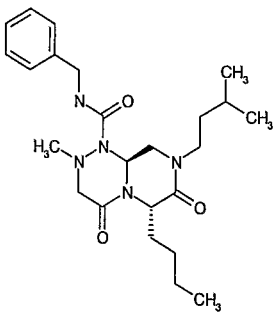
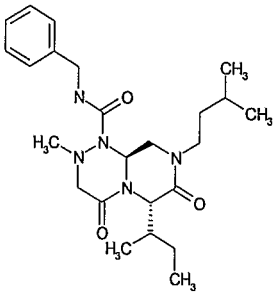
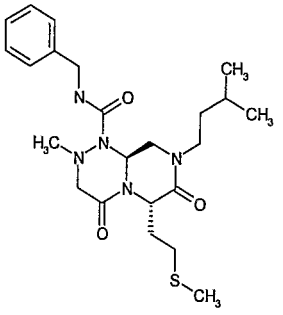
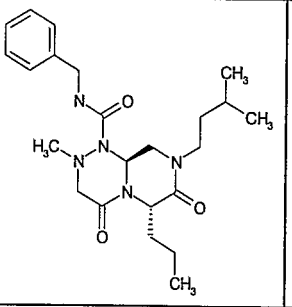
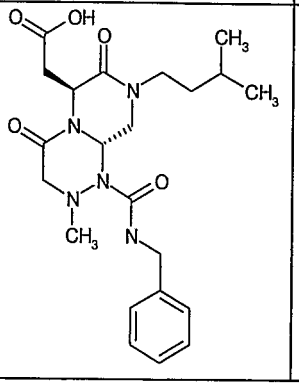
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842		468	469
843		484	485
844		498	499

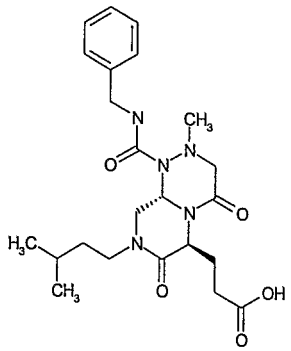
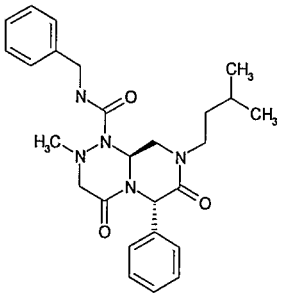
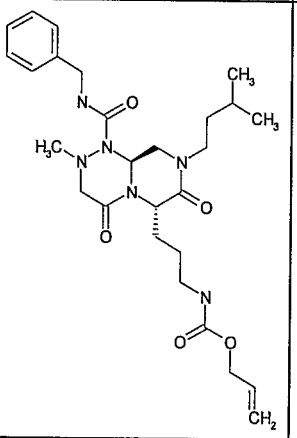
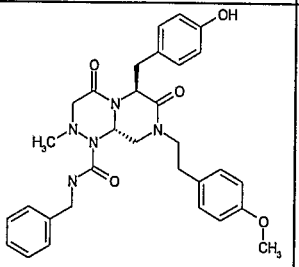
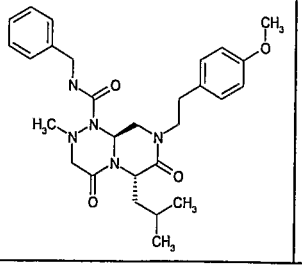
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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846		567	568
847		508	509
848		458	459
849		444	445

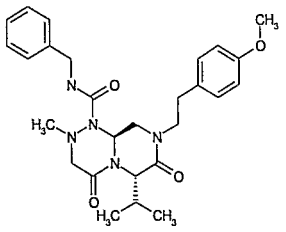
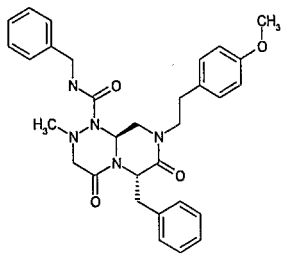
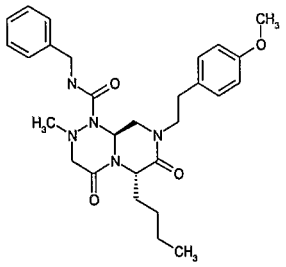
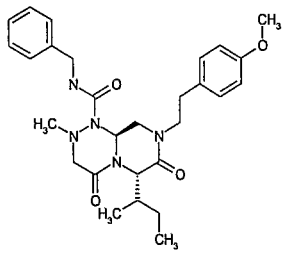
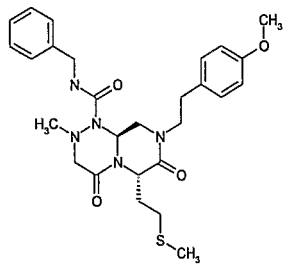
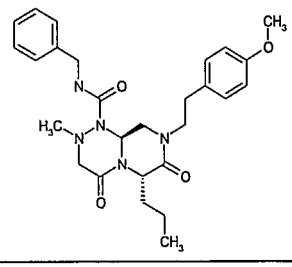
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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851		458	459
852		458	459
853		476	477
854		444	445

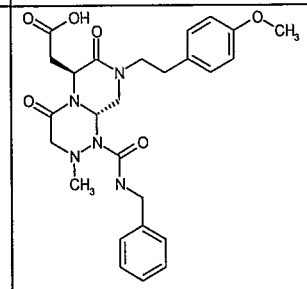
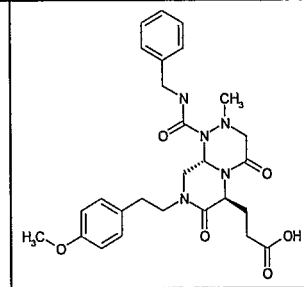
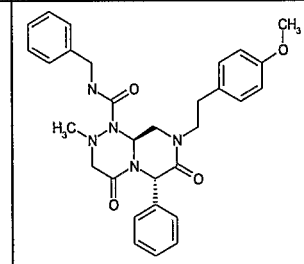
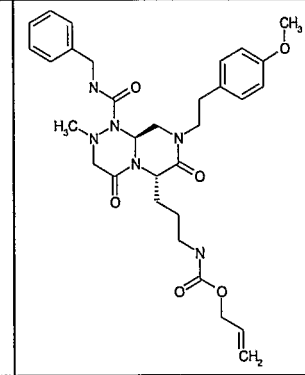
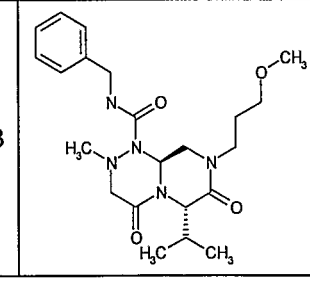
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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856		474	475
857		478	479

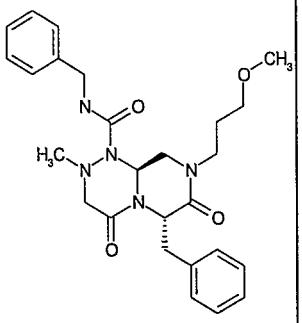
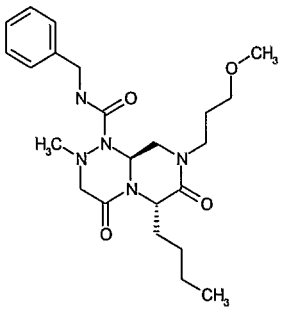
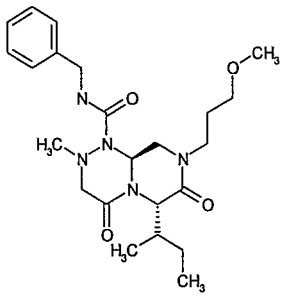
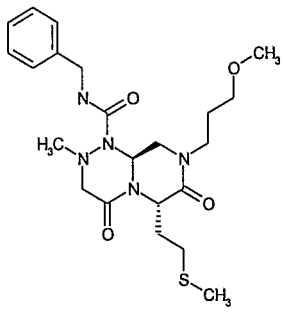
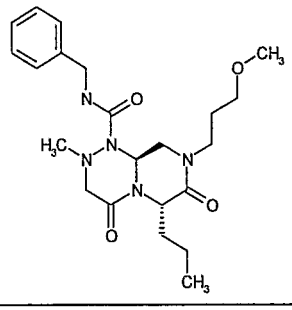
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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859		494	495
860		444	445
861		430	431
862		478	479

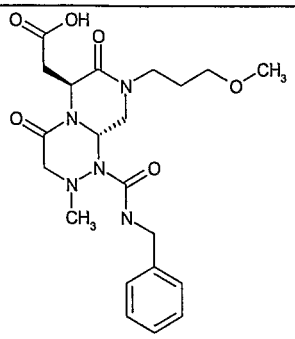
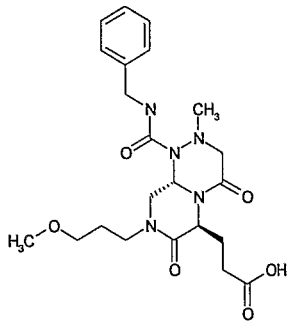
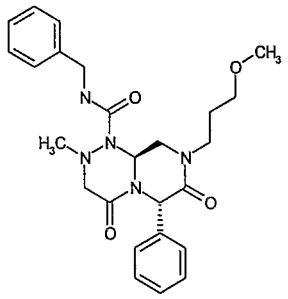
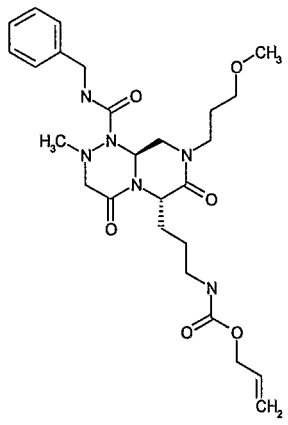
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864		444	445
865		462	463
866		430	431
867		446	447

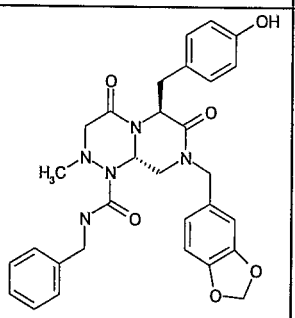
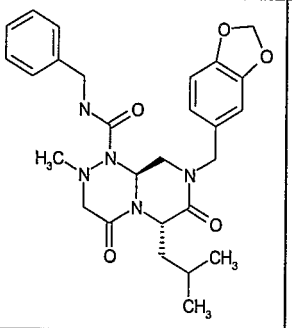
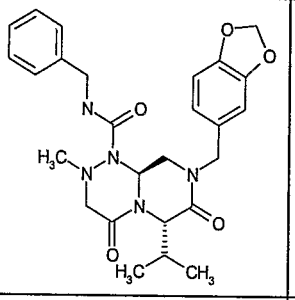
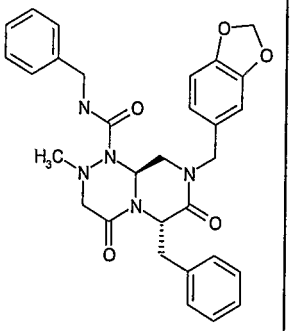
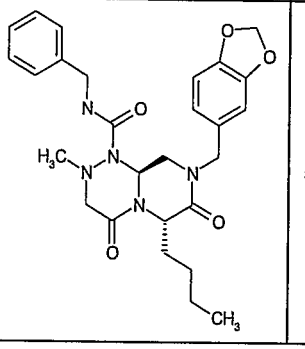
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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869		464	465
870		529	530
871		558	559
872		508	509

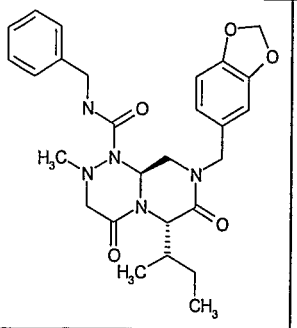
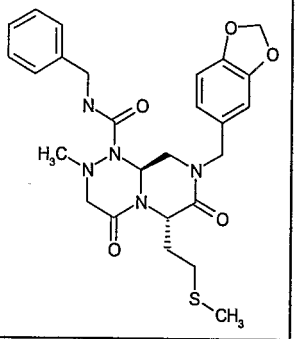
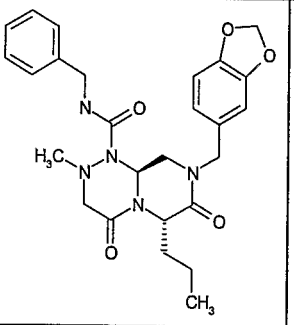
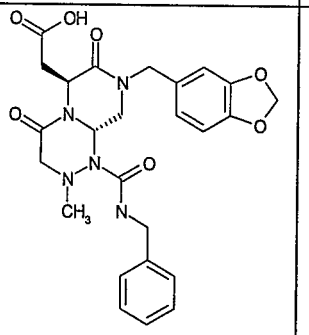
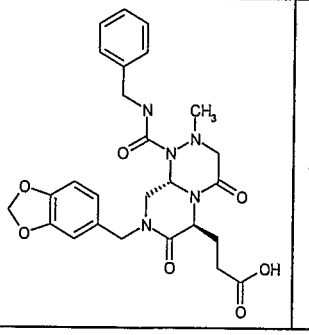
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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874		542	543
875		508	509
876		508	509
877		526	527
878		494	495

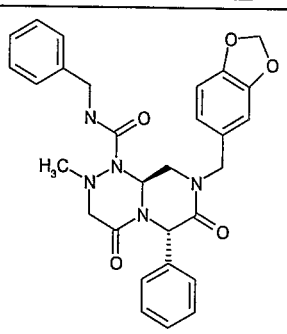
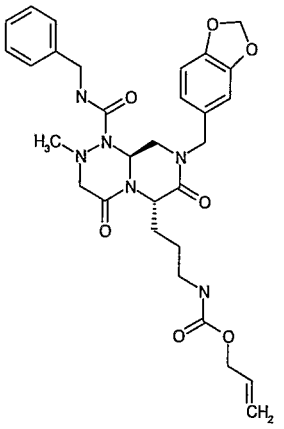
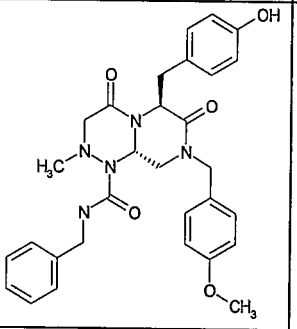
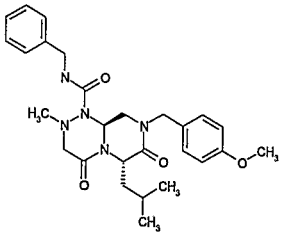
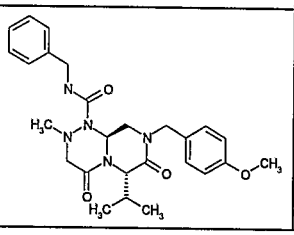
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
879		510	511
880		524	525
881		528	529
882		593	594
883		432	433

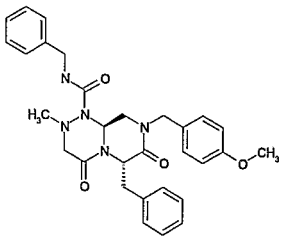
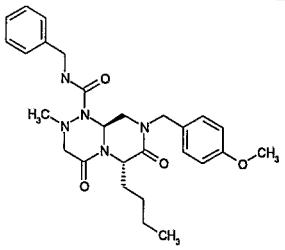
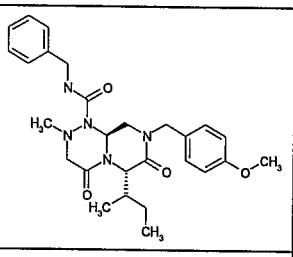
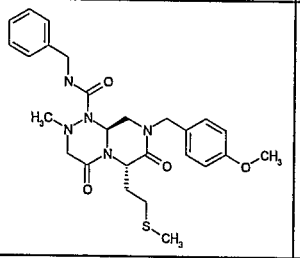
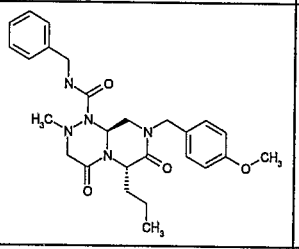
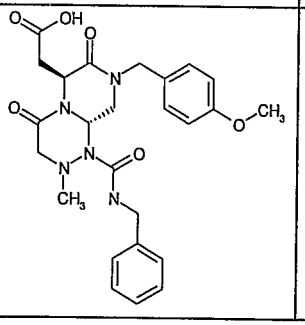
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885		446	447
886		446	447
887		464	465
888		432	433

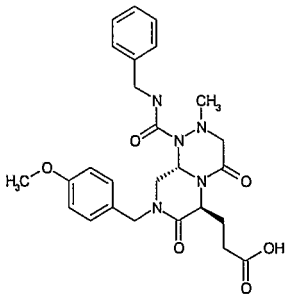
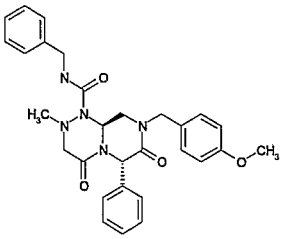
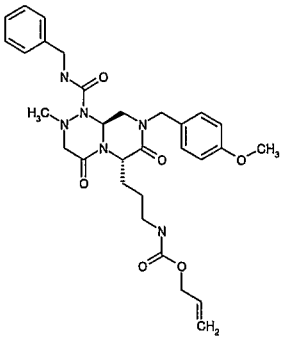
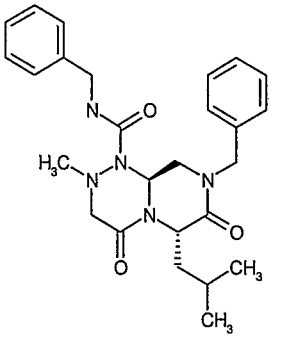
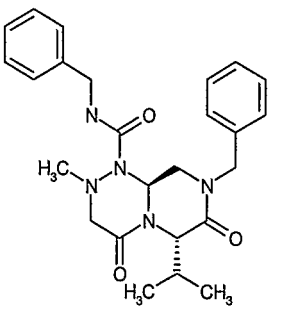
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890		462	463
891		466	467
892		531	532

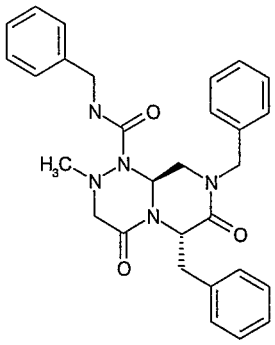
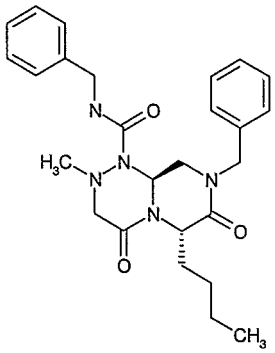
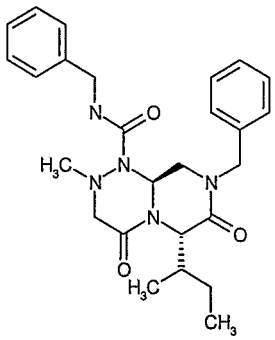
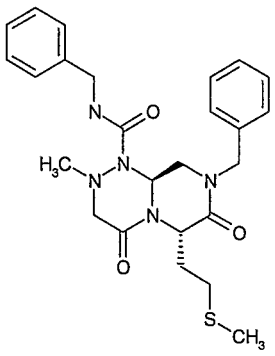
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
893		558	559
894		508	509
895		494	495
896		542	543
897		508	509

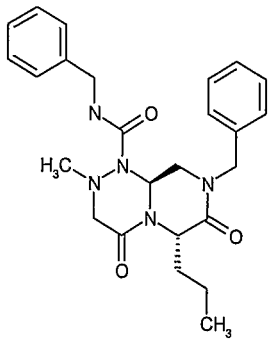
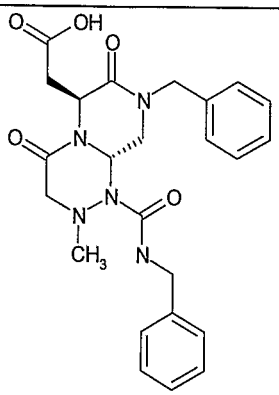
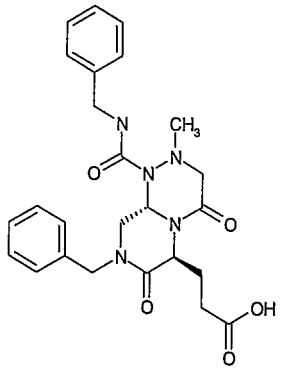
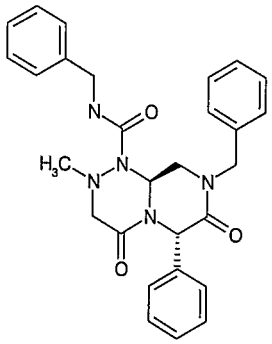
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899		526	527
900		494	495
901		510	511
902		524	525

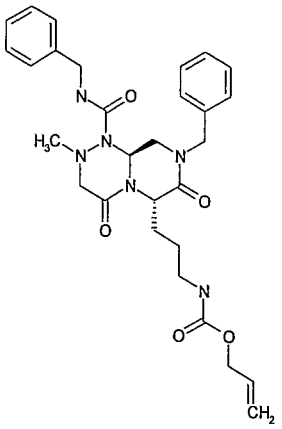
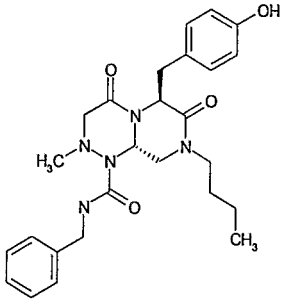
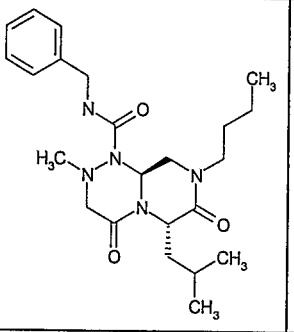
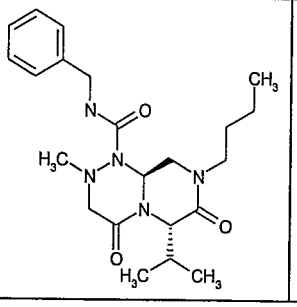
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904		593	594
905		544	545
906		494	495
907		480	481

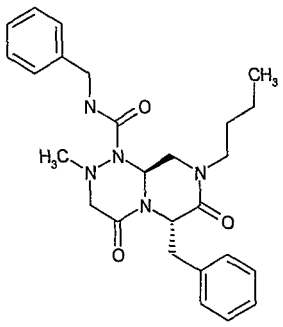
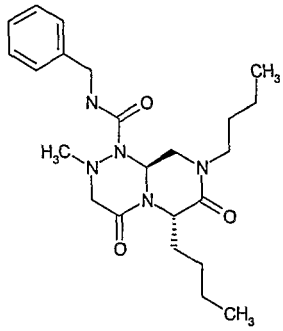
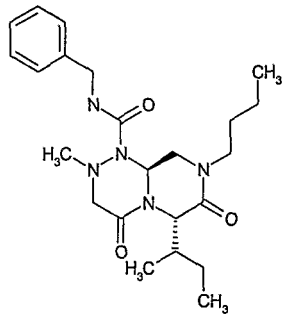
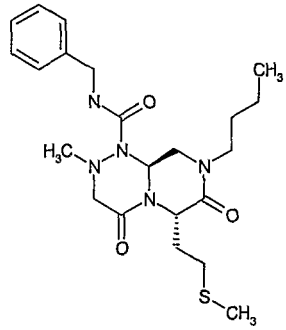
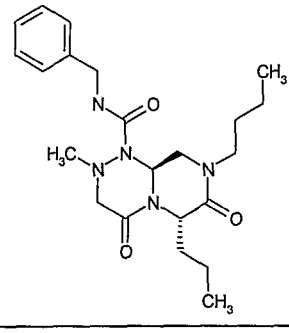
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
908		528	529
909		494	495
910		494	495
911		512	513
912		480	481
913		496	497

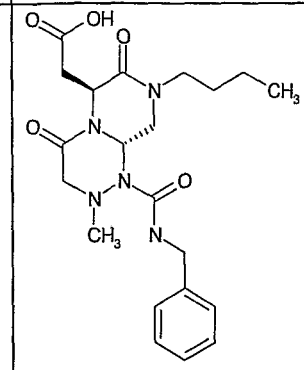
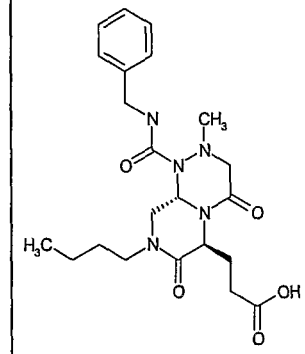
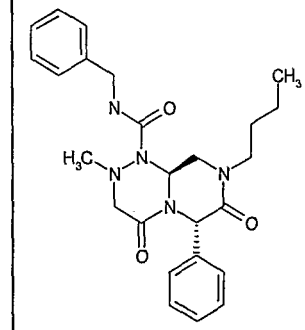
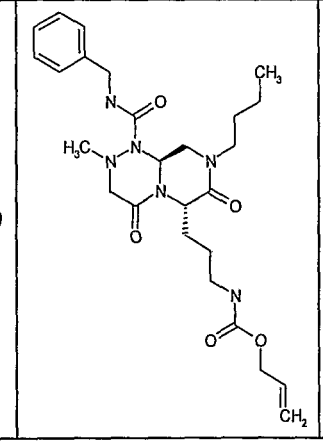
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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915		514	515
916		579	580
917		464	465
918		450	451

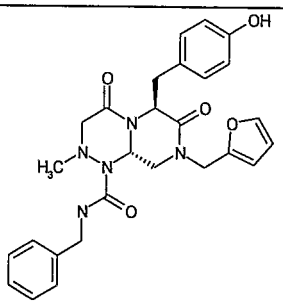
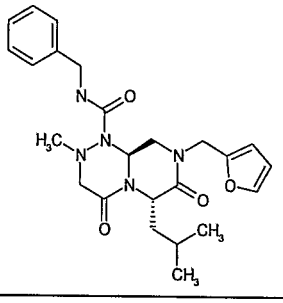
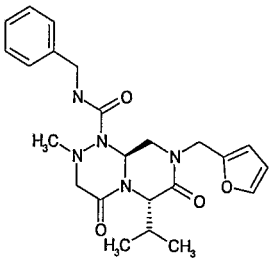
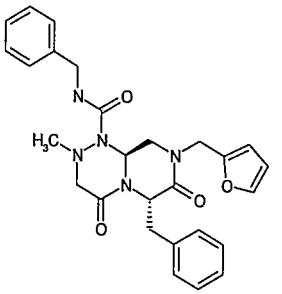
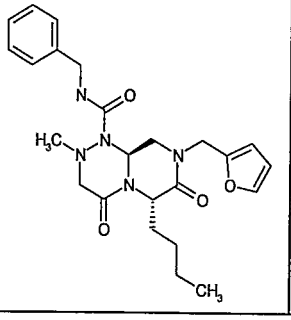
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
919		498	499
920		464	465
921		464	465
922		482	483

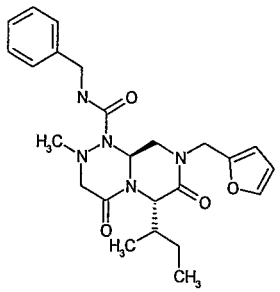
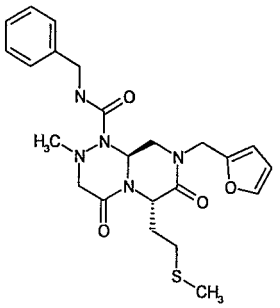
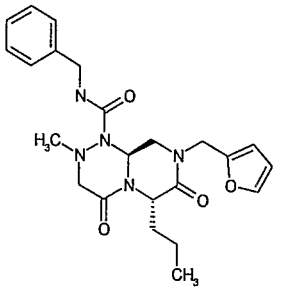
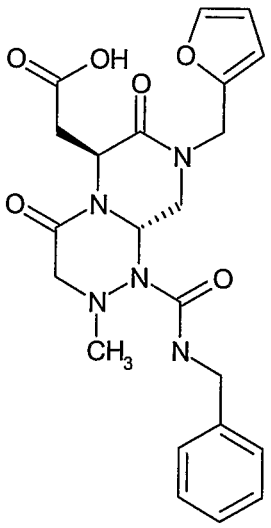
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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924		466	467
925		480	481
926		484	485

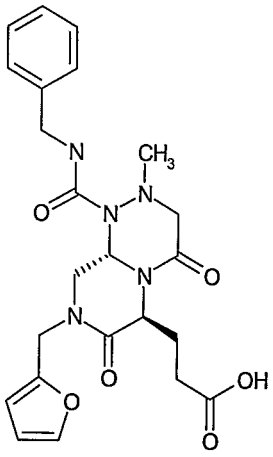
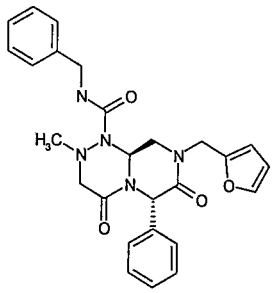
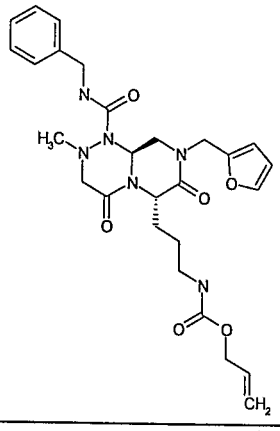
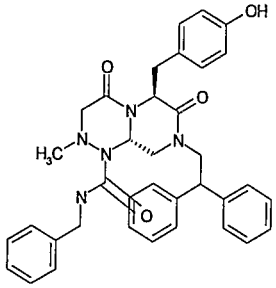
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
927		549	550
928		480	481
929		430	431
930		416	417

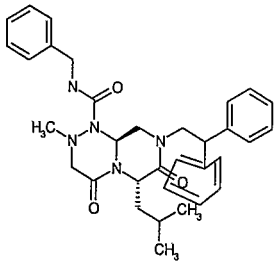
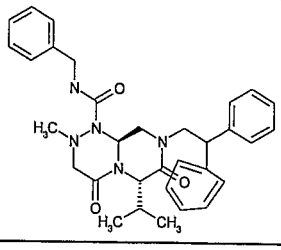
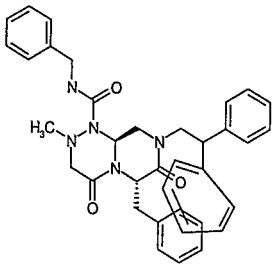
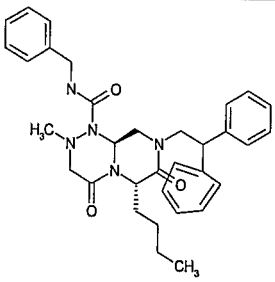
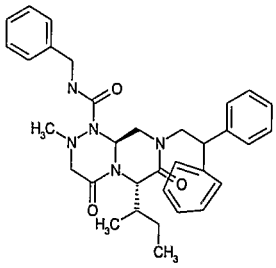
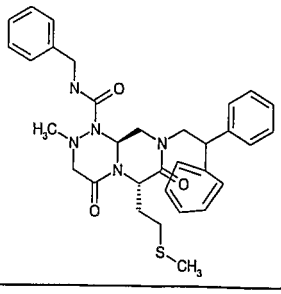
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
931		464	465
932		430	431
933		430	431
934		448	449
935		416	417

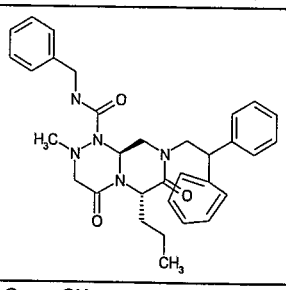
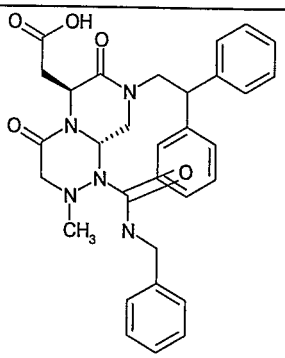
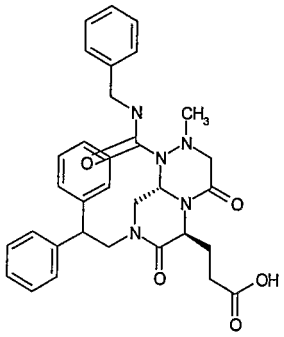
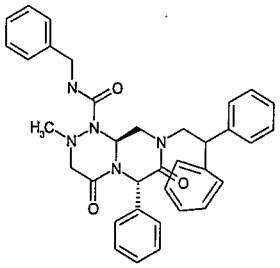
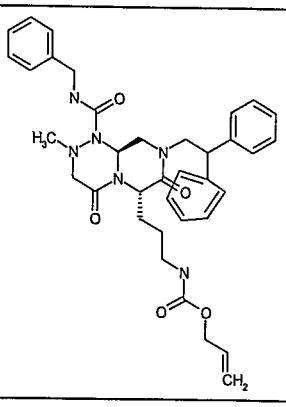
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937		446	447
938		450	451
939		515	516

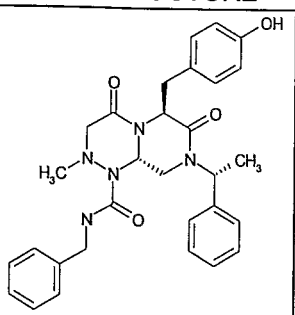
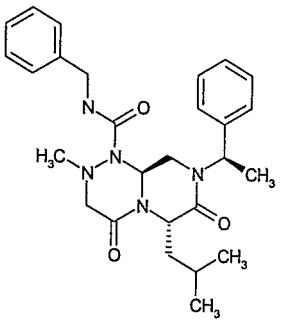
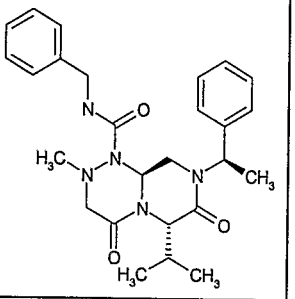
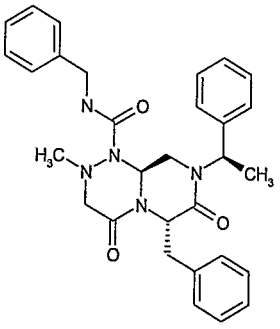
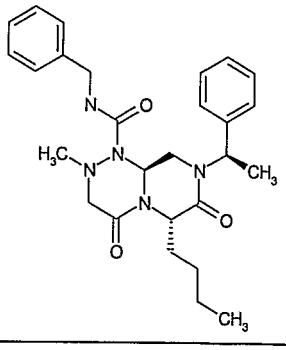
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942		440	441
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944		454	455

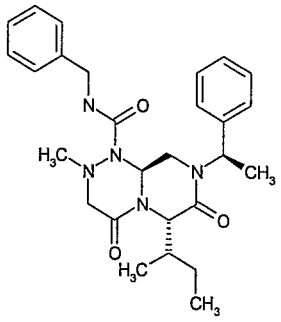
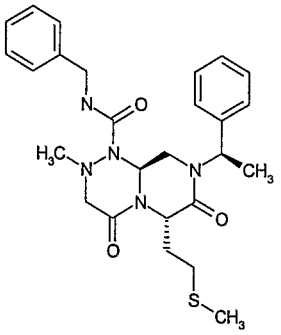
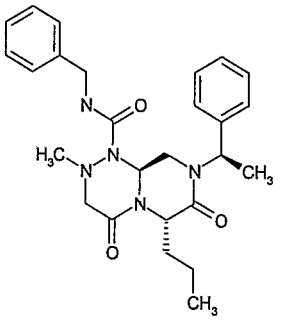
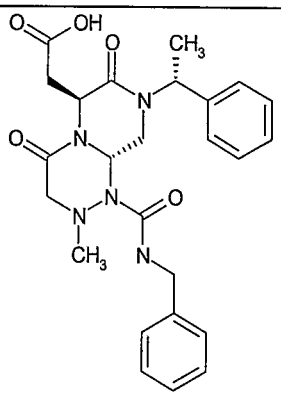
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947		440	441
948		455	456

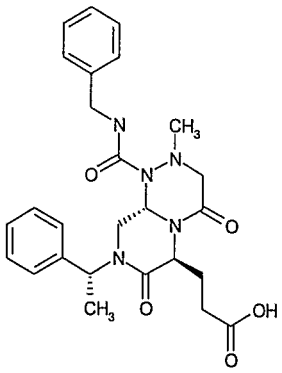
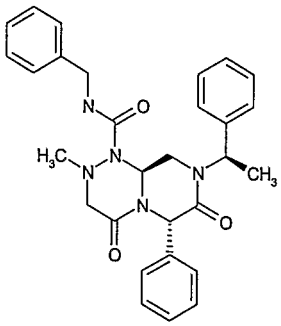
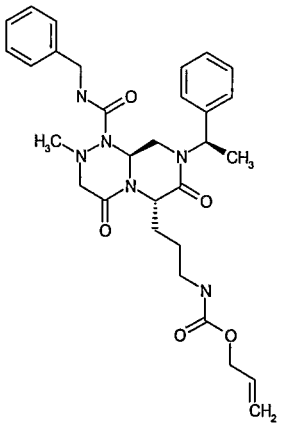
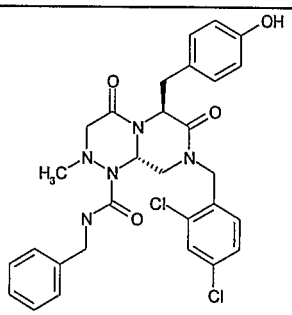
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950		474	475
951		539	540
952		604	605

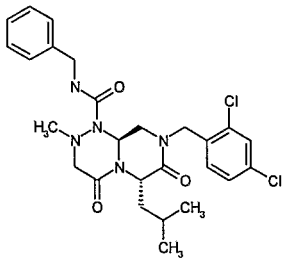
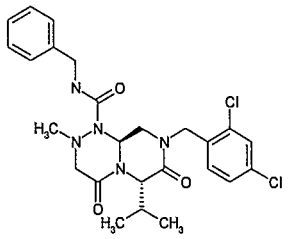
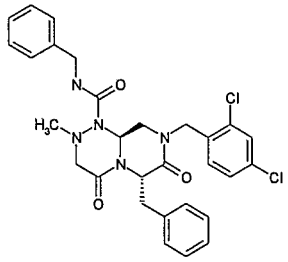
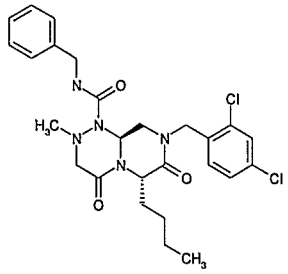
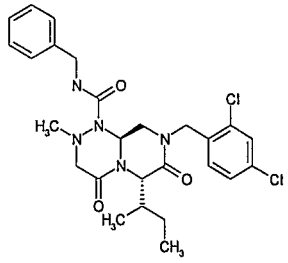
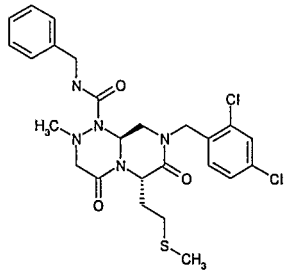
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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954		540	541
955		588	589
956		554	555
957		554	555
958		572	573

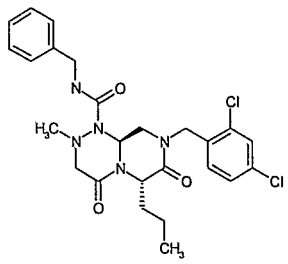
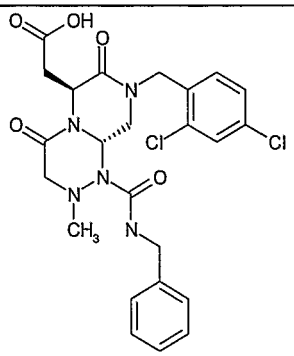
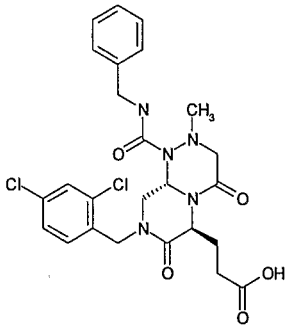
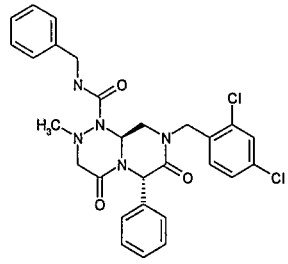
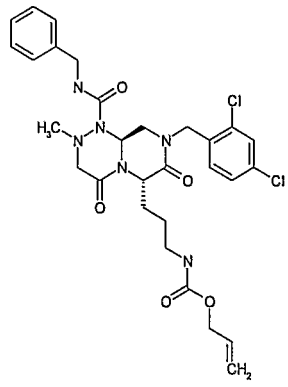
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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961		570	571
962		574	575
963		639	640

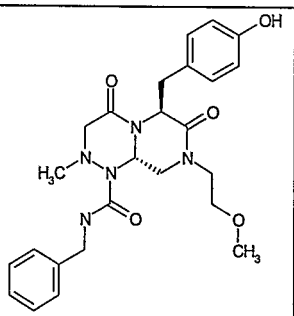
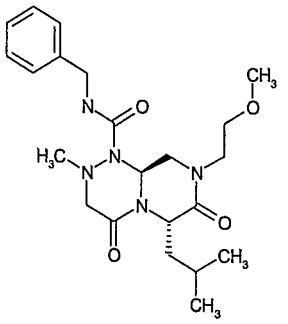
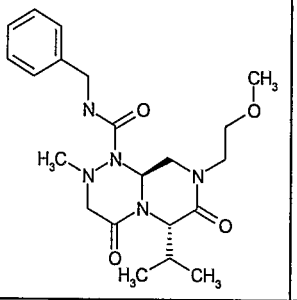
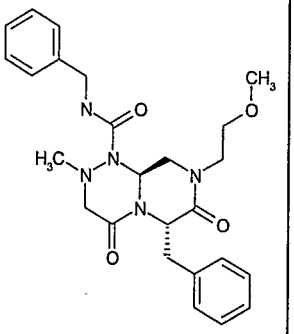
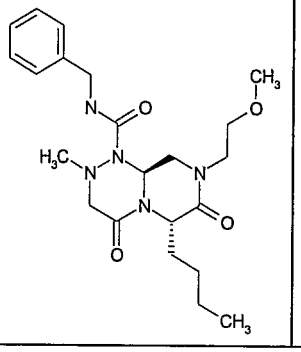
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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965		478	479
966		464	465
967		512	513
968		478	479

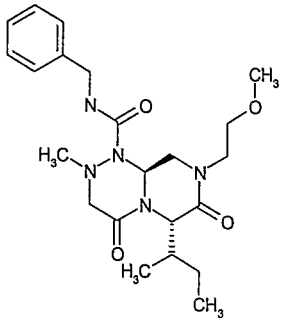
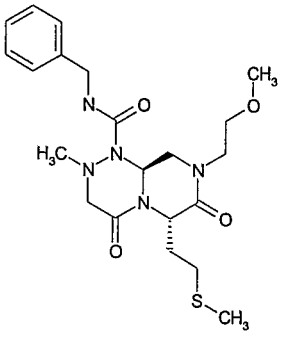
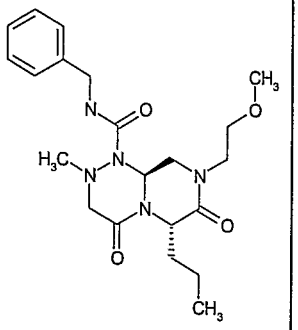
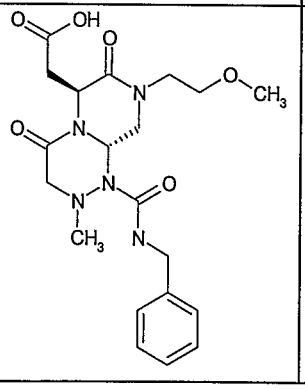
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970		496	497
971		464	465
972		480	481

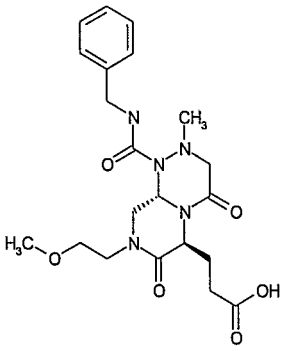
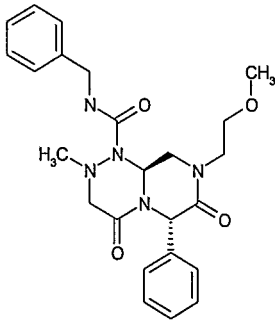
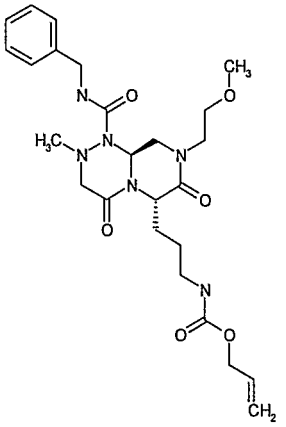
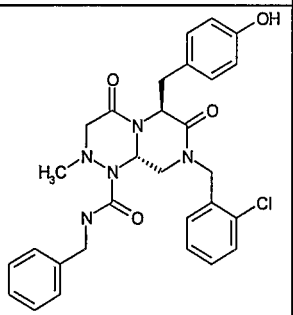
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975		563	564
976		582	583

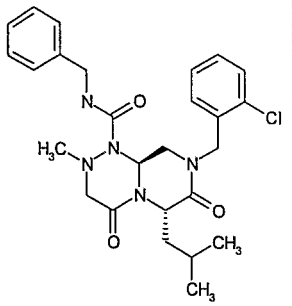
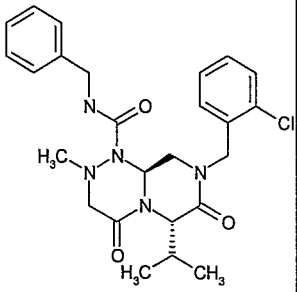
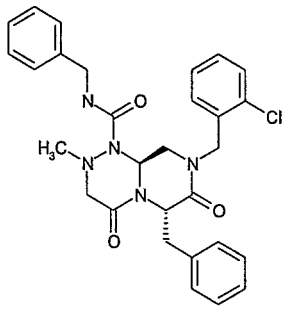
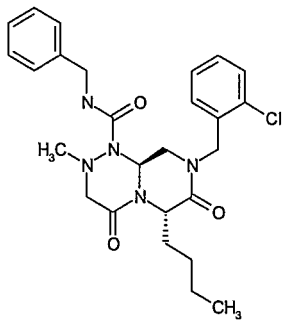
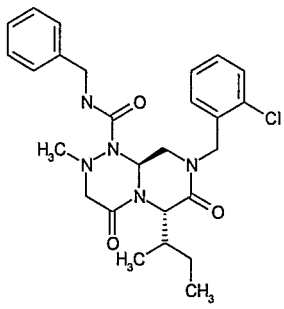
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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980		532	533
981		532	533
982		551	552

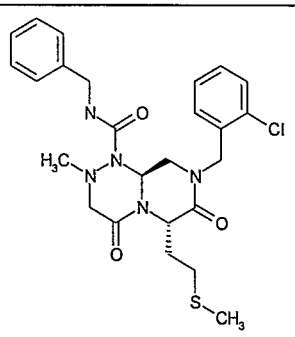
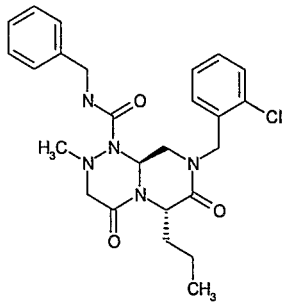
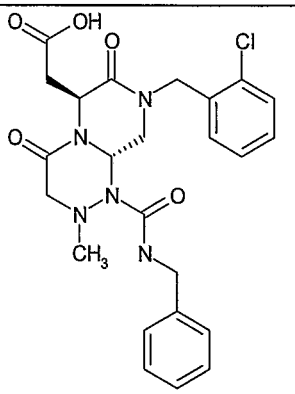
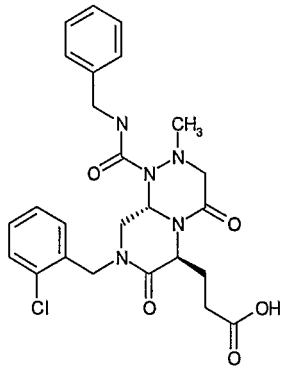
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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985		548	549
986		552	553
987		618	619

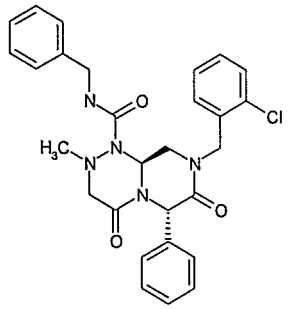
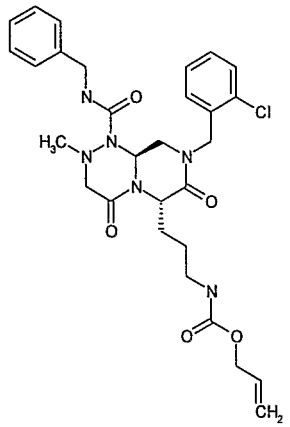
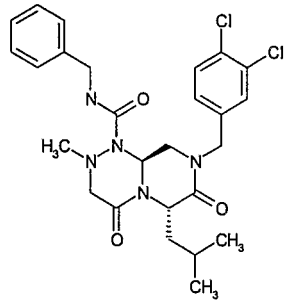
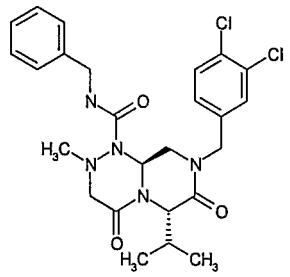
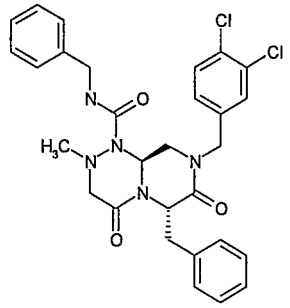
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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989		432	433
990		418	419
991		466	467
992		432	433

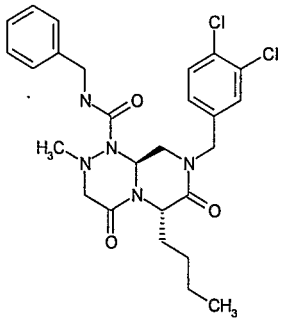
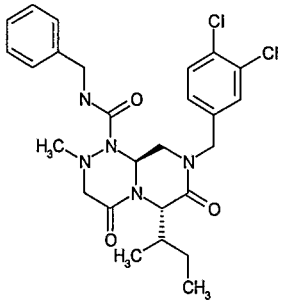
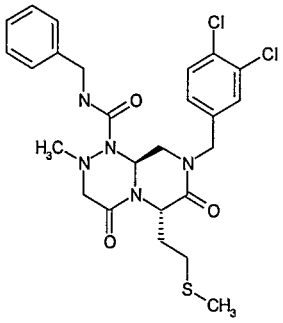
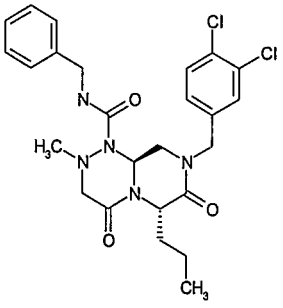
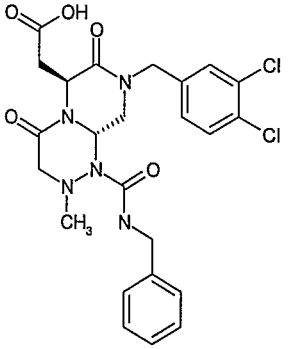
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994		450	451
995		418	419
996		433	434

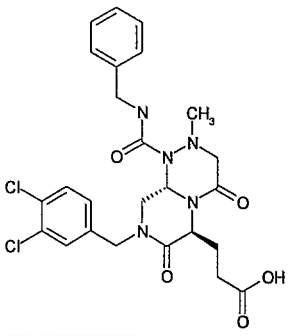
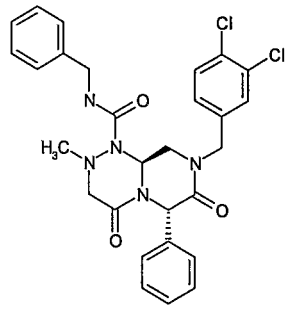
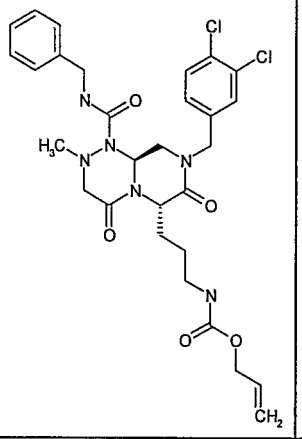
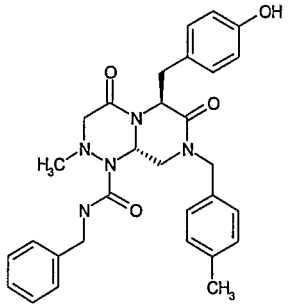
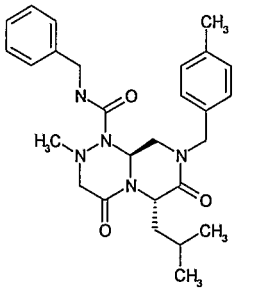
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998		452	453
999		517	518
1000		548	549

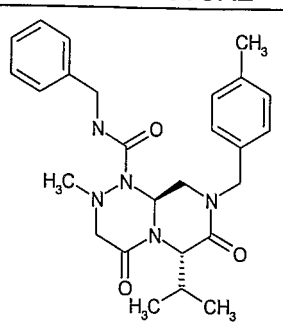
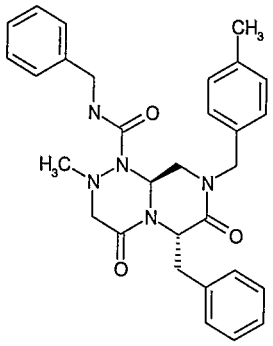
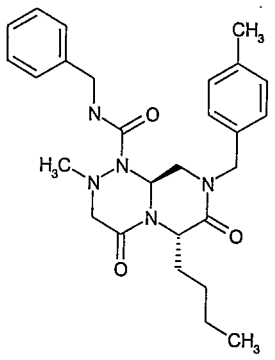
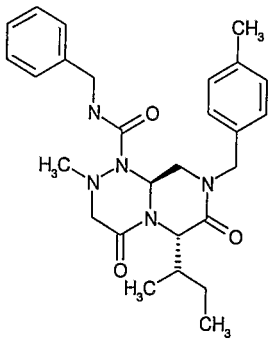
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1003		532	533
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1005		498	499

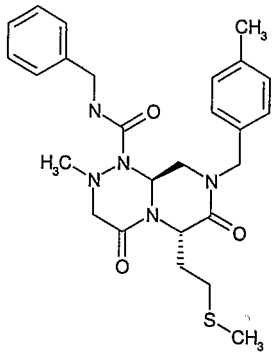
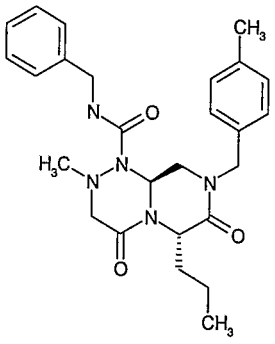
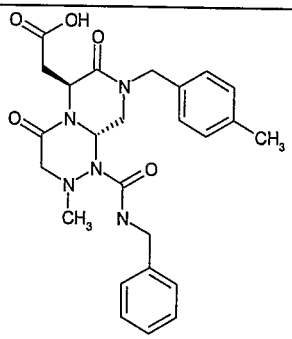
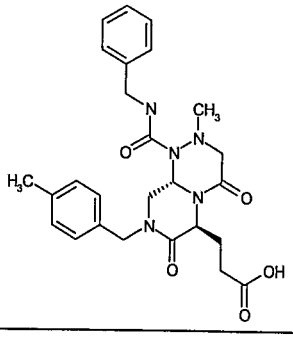
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1007		484	485
1008		500	501
1009		514	515

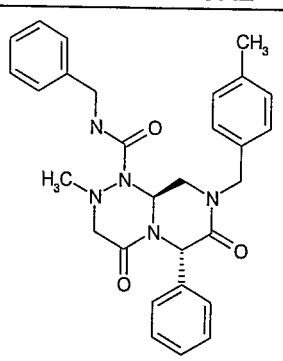
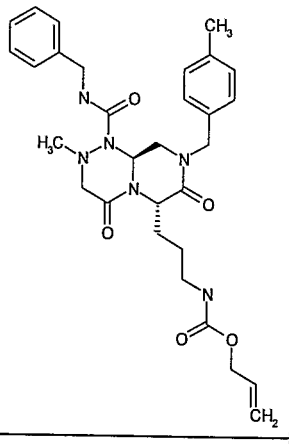
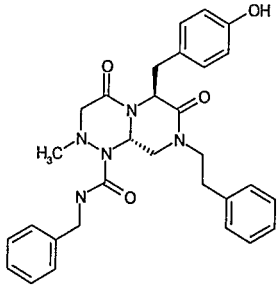
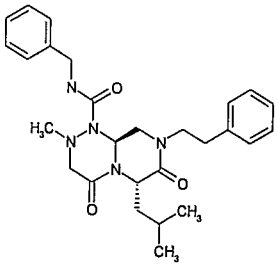
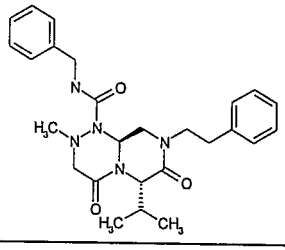
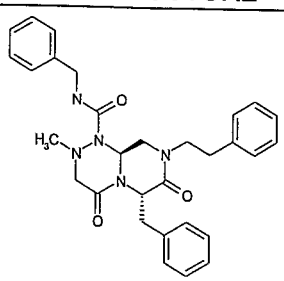
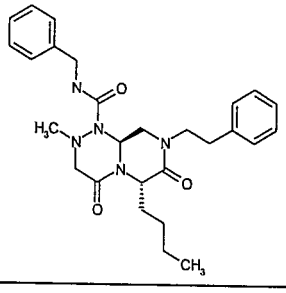
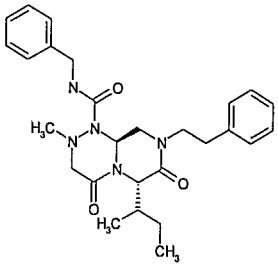
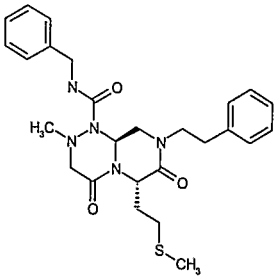
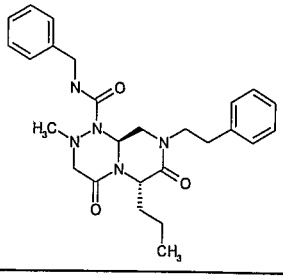
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1011		583	584
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1013		518	519
1014		566	567

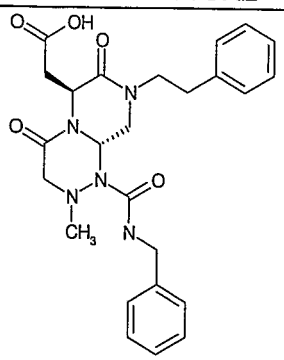
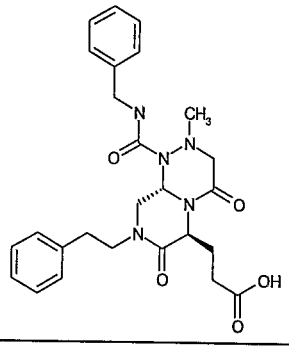
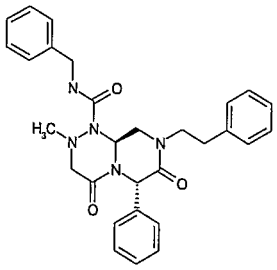
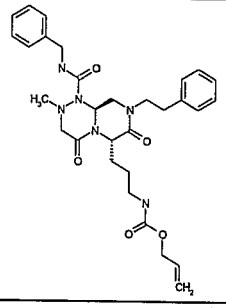
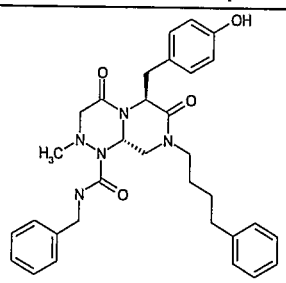
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1017		551	552
1018		518	519
1019		534	535

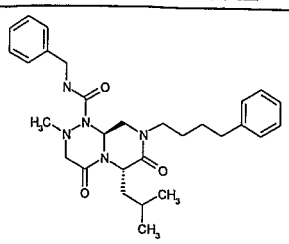
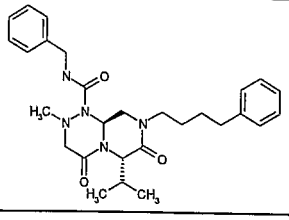
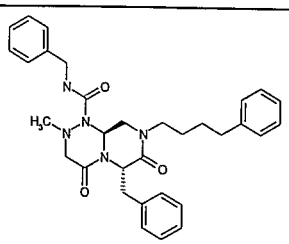
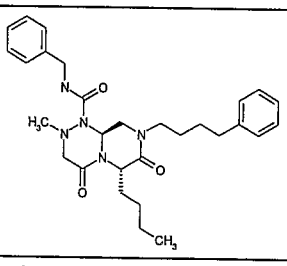
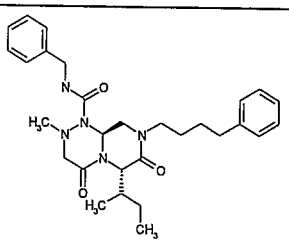
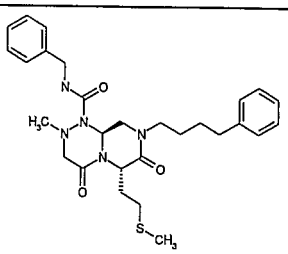
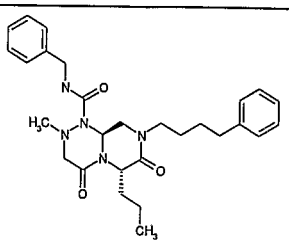
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1021		552	553
1022		618	619
1023		528	529
1024		478	479

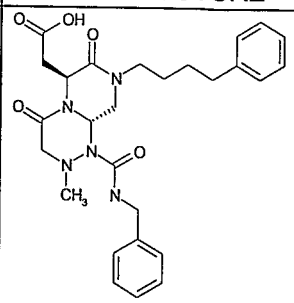
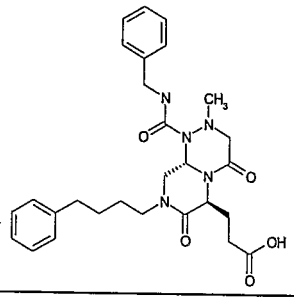
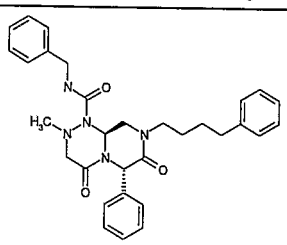
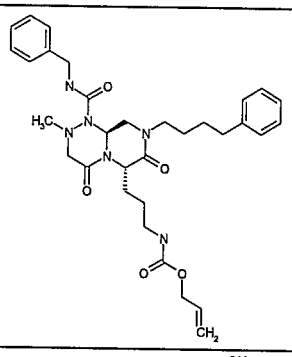
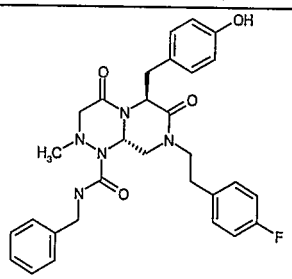
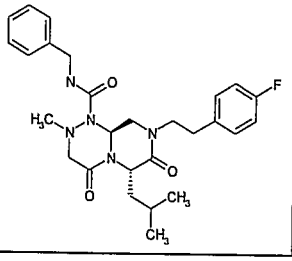
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1025		464	465
1026		512	513
1027		478	479
1028		478	479

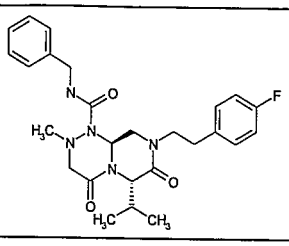
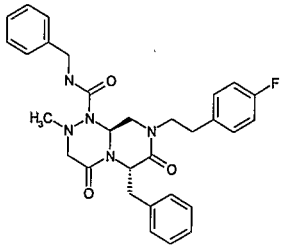
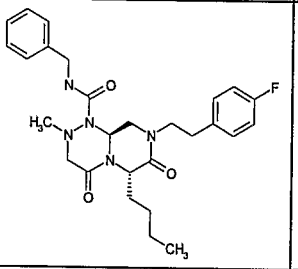
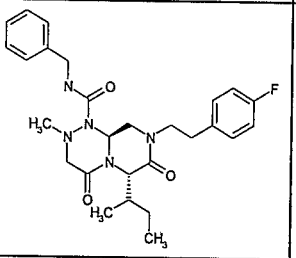
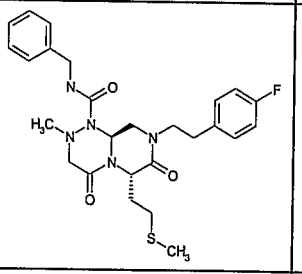
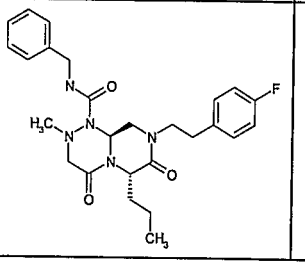
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1030		464	465
1031		480	481
1032		494	495

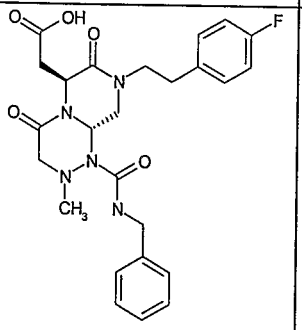
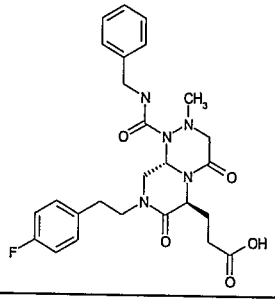
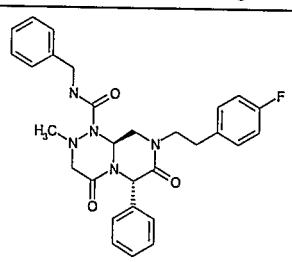
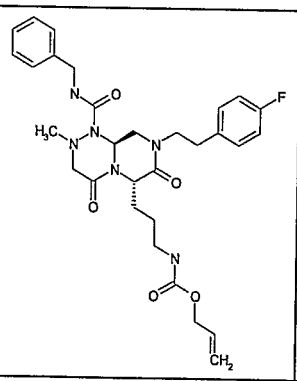
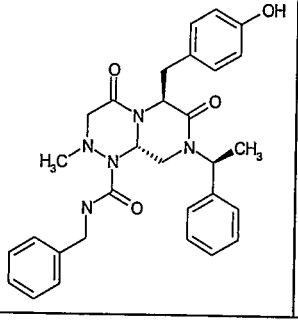
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1034		563	564
1035		528	529
1036		478	479
1037		464	465
1038		512	513
1039		478	479
1040		478	479
1041		496	497
1042		464	465

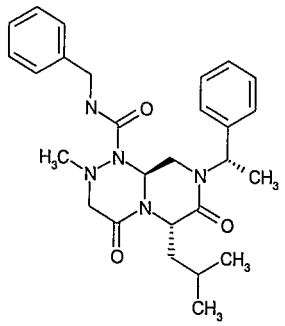
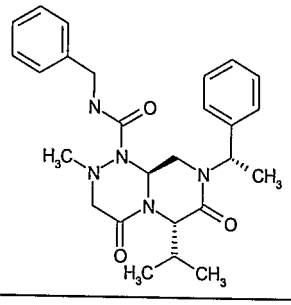
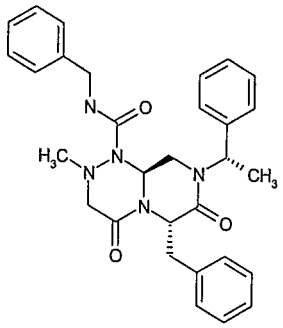
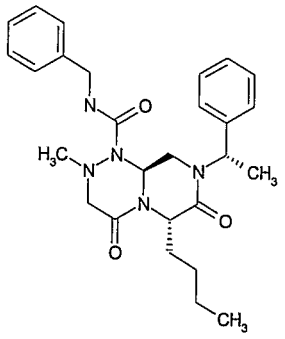
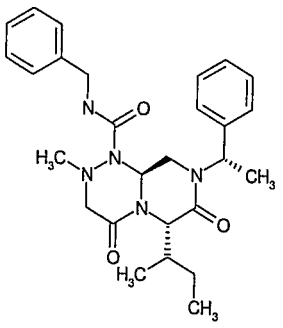
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1044		494	495
1045		498	499
1046		563	564
1047		556	557

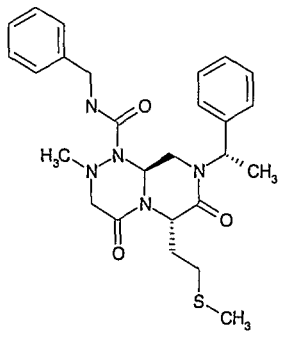
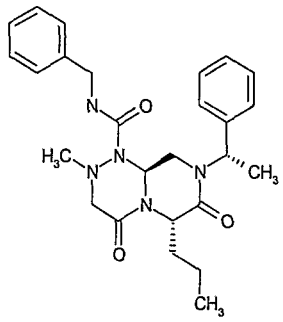
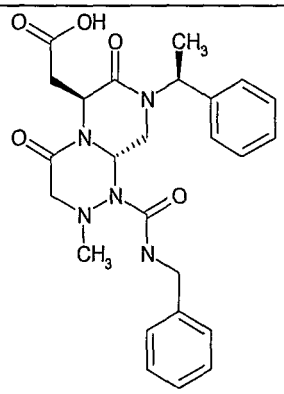
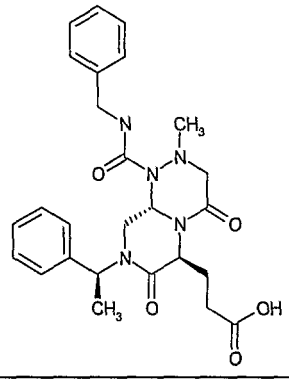
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1051		506	507
1052		506	507
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1054		492	493

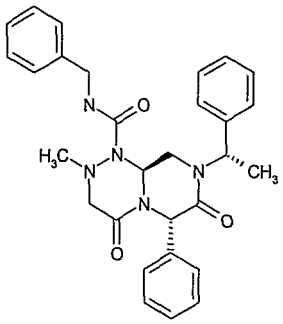
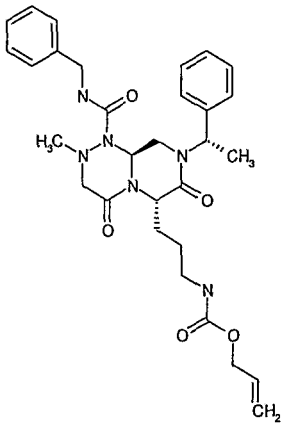
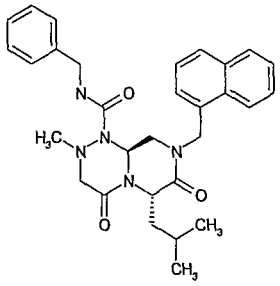
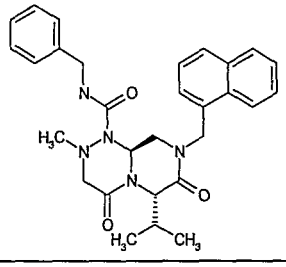
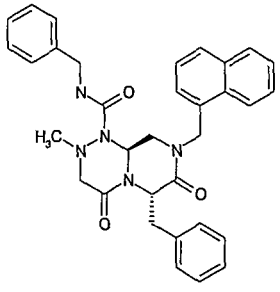
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1056		522	523
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1058		591	592
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1060		496	497

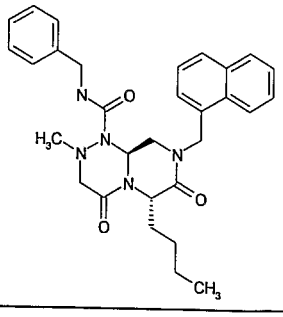
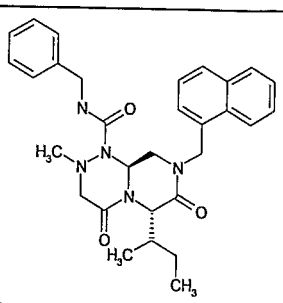
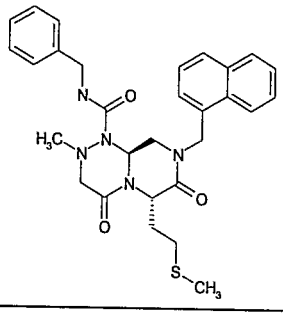
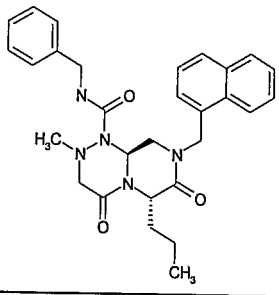
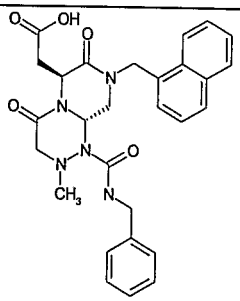
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1062		530	531
1063		496	497
1064		496	497
1065		514	515
1066		482	483

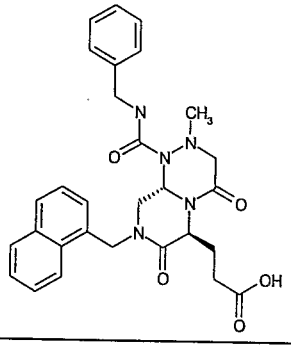
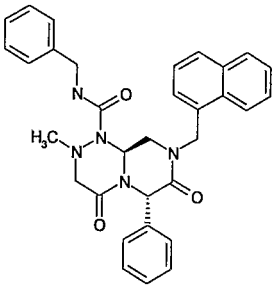
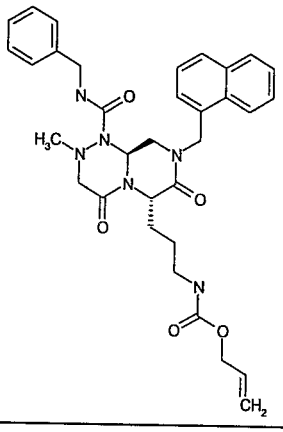
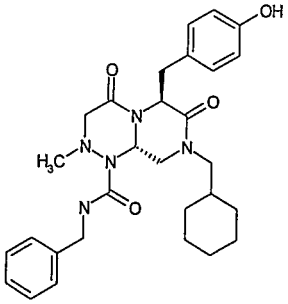
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1068		512	513
1069		516	517
1070		581	582
1071		528	529

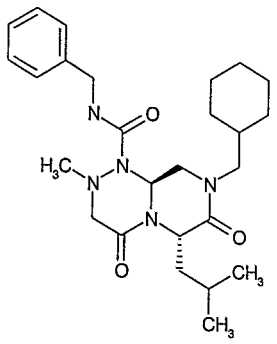
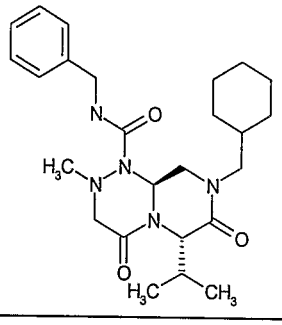
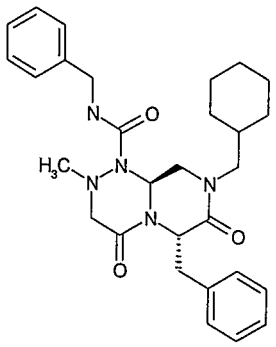
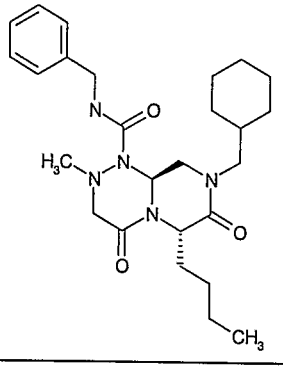
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1073		464	465
1074		512	513
1075		478	479
1076		478	479

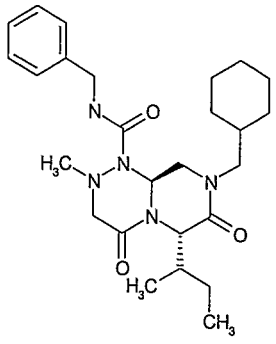
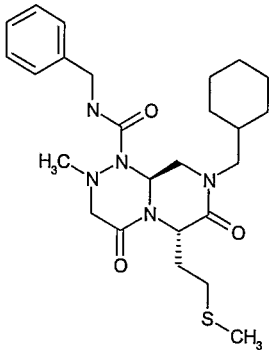
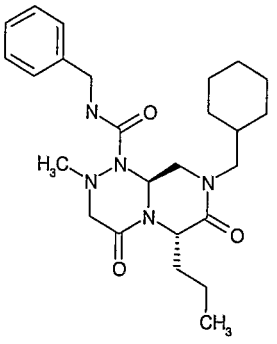
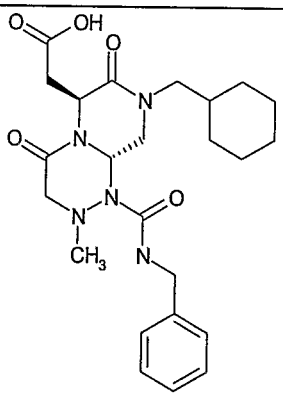
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1078		464	465
1079		480	481
1080		494	495

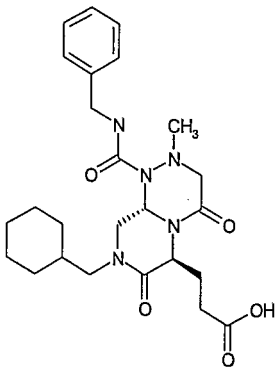
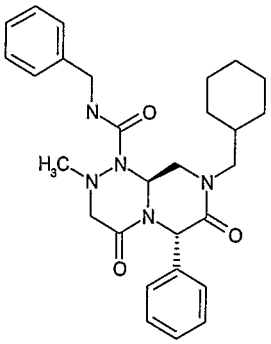
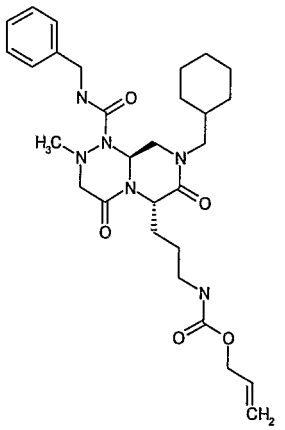
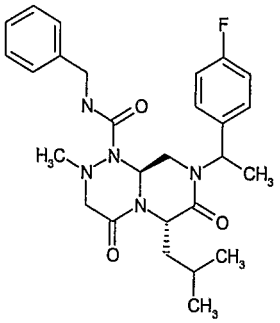
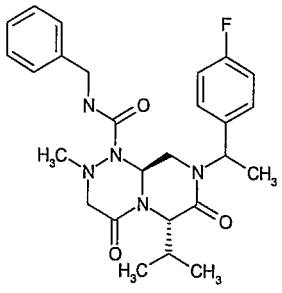
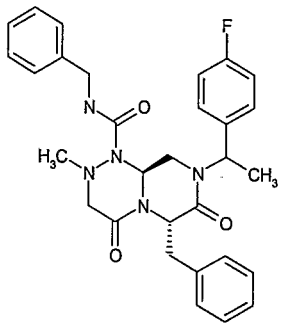
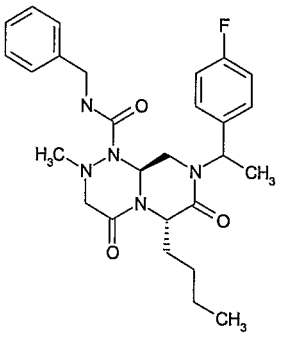
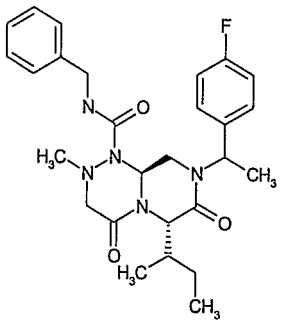
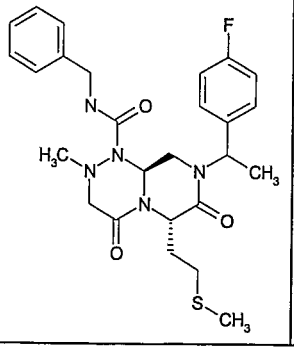
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1082		563	564
1083		514	515
1084		500	501
1085		548	549

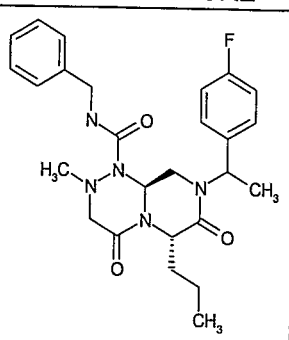
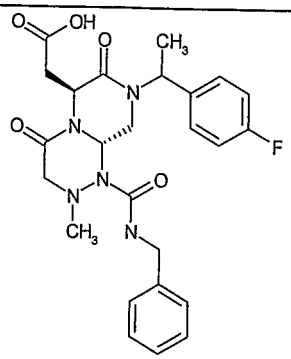
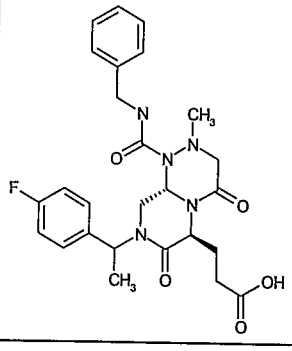
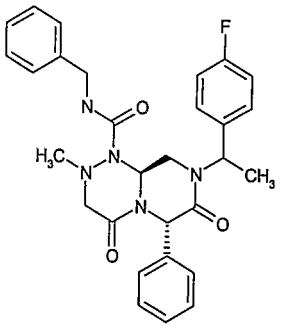
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1088		532	533
1089		500	501
1090		516	517

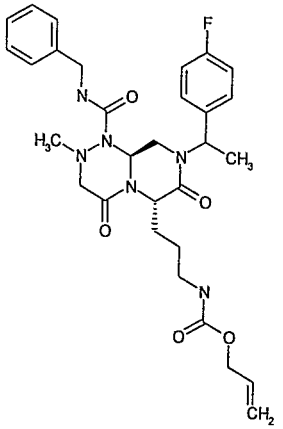
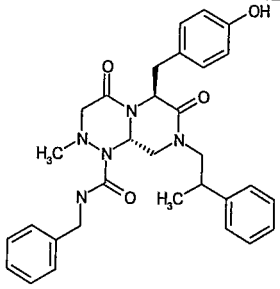
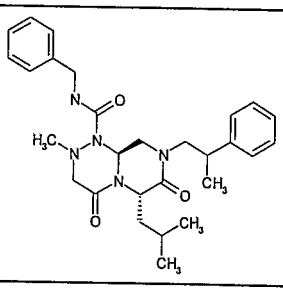
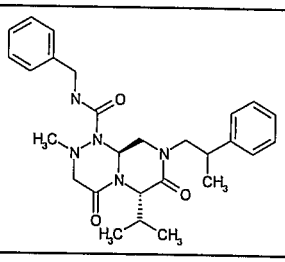
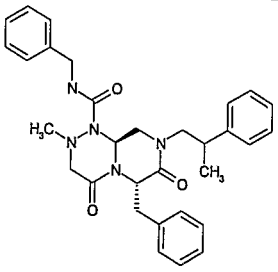
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1092		534	535
1093		599	600
1094		520	521

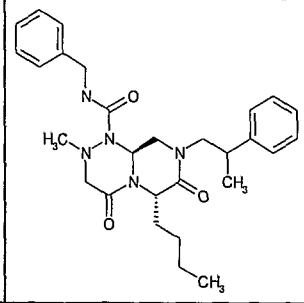
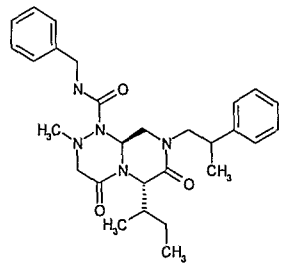
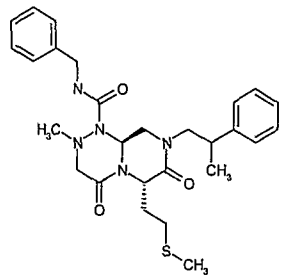
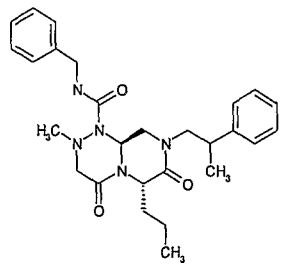
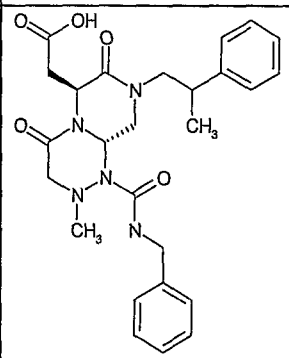
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1096		456	457
1097		504	505
1098		470	471

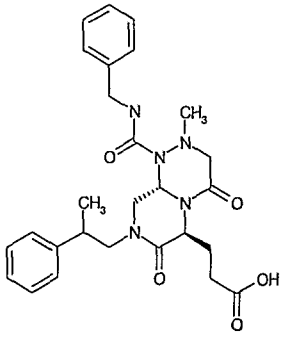
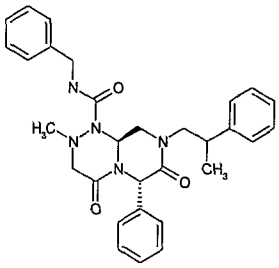
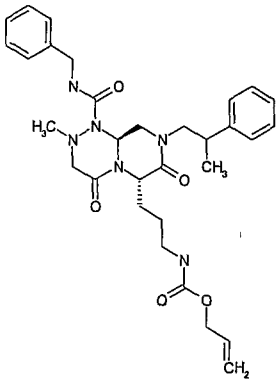
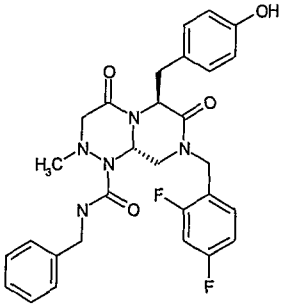
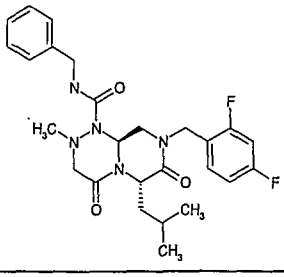
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1100		488	489
1101		456	457
1102		472	473

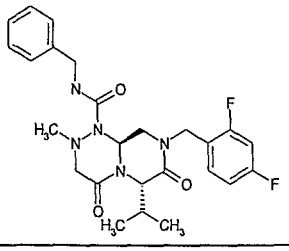
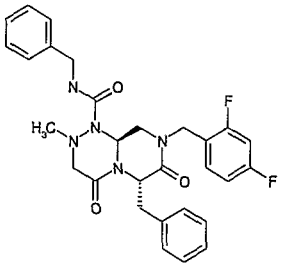
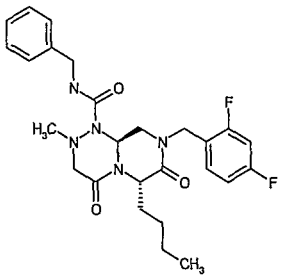
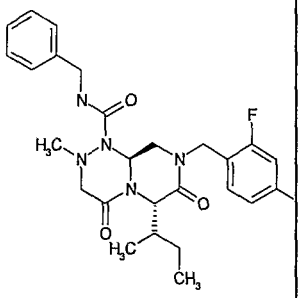
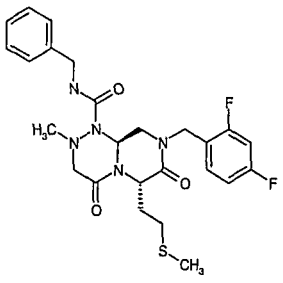
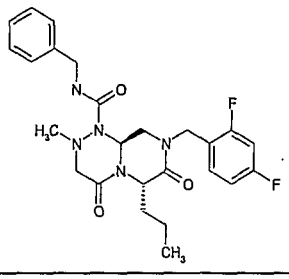
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1104		490	491
1105		555	556
1106		496	497
1107		482	483
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1109		496	497
1110		496	497
1111		514	515

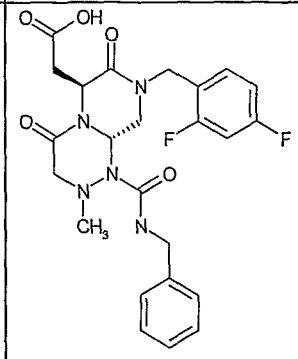
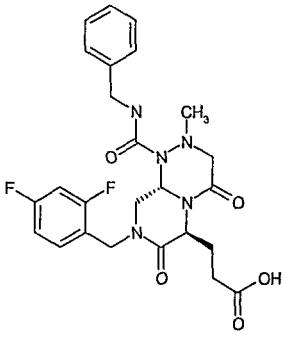
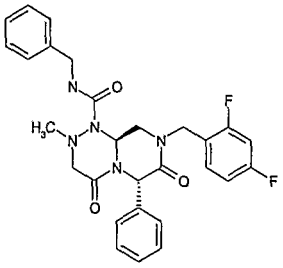
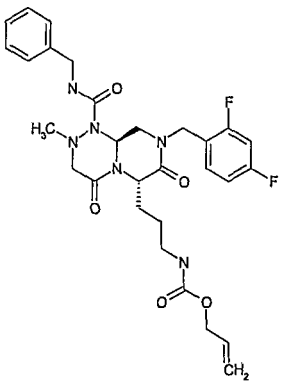
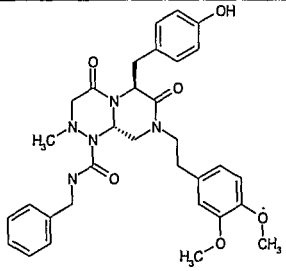
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1113		498	499
1114		512	513
1115		516	517

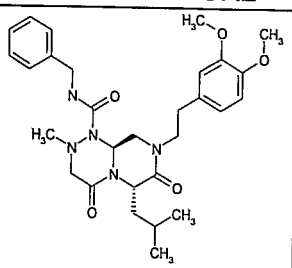
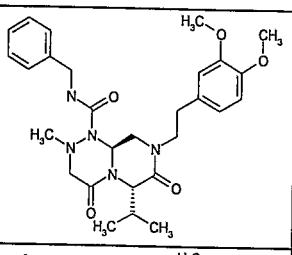
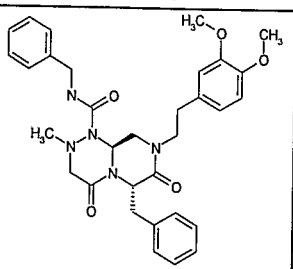
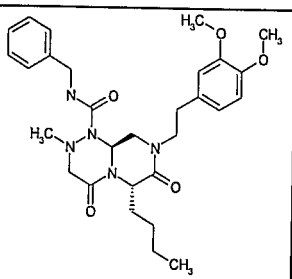
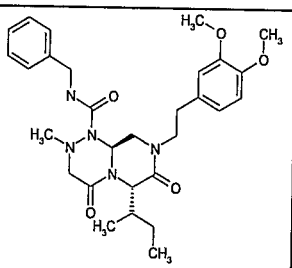
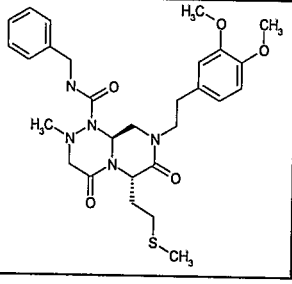
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1116		581	582
1117		542	543
1118		492	493
1119		478	479
1120		526	527

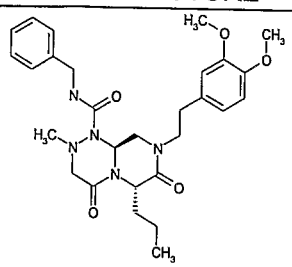
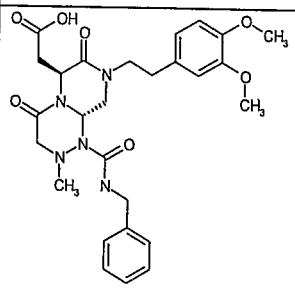
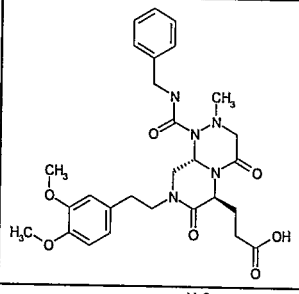
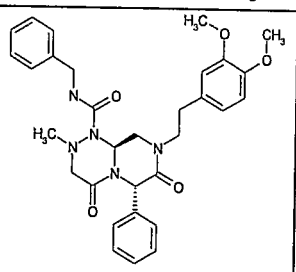
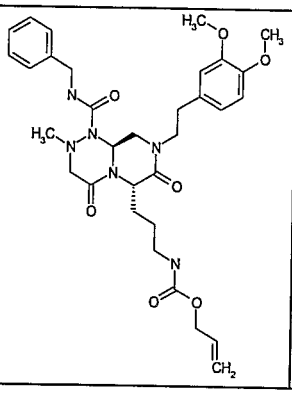
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1123		510	511
1124		478	479
1125		494	495

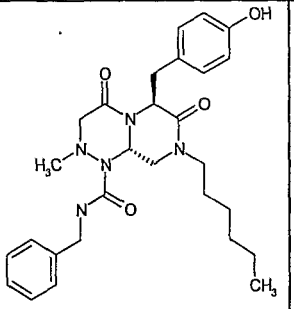
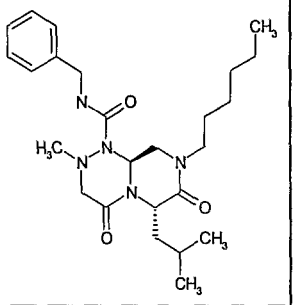
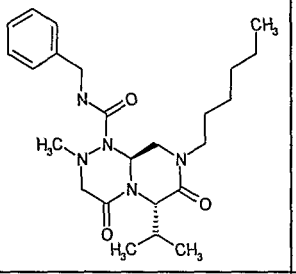
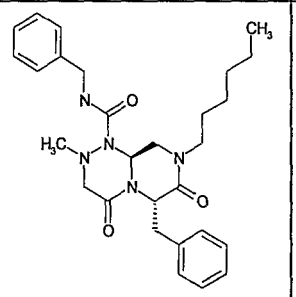
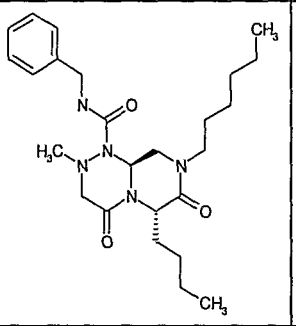
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1128		577	578
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1130		500	501

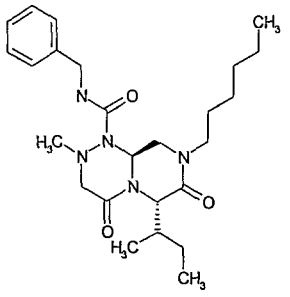
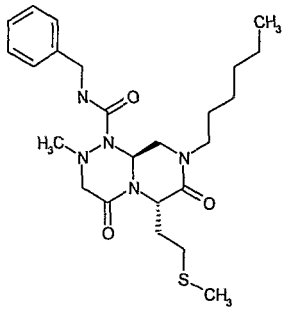
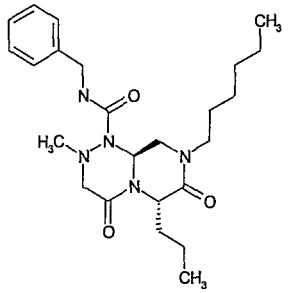
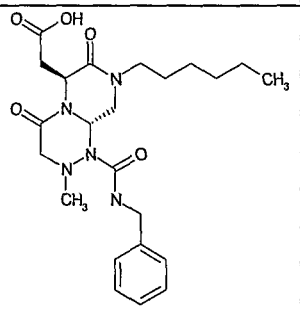
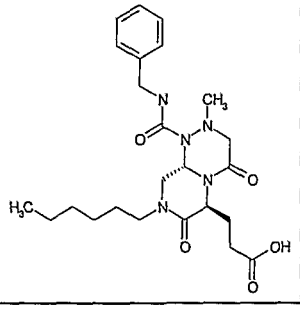
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1132		534	535
1133		500	501
1134		500	501
1135		518	519
1136		486	487

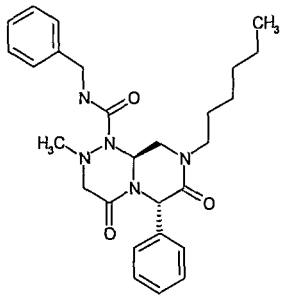
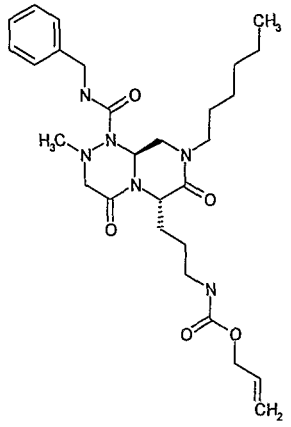
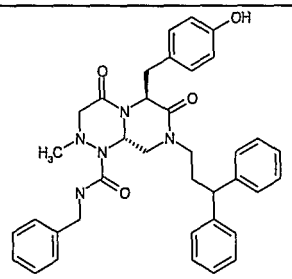
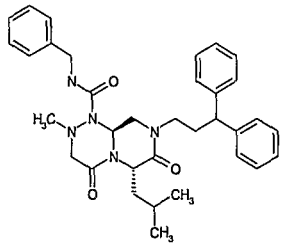
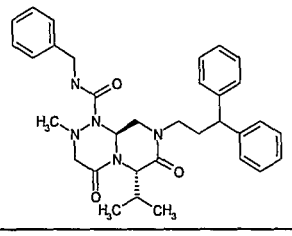
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1138		516	517
1139		520	521
1140		585	586
1141		588	589

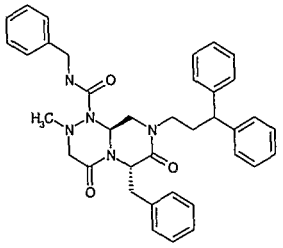
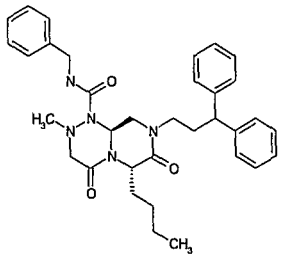
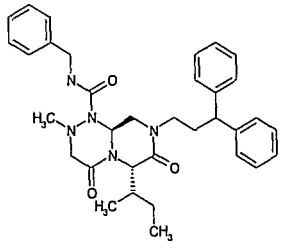
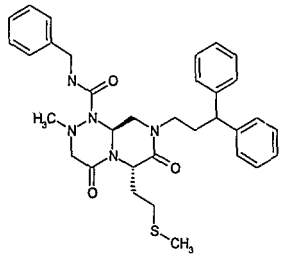
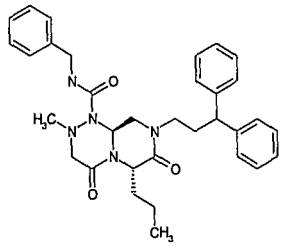
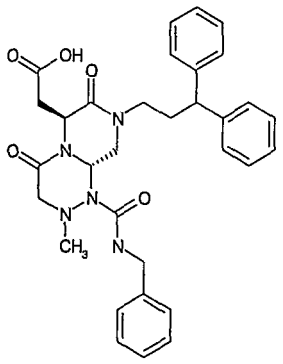
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1143		524	525
1144		572	573
1145		538	539
1146		538	539
1147		556	557

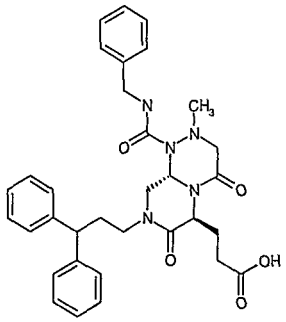
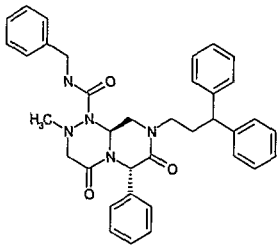
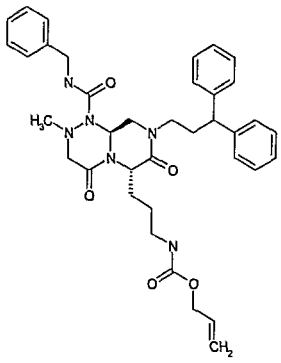
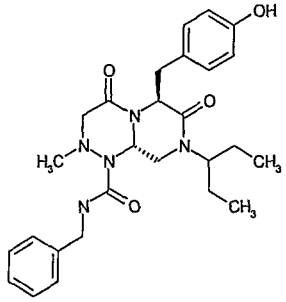
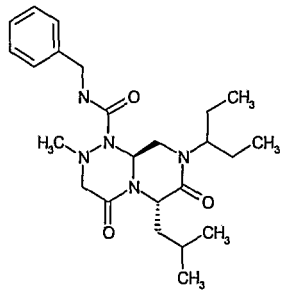
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1149		540	541
1150		554	555
1151		558	559
1152		623	624

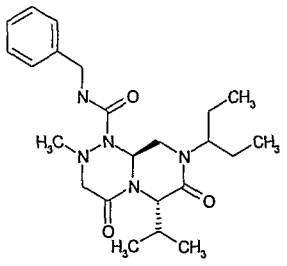
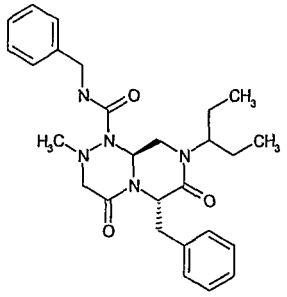
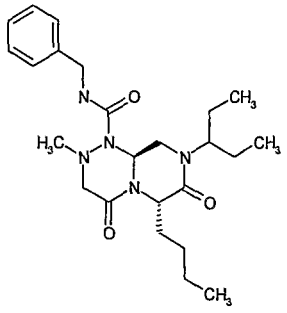
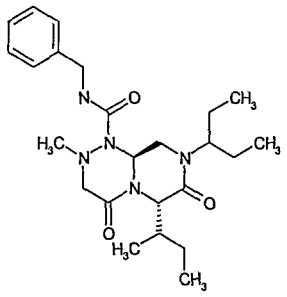
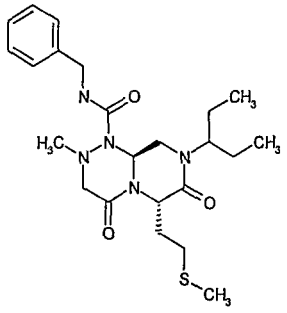
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1153		508	509
1154		458	459
1155		444	445
1156		492	493
1157		458	459

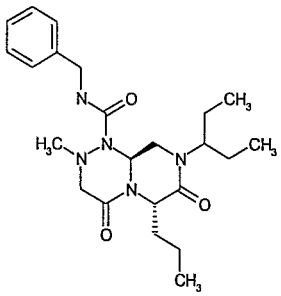
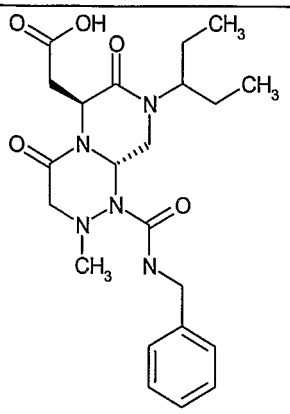
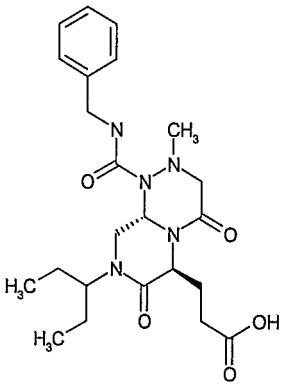
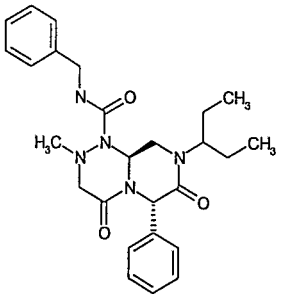
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1158		458	459
1159		476	477
1160		444	445
1161		460	461
1162		474	475

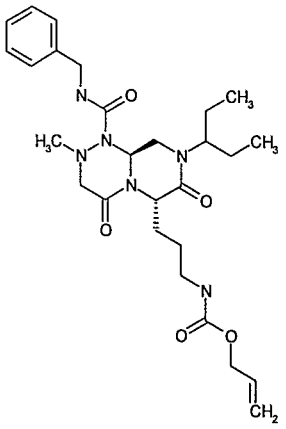
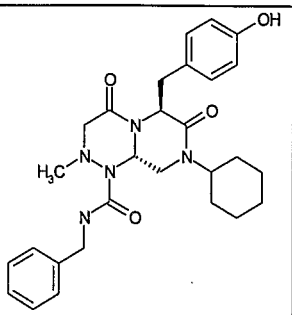
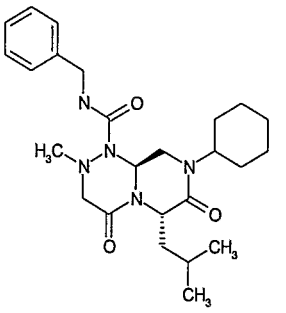
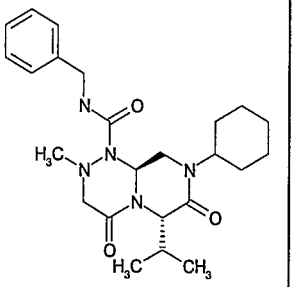
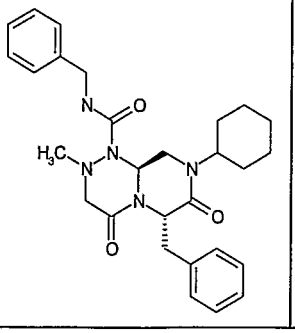
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1163		478	479
1164		543	544
1165		618	619
1166		568	569
1167		554	555

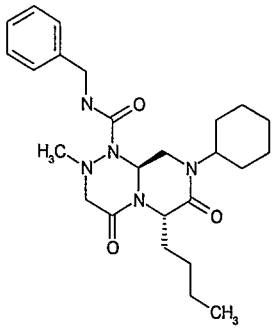
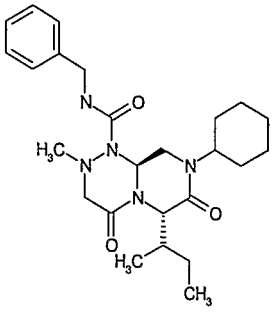
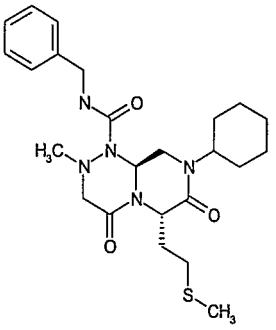
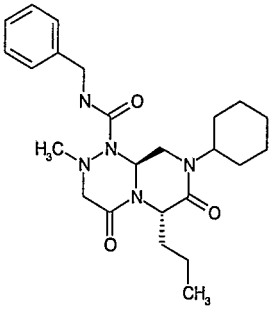
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1169		568	569
1170		568	569
1171		586	587
1172		554	555
1173		570	571

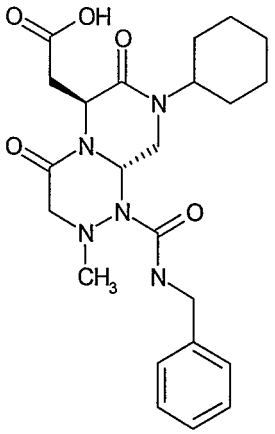
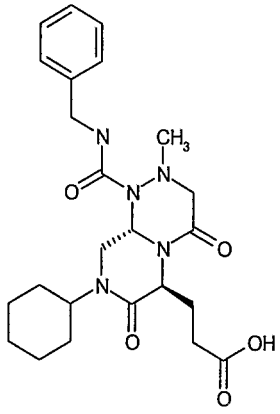
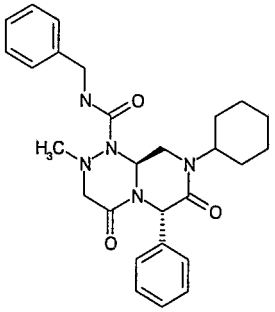
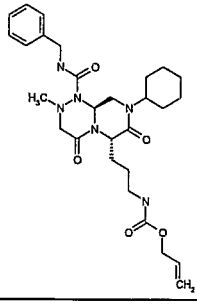
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1174		584	585
1175		588	589
1176		653	654
1177		494	495
1178		444	445

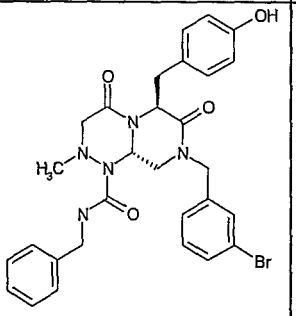
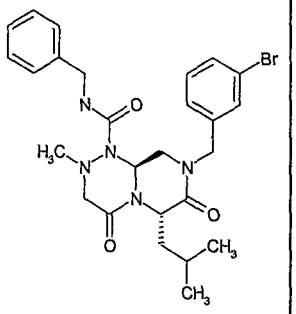
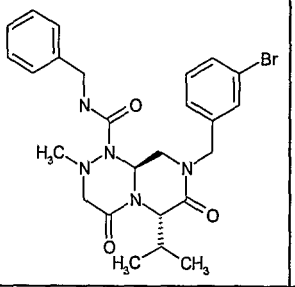
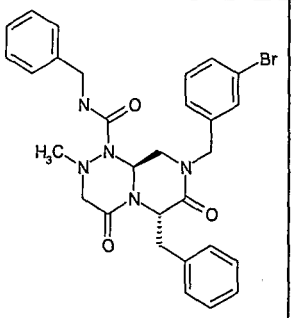
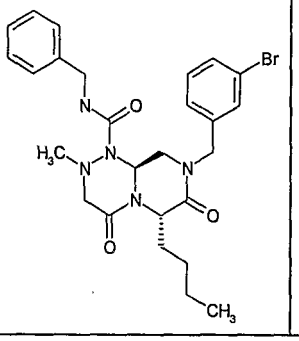
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1179		430	431
1180		478	479
1181		444	445
1182		444	445
1183		462	463

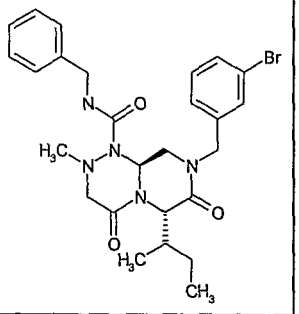
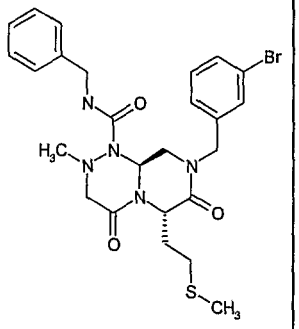
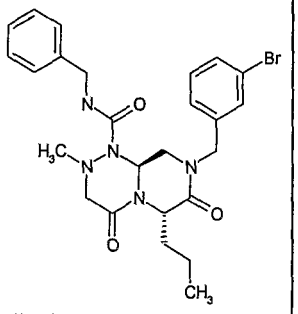
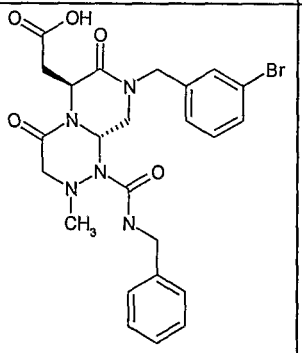
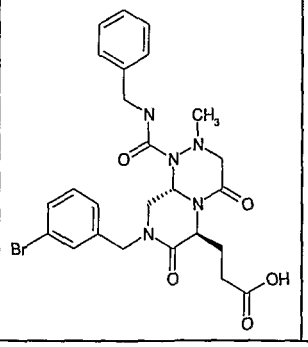
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1184		430	431
1185		446	447
1186		460	461
1187		464	465

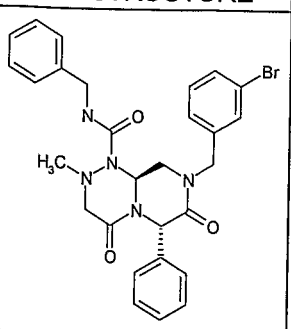
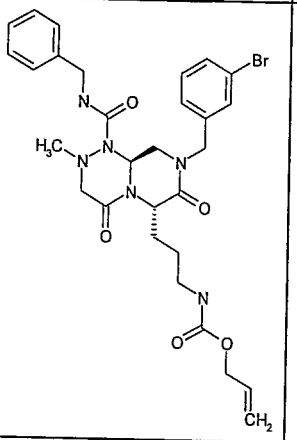
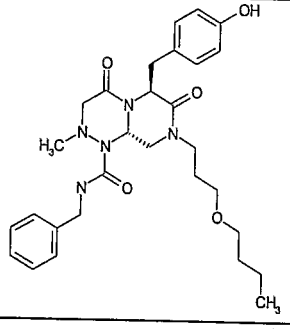
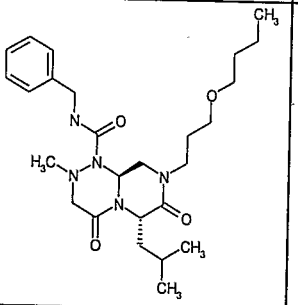
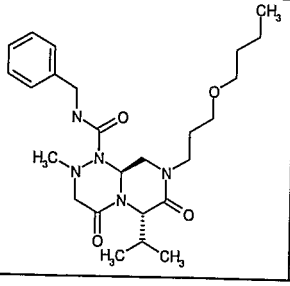
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1188		529	530
1189		506	507
1190		456	457
1191		442	443
1192		490	491

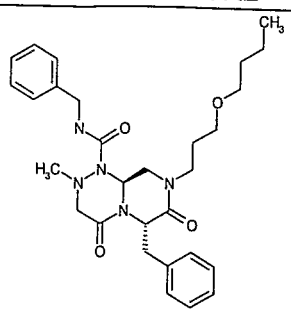
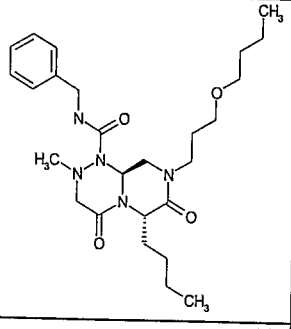
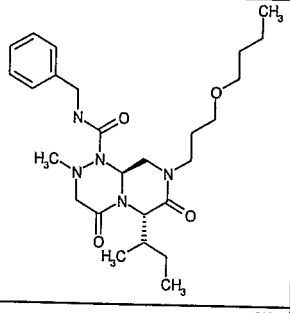
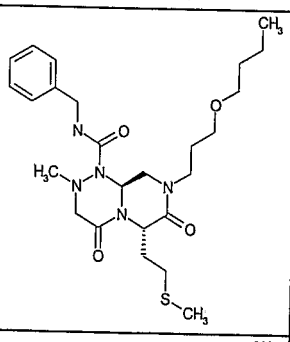
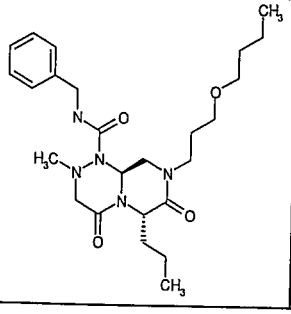
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1194		456	457
1195		474	475
1196		442	443

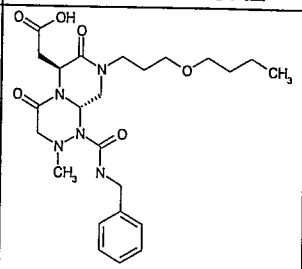
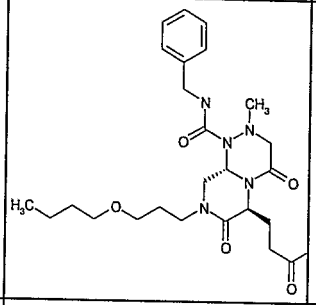
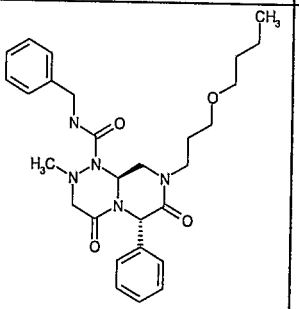
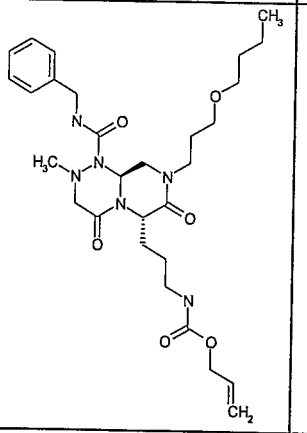
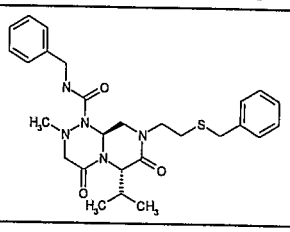
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1198		472	473
1199		476	477
1200		541	542

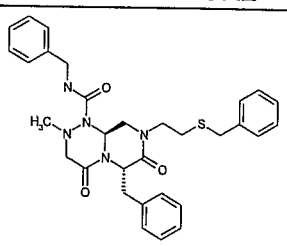
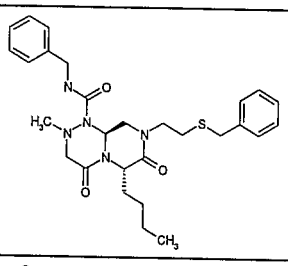
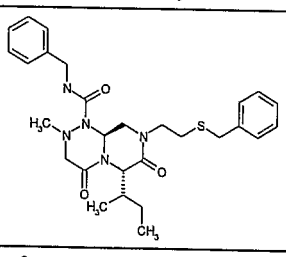
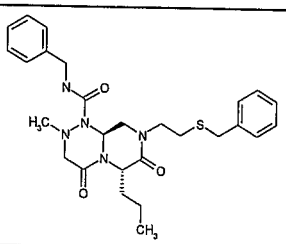
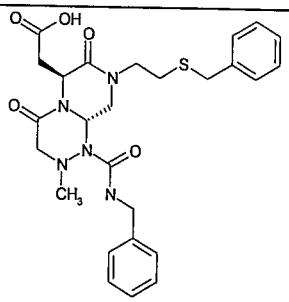
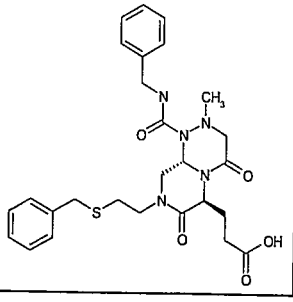
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1201		592	593
1202		542	543
1203		528	529
1204		576	577
1205		542	543

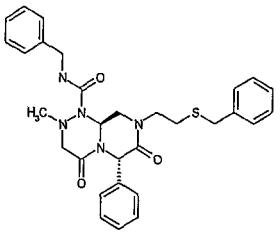
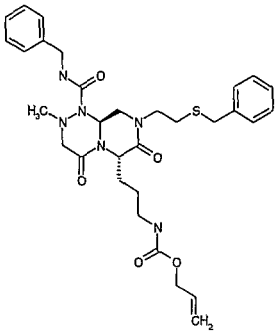
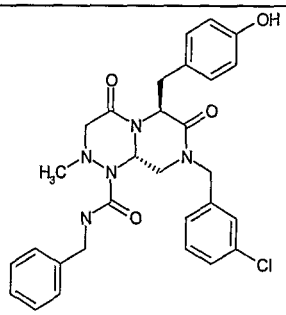
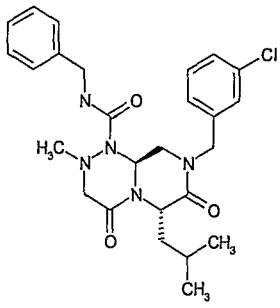
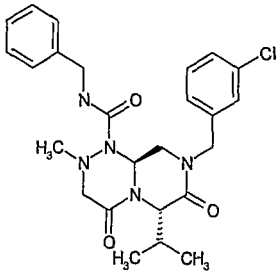
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1207		561	562
1208		528	529
1209		544	545
1210		558	559

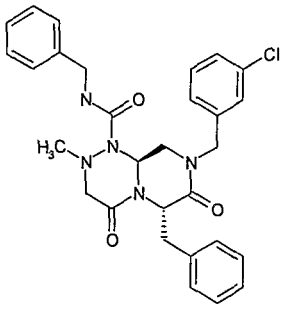
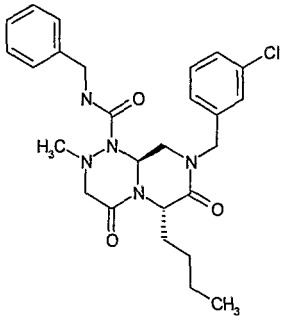
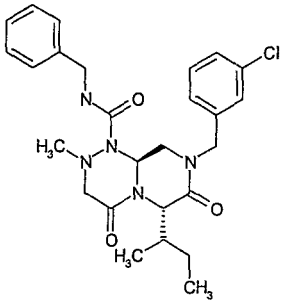
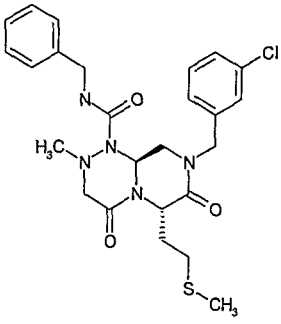
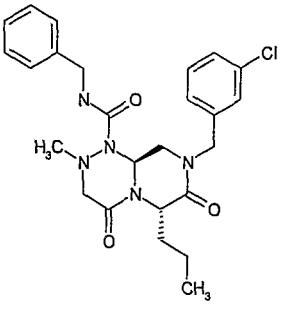
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1211		562	563
1212		628	629
1213		538	539
1214		488	489
1215		474	475

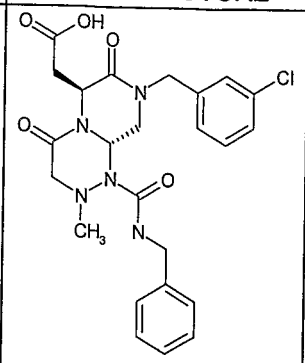
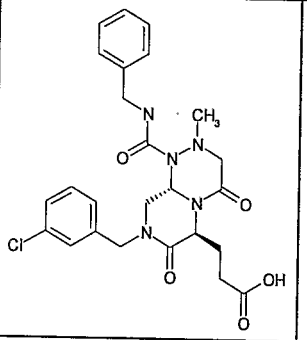
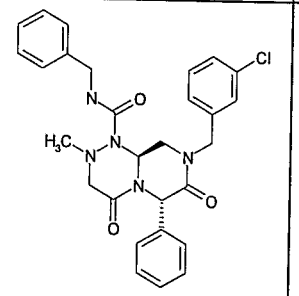
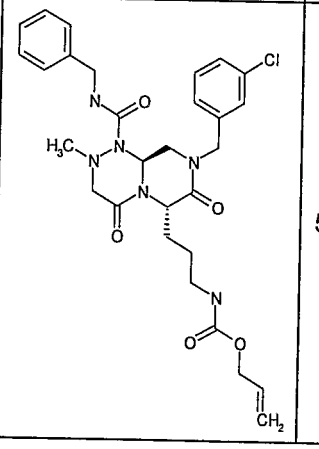
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1218		488	489
1219		506	507
1220		474	475

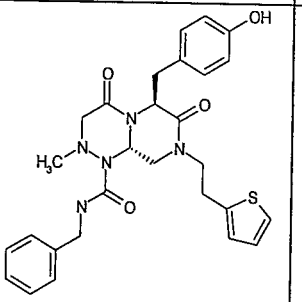
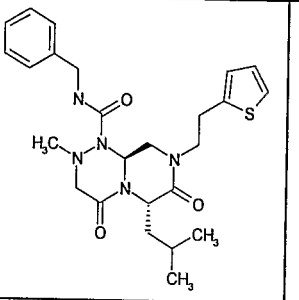
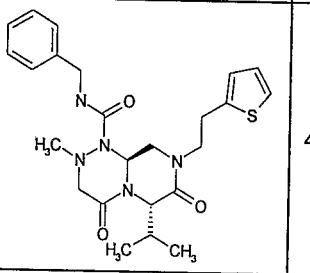
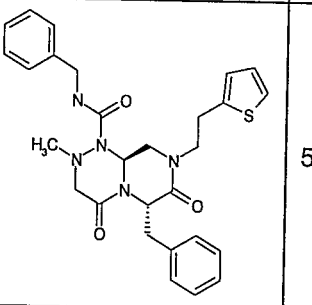
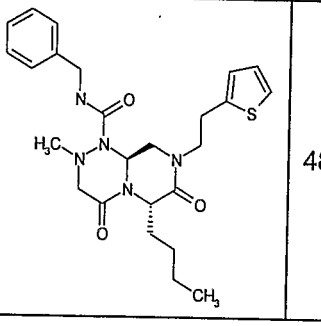
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1222		504	505
1223		508	509
1224		573	574
1225		510	511

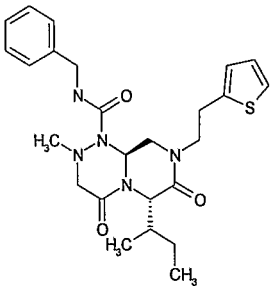
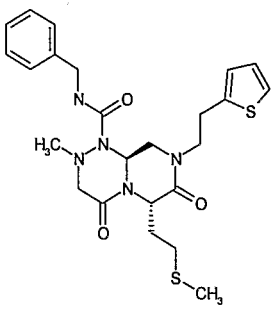
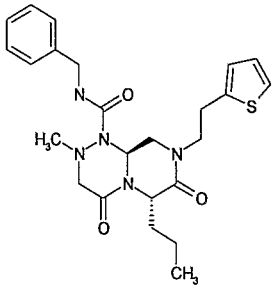
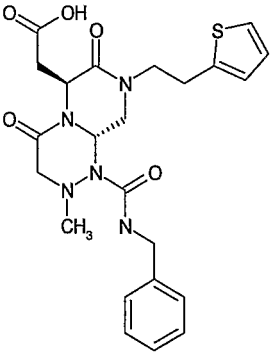
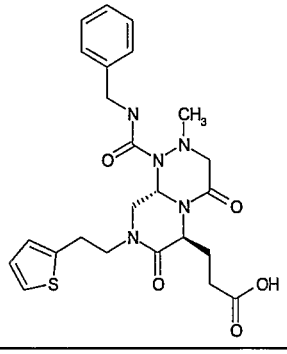
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1227		524	525
1228		524	525
1229		510	511
1230		526	527
1231		540	541

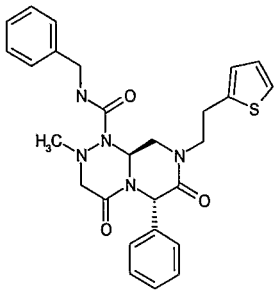
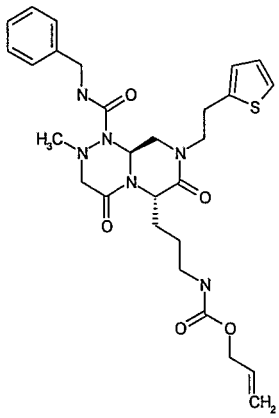
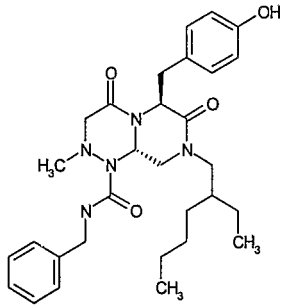
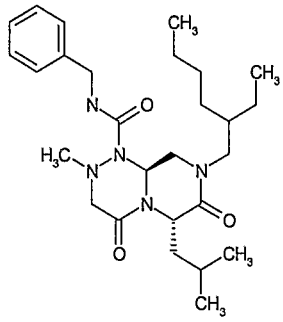
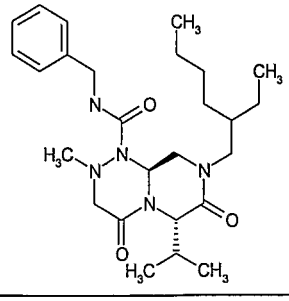
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1232		544	545
1233		609	610
1234		548	549
1235		498	499
1236		484	485

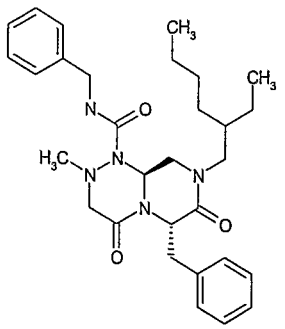
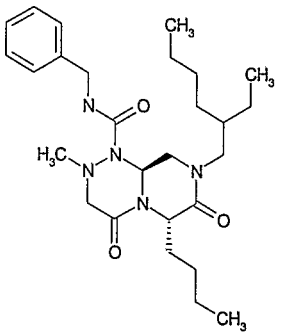
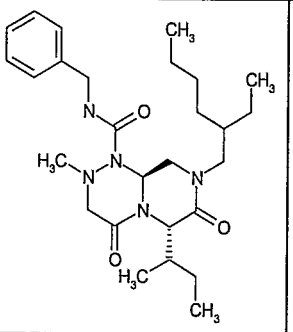
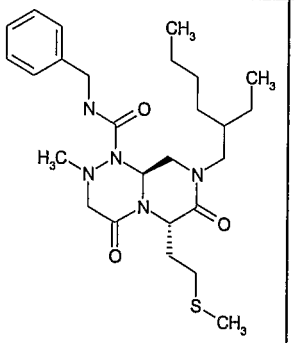
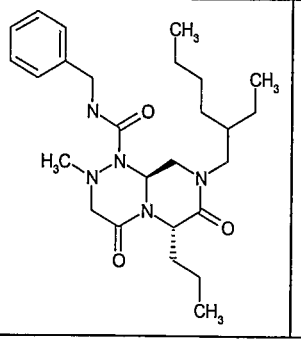
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1238		498	499
1239		498	499
1240		516	517
1241		484	485

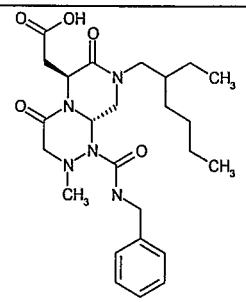
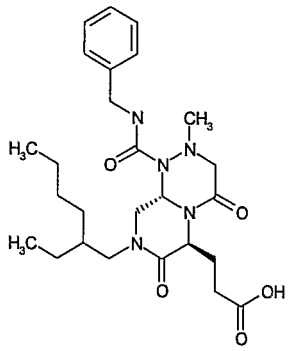
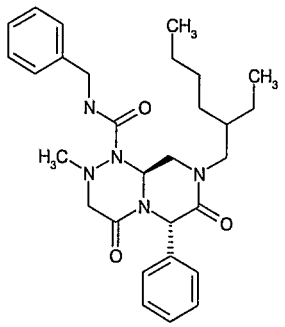
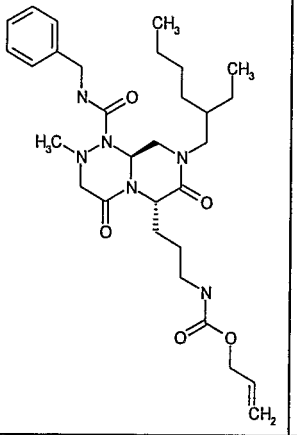
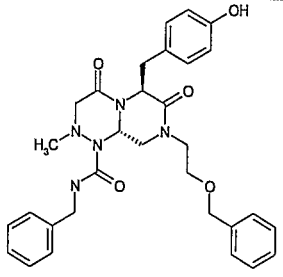
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1243		514	515
1244		518	519
1245		583	584

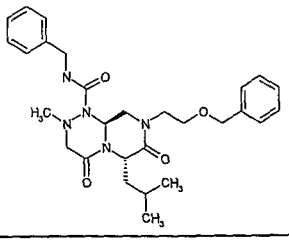
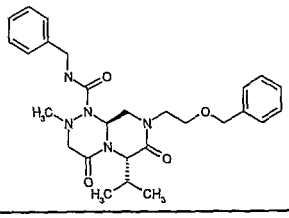
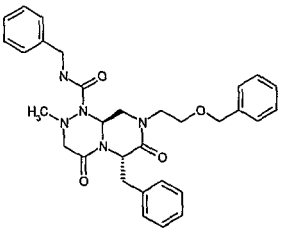
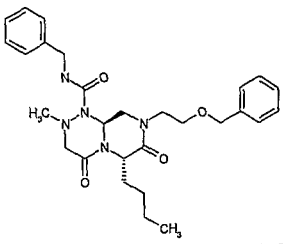
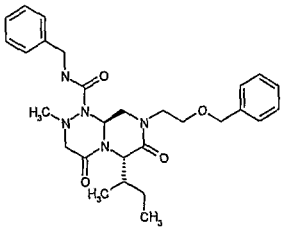
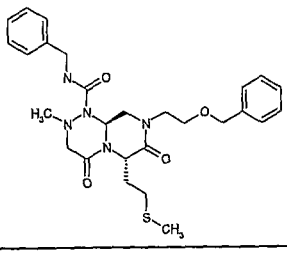
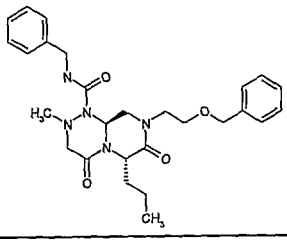
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1247		484	485
1248		470	471
1249		518	519
1250		484	485

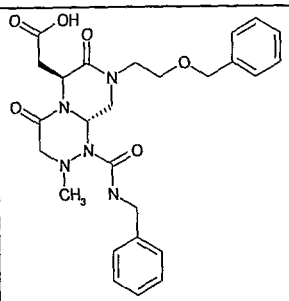
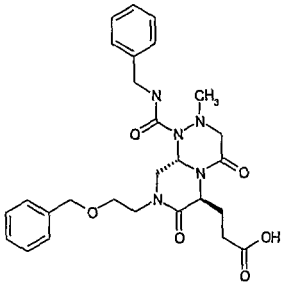
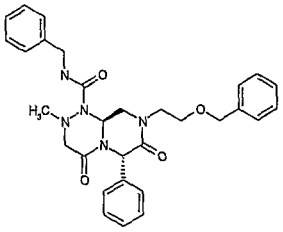
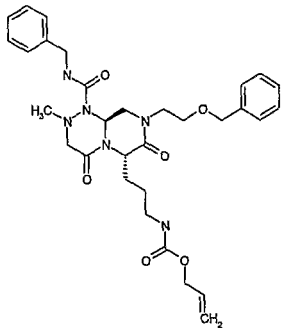
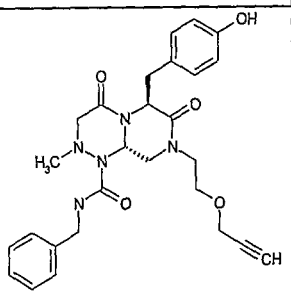
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1252		502	503
1253		470	471
1254		486	487
1255		500	501

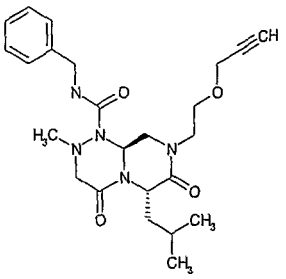
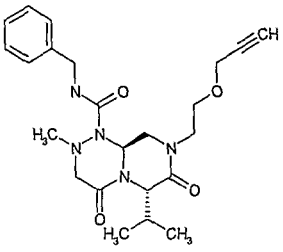
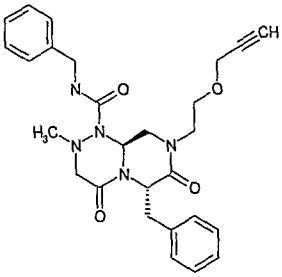
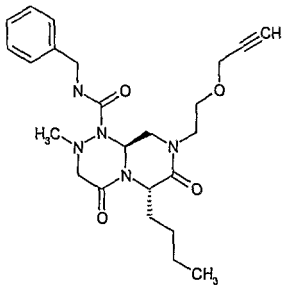
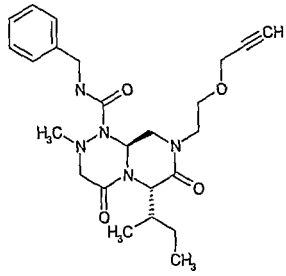
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1257		569	570
1258		536	537
1259		486	487
1260		472	473

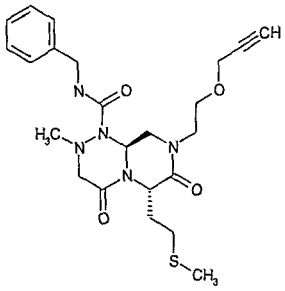
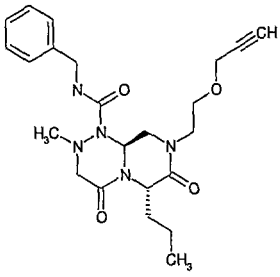
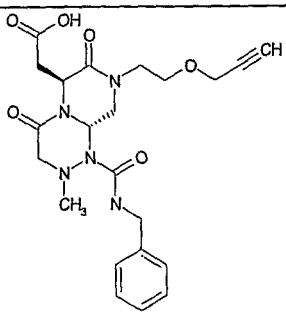
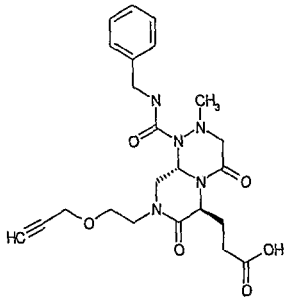
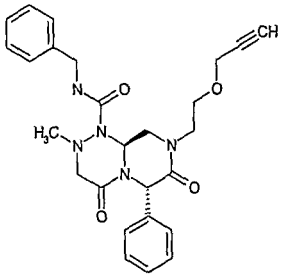
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1261		520	521
1262		486	487
1263		486	487
1264		504	505
1265		472	473

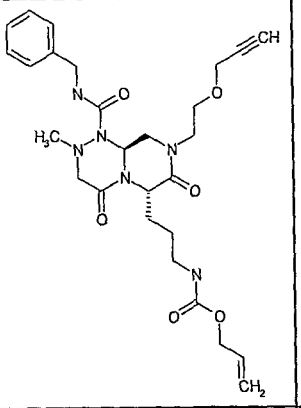
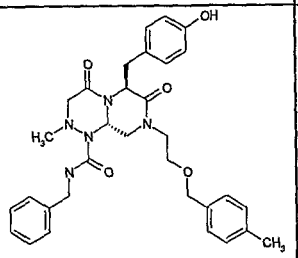
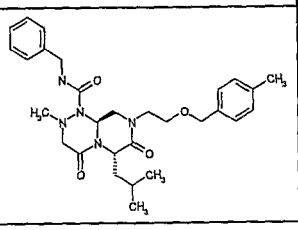
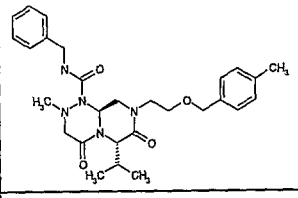
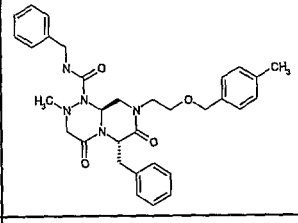
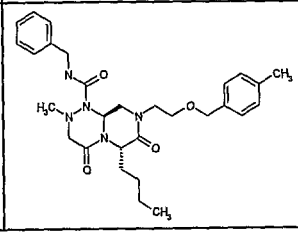
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1267		502	503
1268		506	507
1269		571	572
1270		558	559

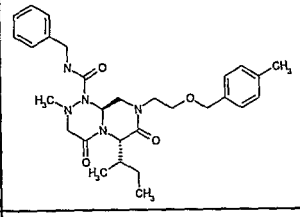
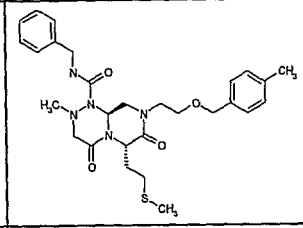
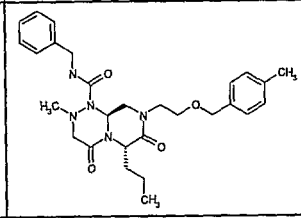
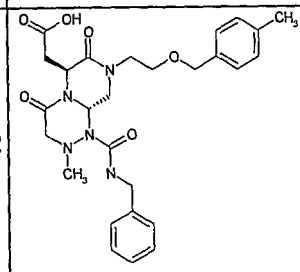
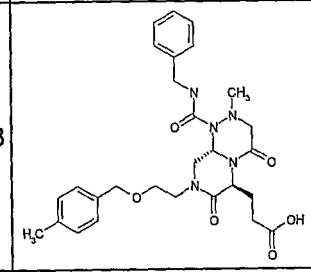
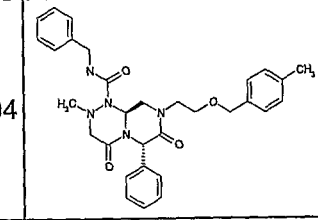
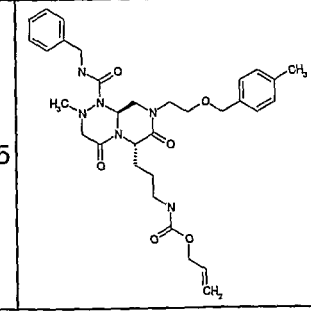
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1272		494	495
1273		542	543
1274		508	509
1275		508	509
1276		526	527
1277		494	495

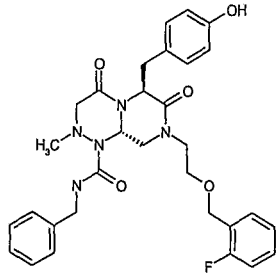
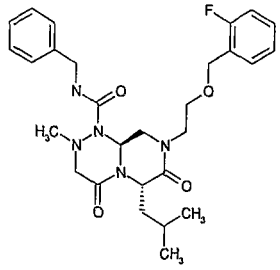
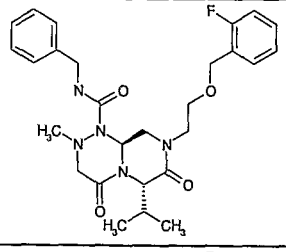
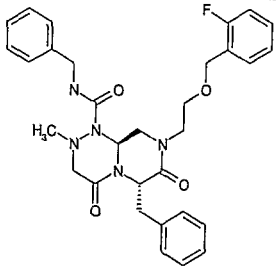
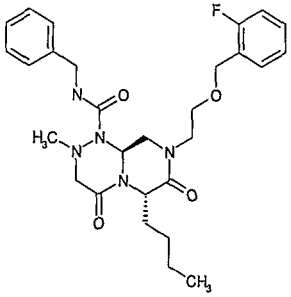
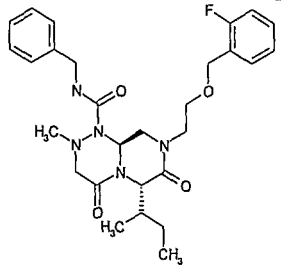
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1279		524	525
1280		528	529
1281		593	594
1282		506	507

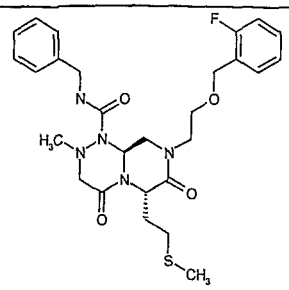
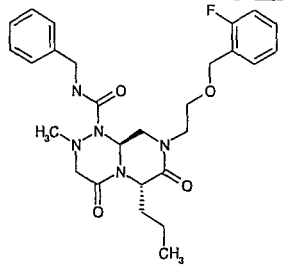
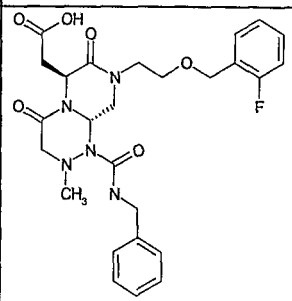
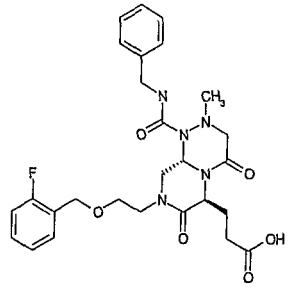
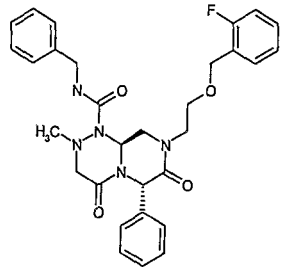
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1284		442	443
1285		490	491
1286		456	457
1287		456	457

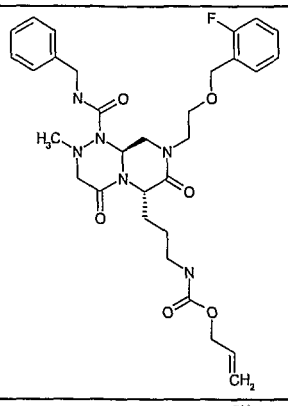
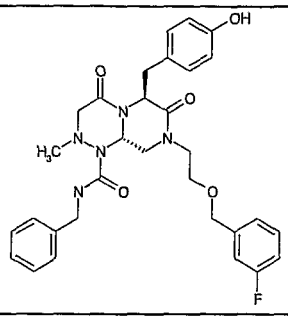
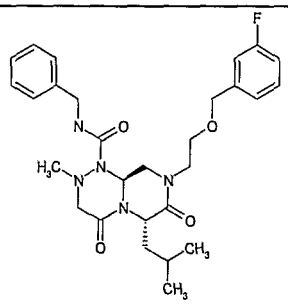
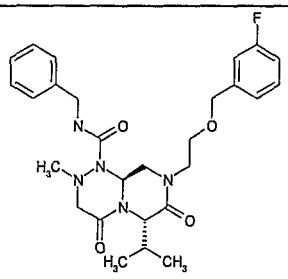
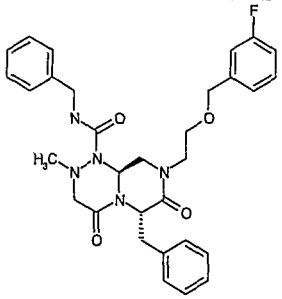
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1289		442	443
1290		457	458
1291		472	473
1292		476	477

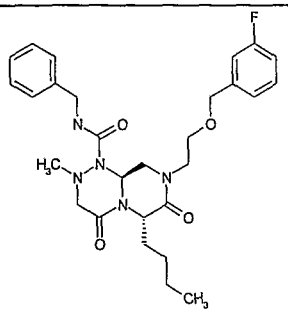
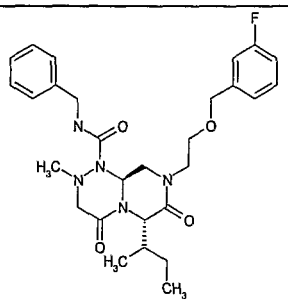
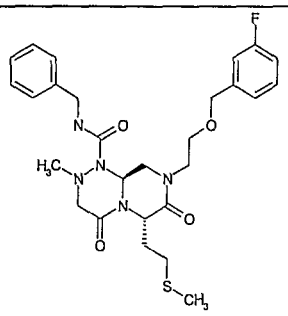
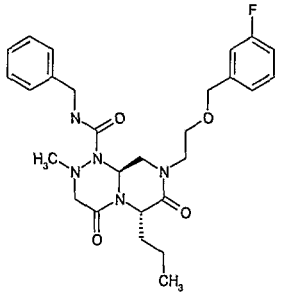
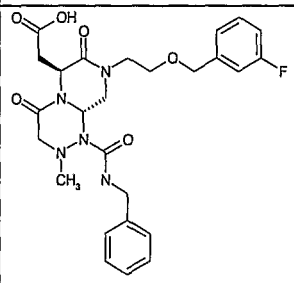
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1294		572	573
1295		522	523
1296		508	509
1297		556	557
1298		522	523

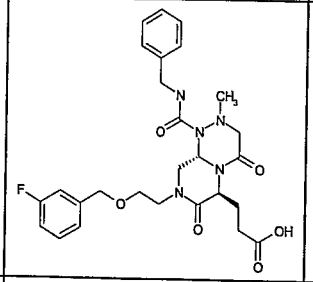
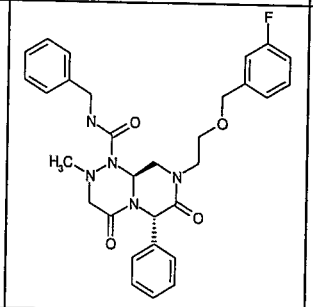
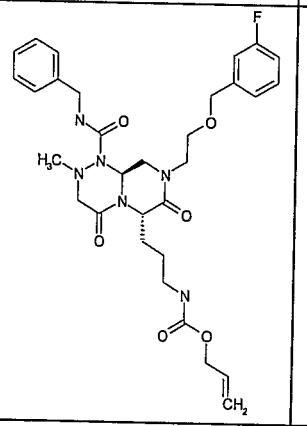
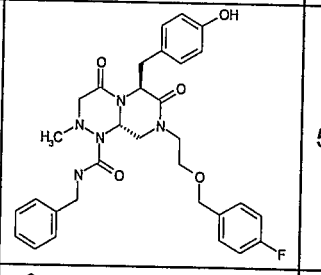
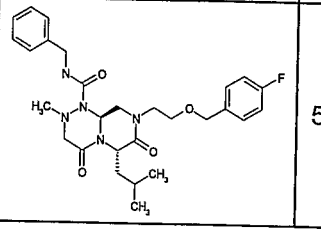
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1299		522	523
1300		540	541
1301		508	509
1302		524	525
1303		538	539
1304		542	543
1305		607	608

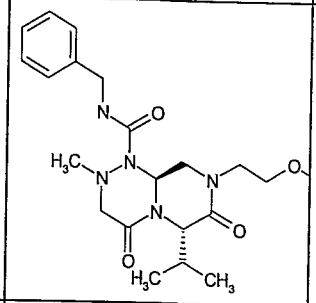
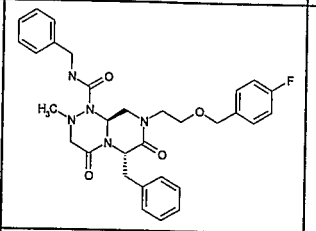
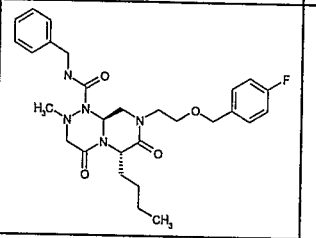
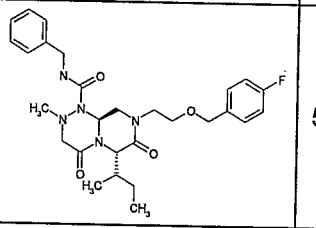
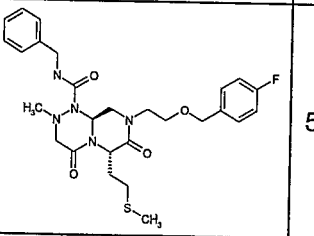
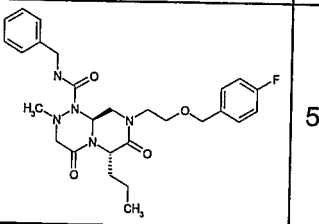
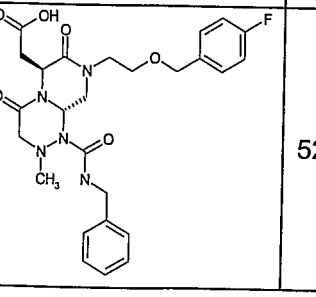
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1307		526	527
1308		512	513
1309		560	561
1310		526	527
1311		526	527

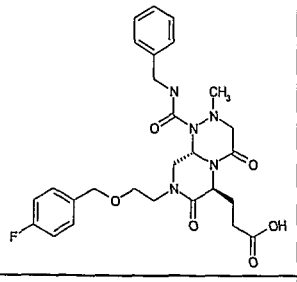
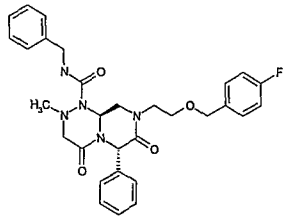
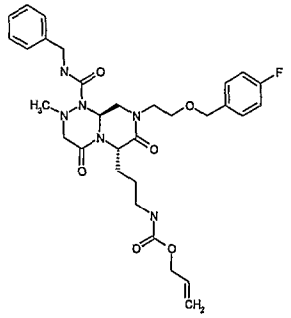
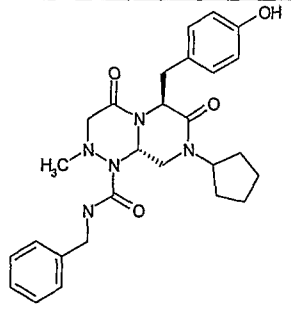
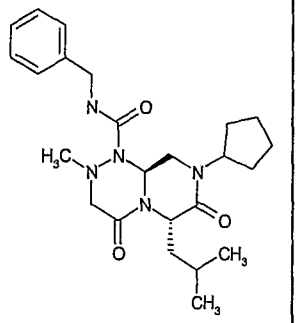
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1314		528	529
1315		542	543
1316		546	547

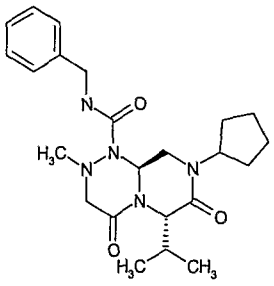
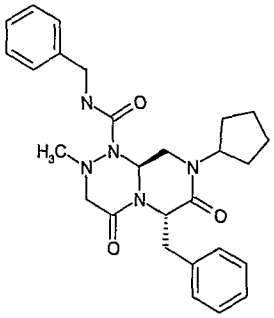
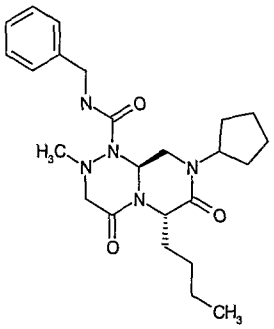
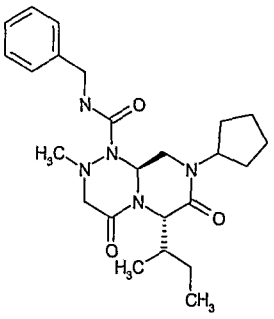
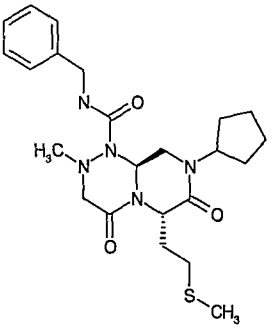
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1317		611	612
1318		576	577
1319		526	527
1320		512	513
1321		560	561

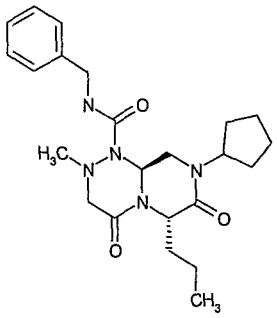
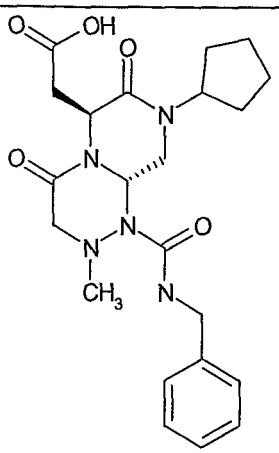
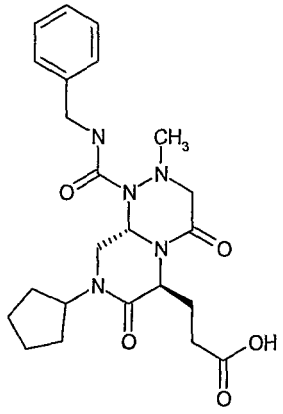
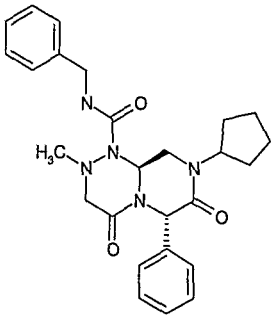
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1322		526	527
1323		526	527
1324		544	545
1325		512	513
1326		528	529

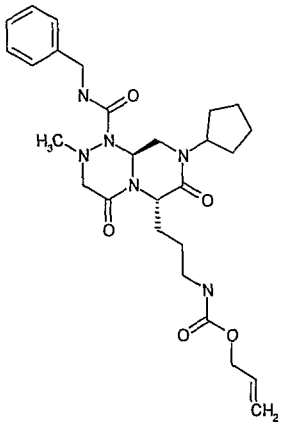
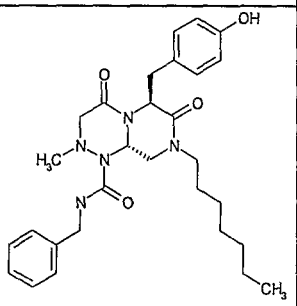
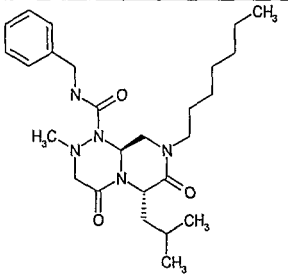
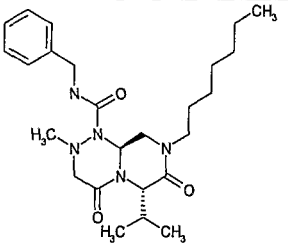
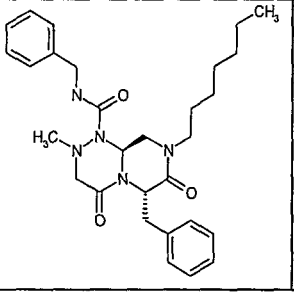
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1327		542	543
1328		546	547
1329		611	612
1330		576	577
1331		526	527

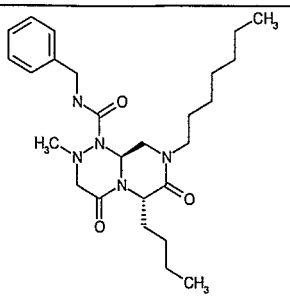
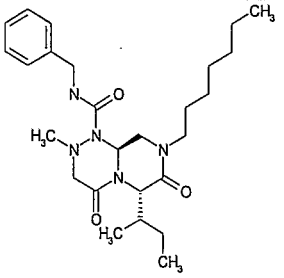
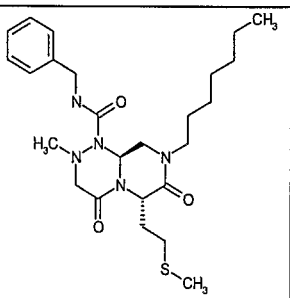
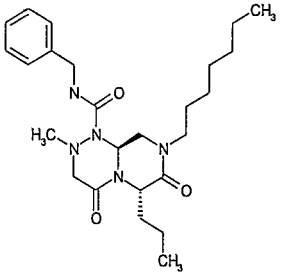
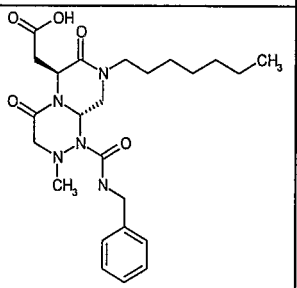
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1333		560	561
1334		526	527
1335		526	527
1336		544	545
1337		512	513
1338		528	529

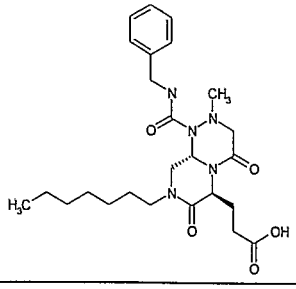
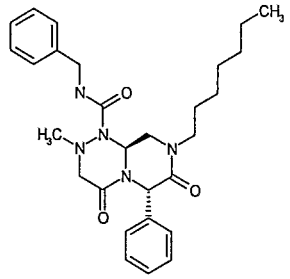
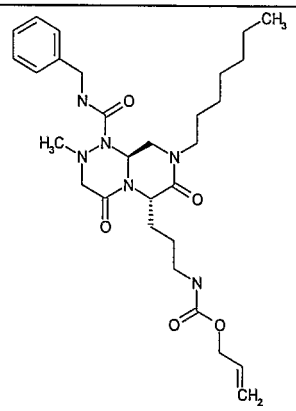
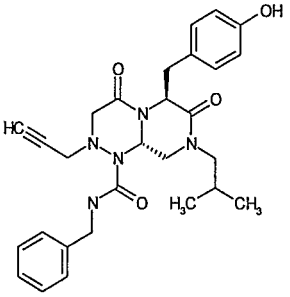
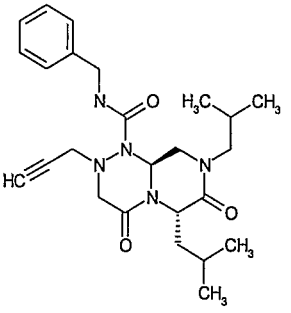
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1340		546	547
1341		611	612
1342		492	493
1343		442	443

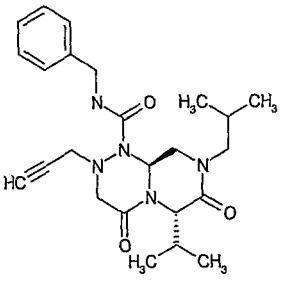
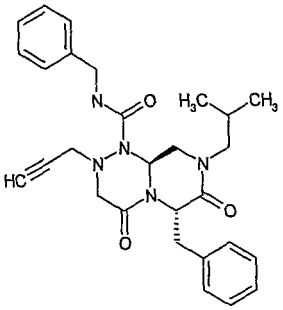
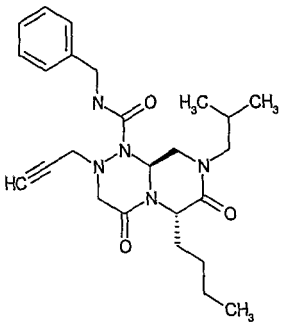
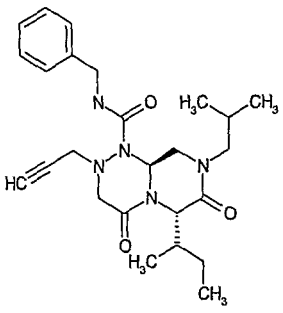
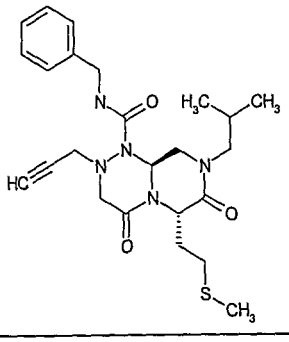
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1344		428	429
1345		476	477
1346		442	443
1347		442	443
1348		460	461

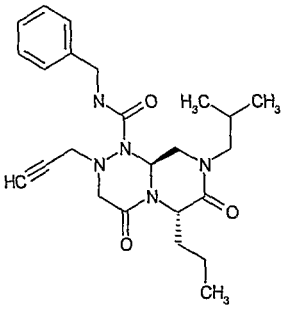
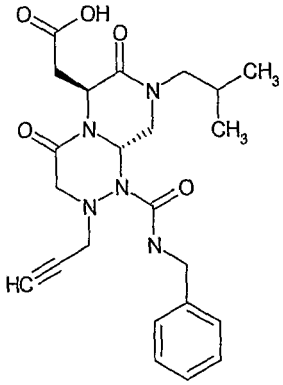
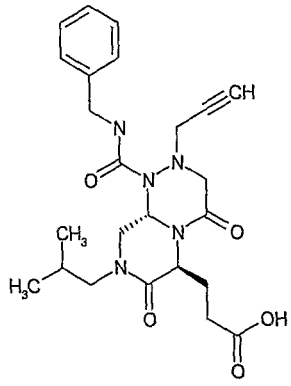
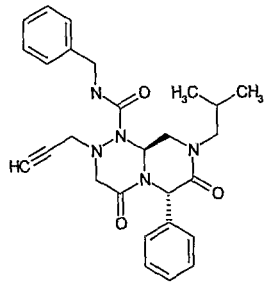
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1349		428	429
1350		444	445
1351		458	459
1352		462	463

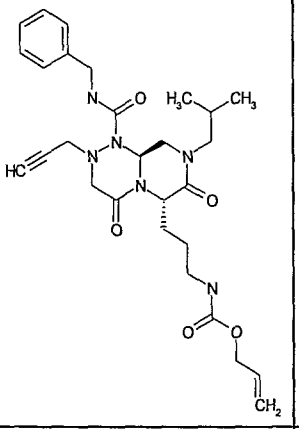
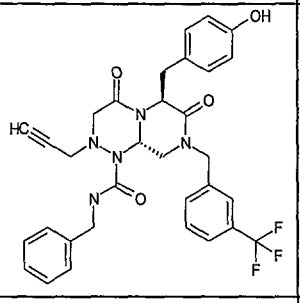
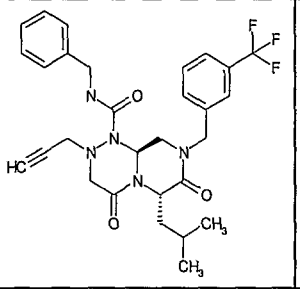
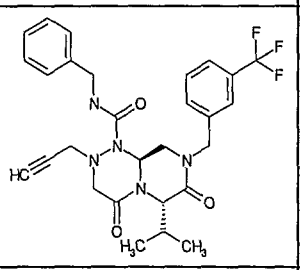
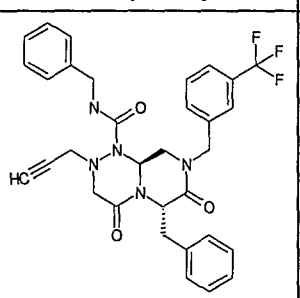
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1353		527	528
1354		522	523
1355		472	473
1356		458	459
1357		506	507

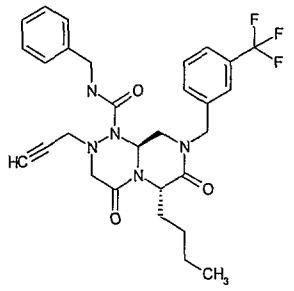
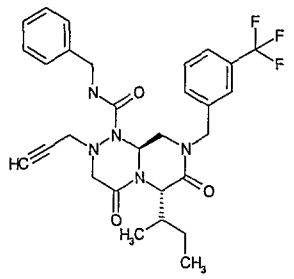
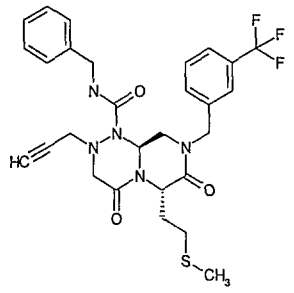
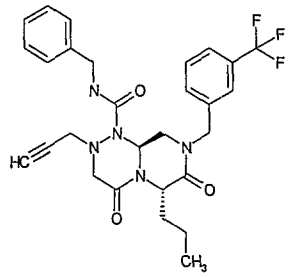
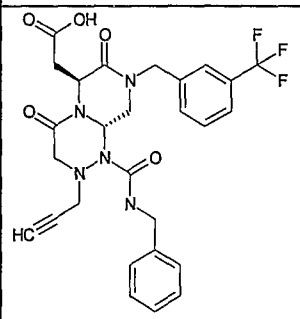
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1359		472	473
1360		490	491
1361		458	459
1362		474	475

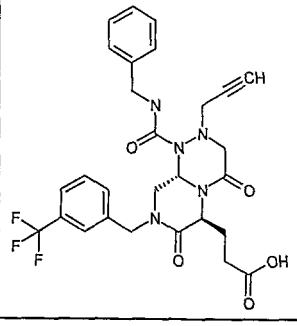
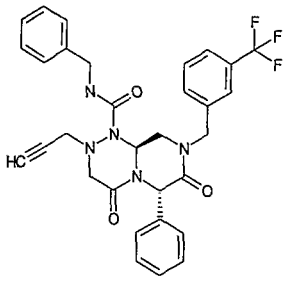
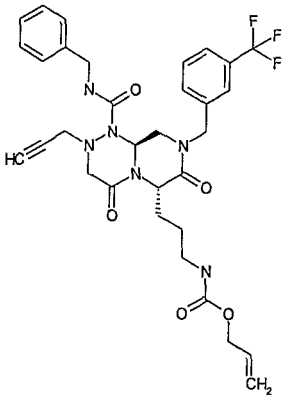
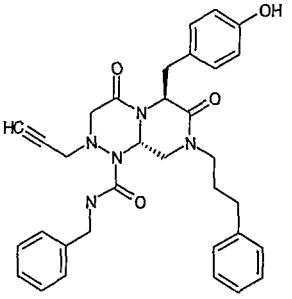
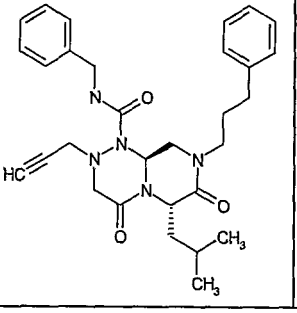
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1363		488	489
1364		492	493
1365		557	558
1366		504	505
1367		454	455

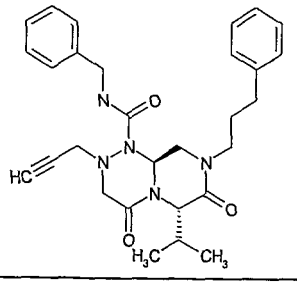
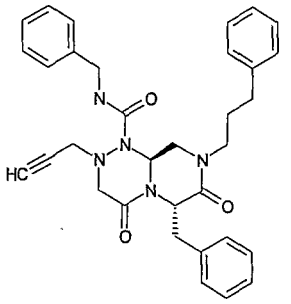
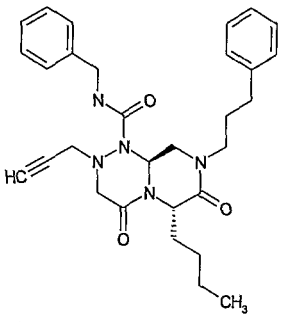
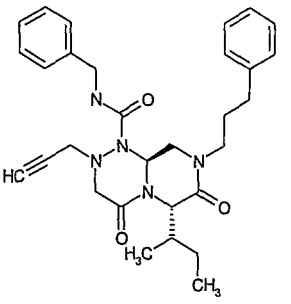
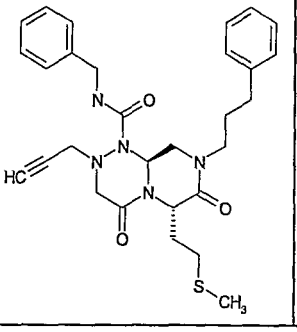
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1369		488	489
1370		454	455
1371		454	455
1372		472	473

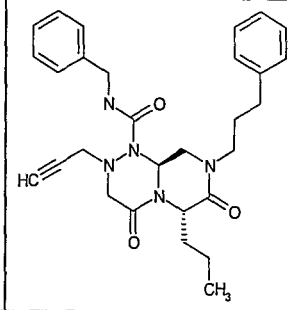
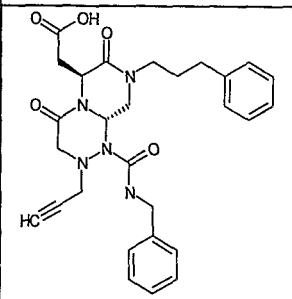
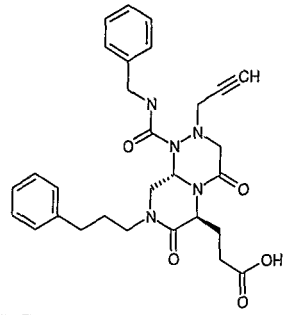
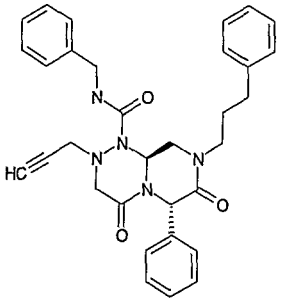
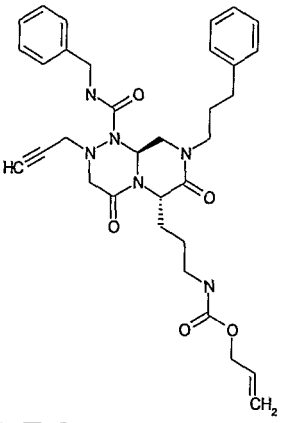
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1374		456	457
1375		470	471
1376		474	475

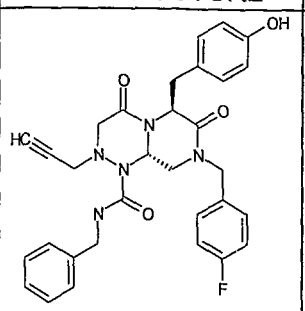
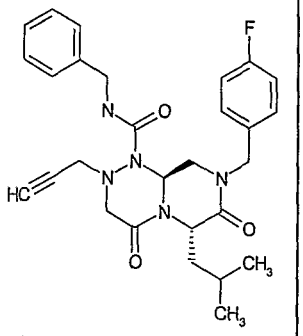
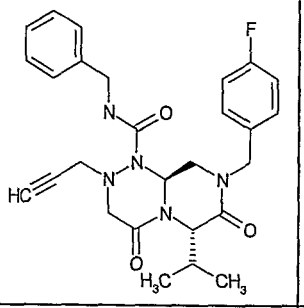
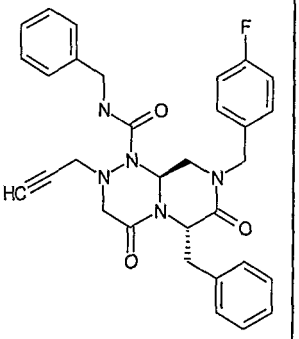
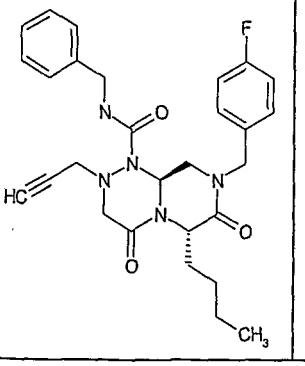
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1377		539	540
1378		606	607
1379		556	557
1380		542	543
1381		590	591

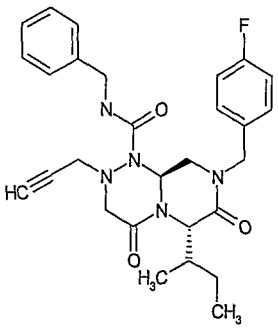
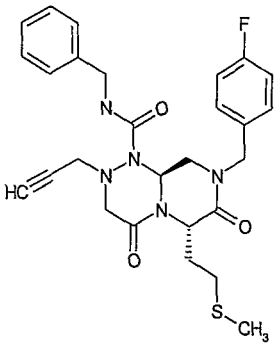
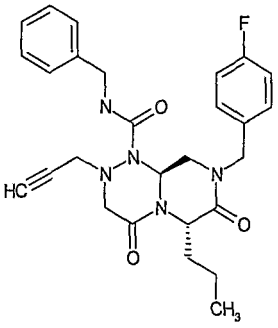
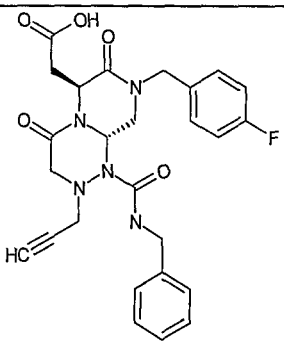
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1383		556	557
1384		574	575
1385		542	543
1386		558	559

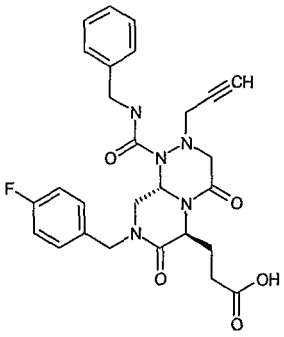
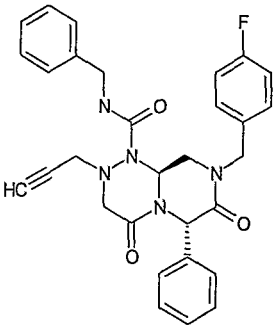
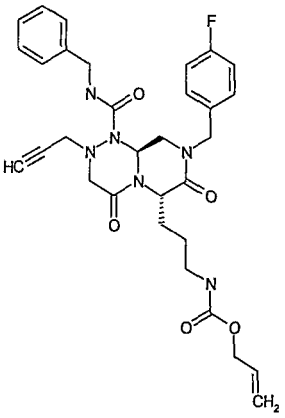
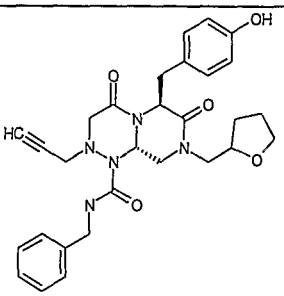
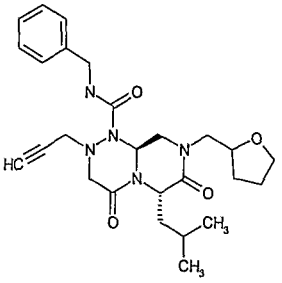
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1388		576	577
1389		641	642
1390		566	567
1391		516	517

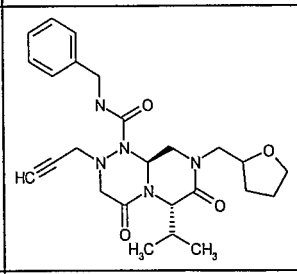
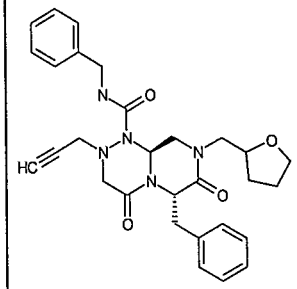
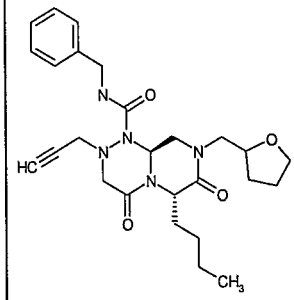
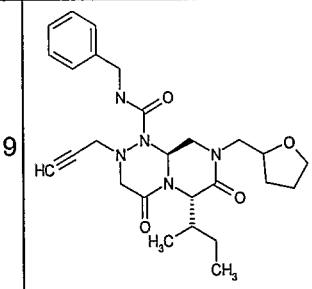
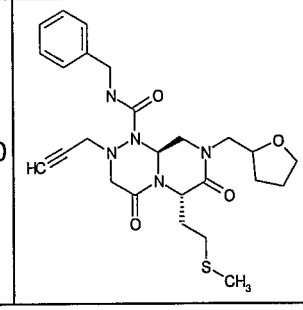
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1392		502	503
1393		550	551
1394		516	517
1395		516	517
1396		534	535

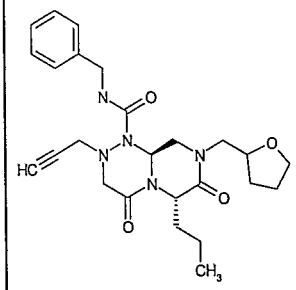
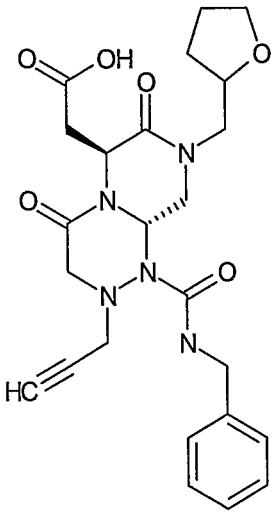
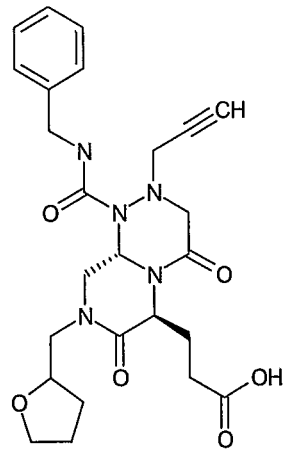
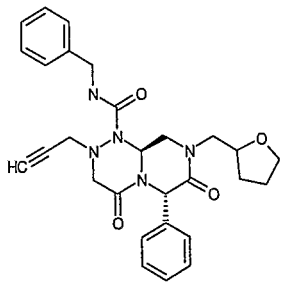
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1397		502	503
1398		518	519
1399		532	533
1400		536	537
1401		601	602

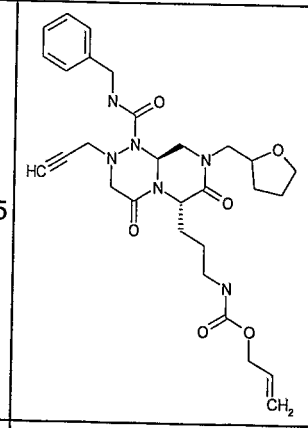
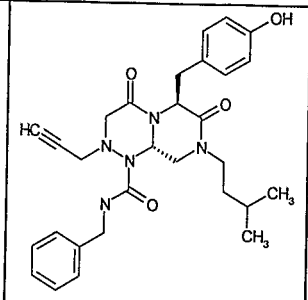
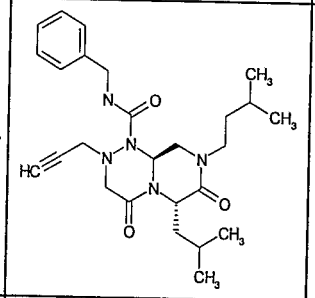
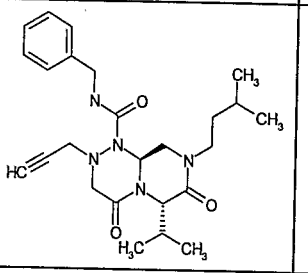
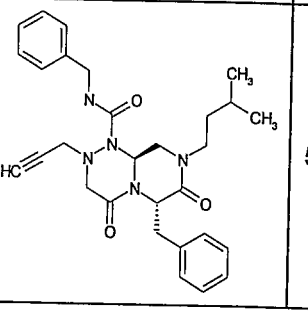
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1402		556	557
1403		506	507
1404		492	493
1405		540	541
1406		506	507

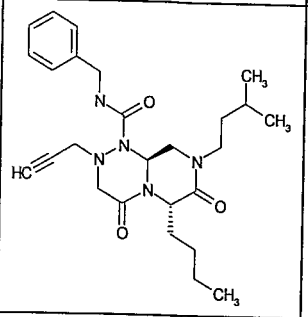
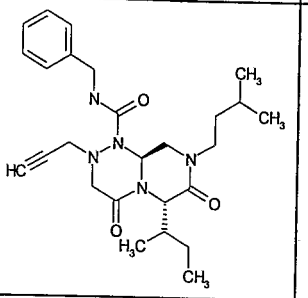
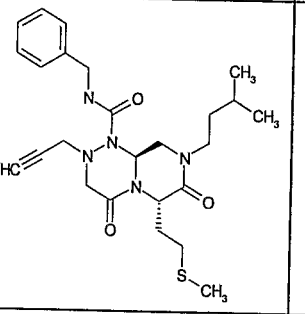
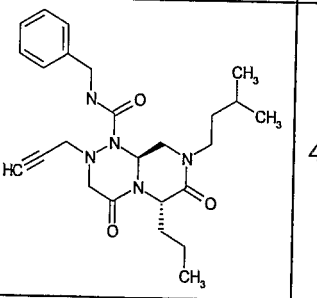
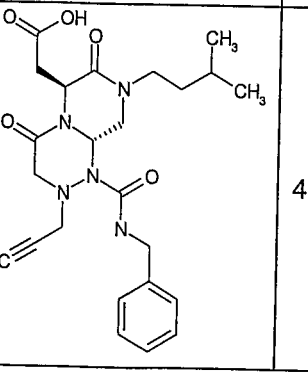
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1408		524	525
1409		492	493
1410		508	509

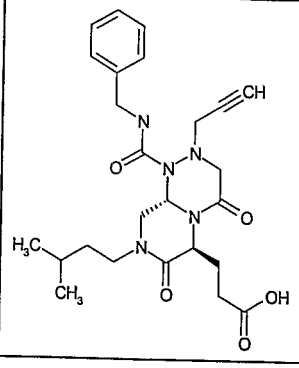
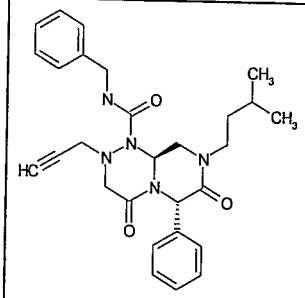
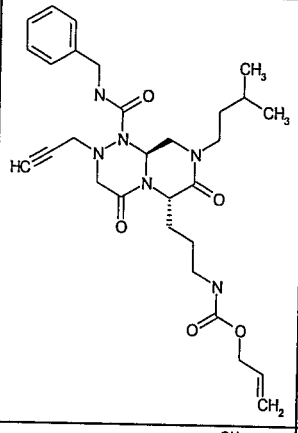
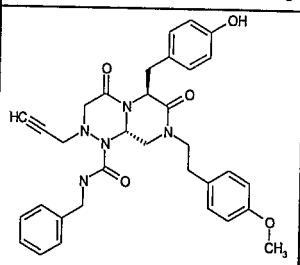
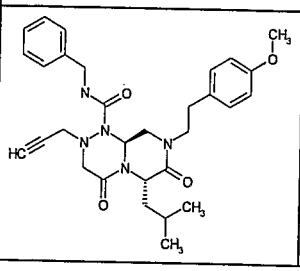
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1411		522	523
1412		526	527
1413		591	592
1414		532	533
1415		482	483

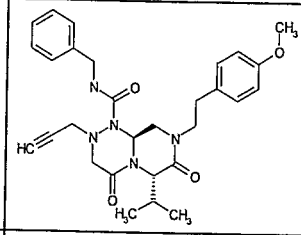
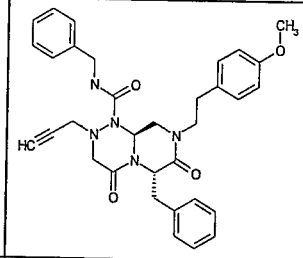
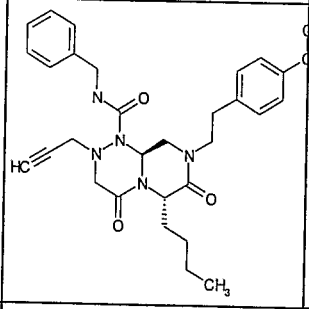
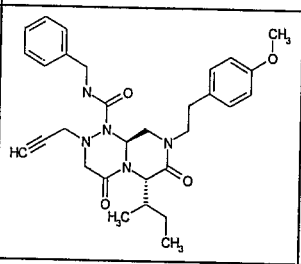
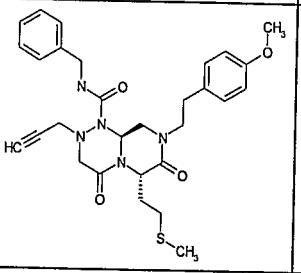
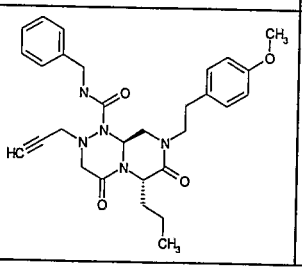
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1416		468	469
1417		516	517
1418		482	483
1419		482	483
1420		500	501

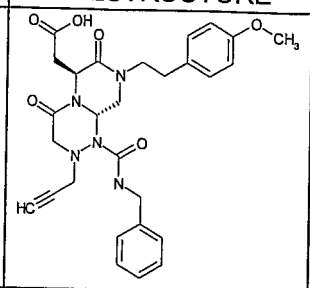
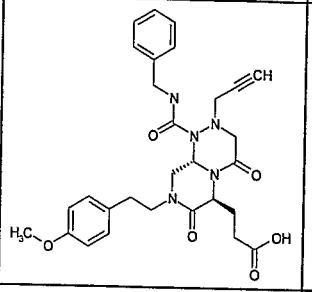
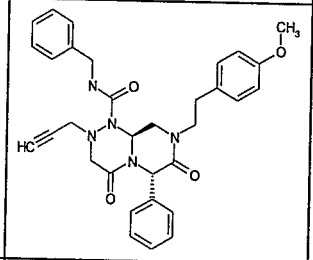
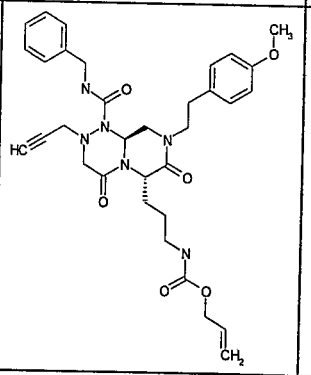
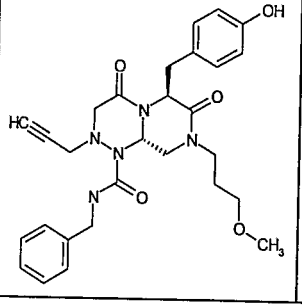
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1421		468	469
1422		484	485
1423		498	499
1424		502	503

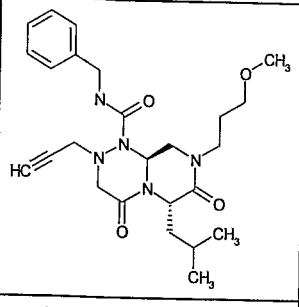
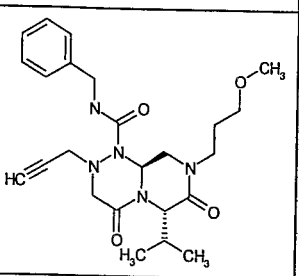
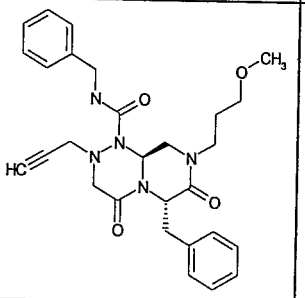
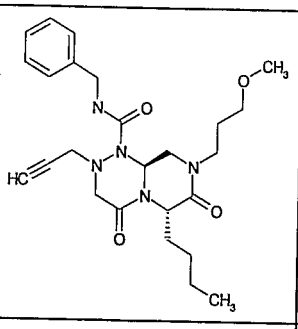
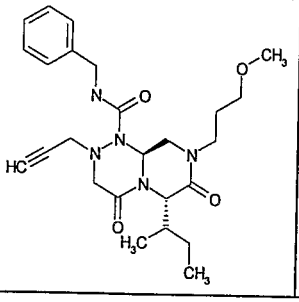
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1425		567	568
1426		518	519
1427		468	469
1428		454	455
1429		502	503

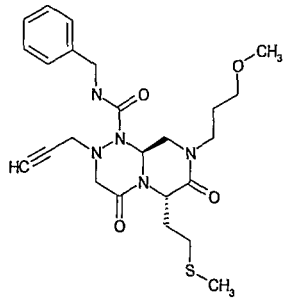
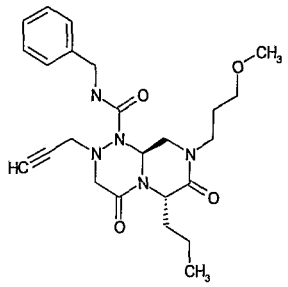
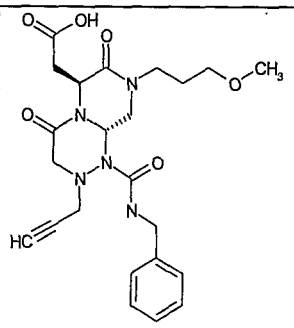
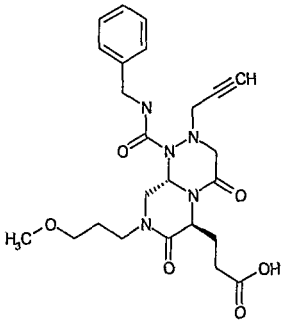
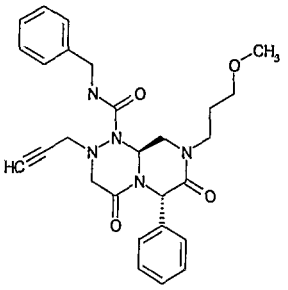
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1430		468	469
1431		468	469
1432		486	487
1433		454	455
1434		470	471

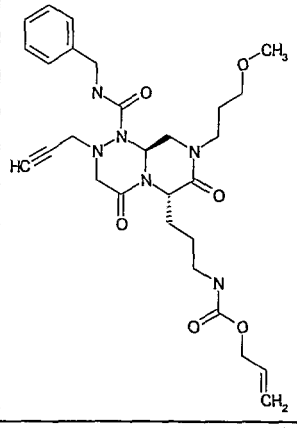
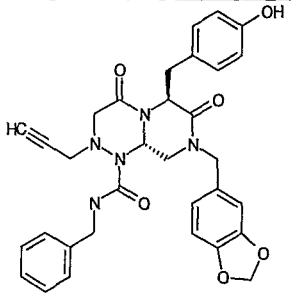
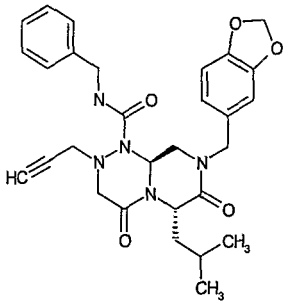
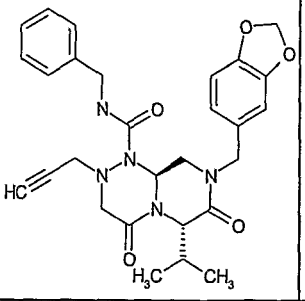
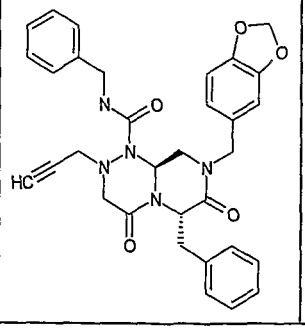
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1435		484	485
1436		488	489
1437		553	554
1438		582	583
1439		532	533

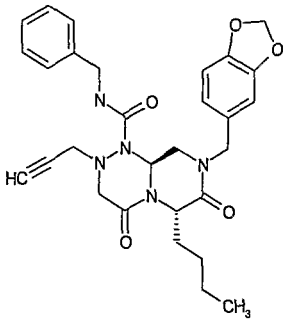
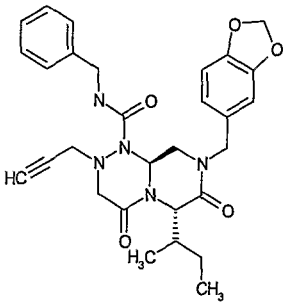
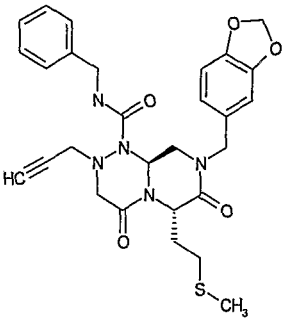
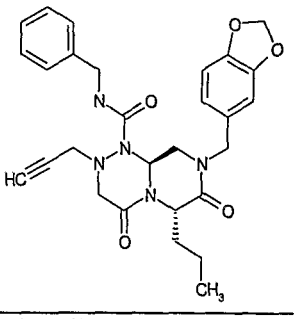
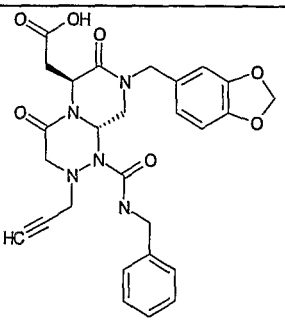
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1441		566	567
1442		532	533
1443		532	533
1444		550	551
1445		518	519

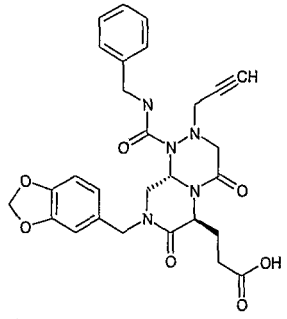
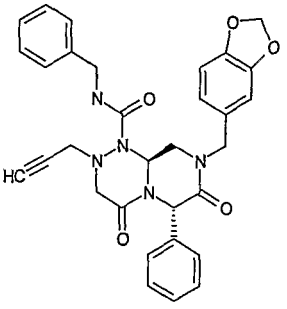
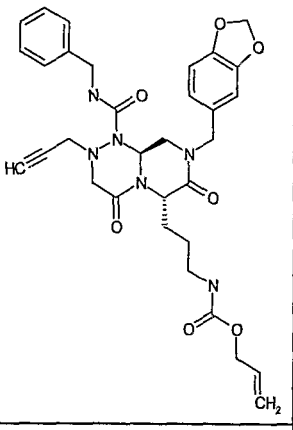
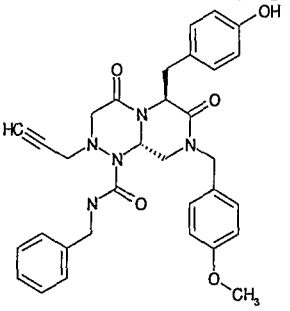
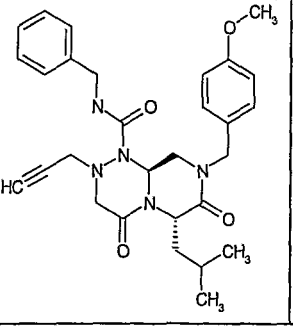
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1446		534	535
1447		548	549
1448		552	553
1449		617	618
1450		520	521

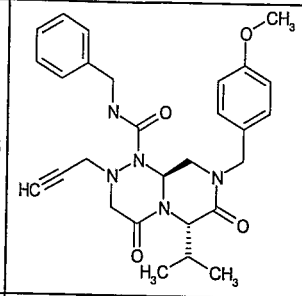
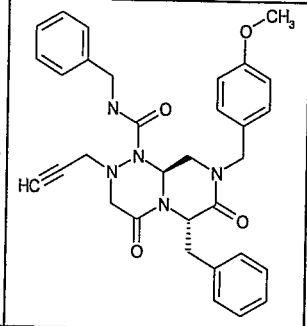
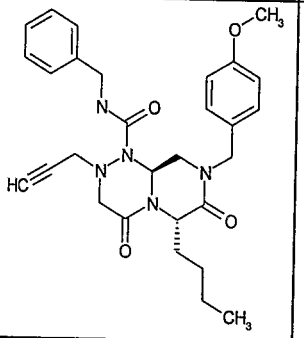
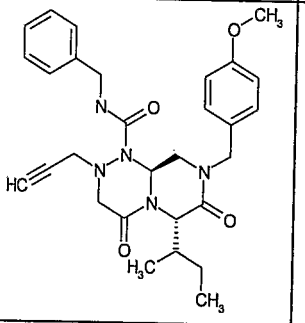
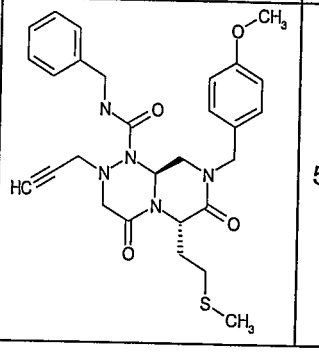
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1451		470	471
1452		456	457
1453		504	505
1454		470	471
1455		470	471

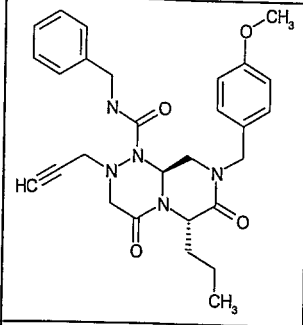
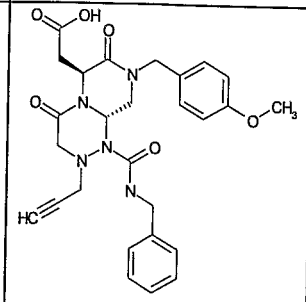
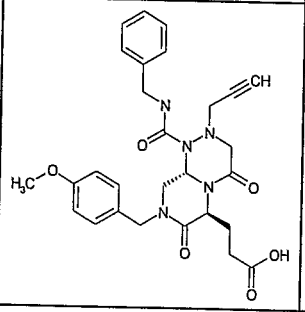
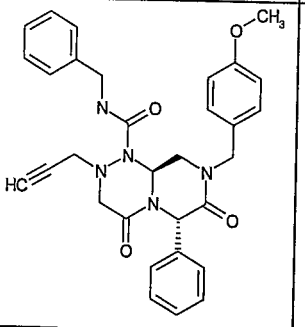
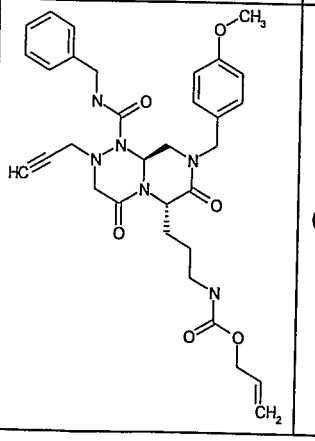
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1457		456	457
1458		472	473
1459		486	487
1460		490	491

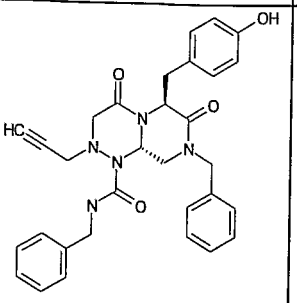
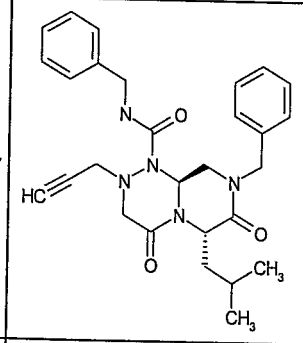
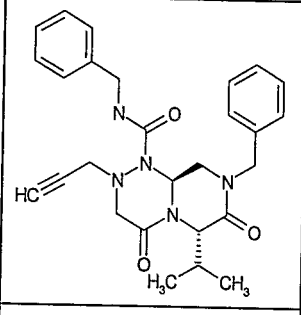
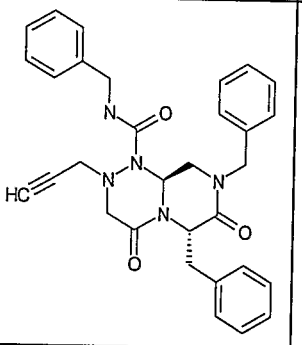
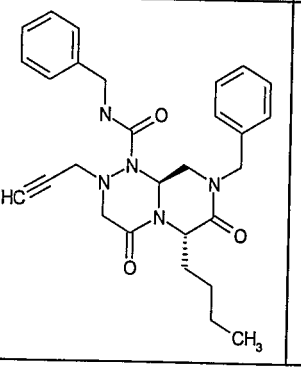
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1461		555	556
1462		582	583
1463		532	533
1464		518	519
1465		566	567

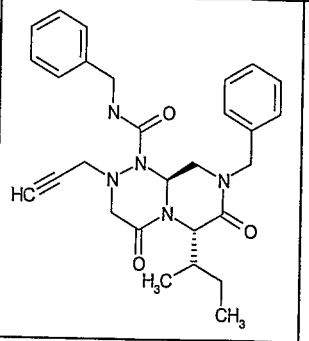
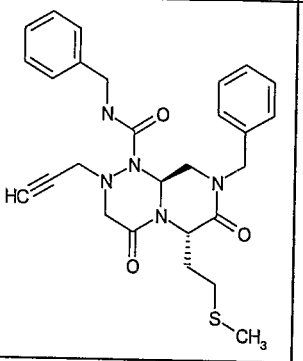
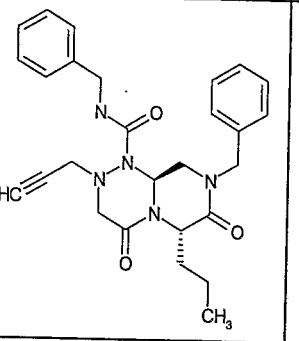
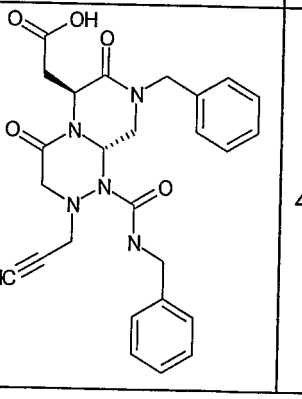
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1466		532	533
1467		532	533
1468		550	551
1469		518	519
1470		534	535

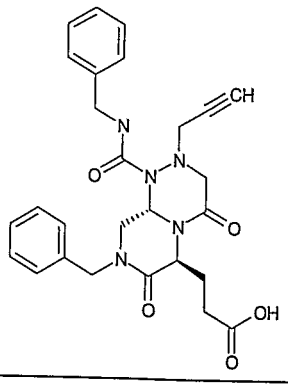
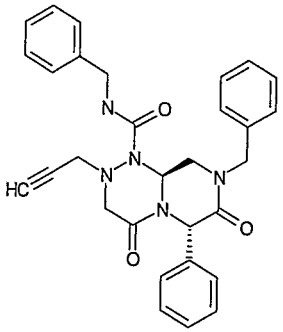
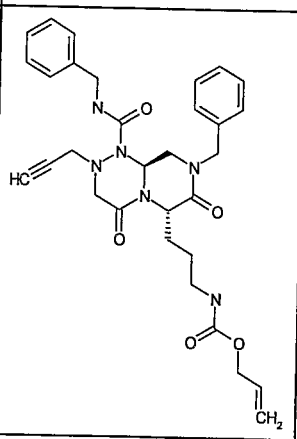
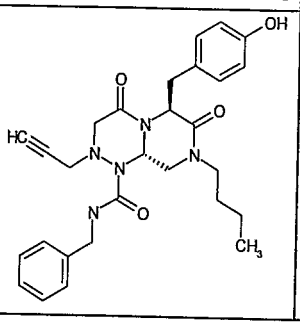
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1471		548	549
1472		552	553
1473		617	618
1474		568	569
1475		518	519

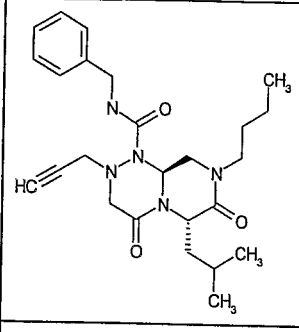
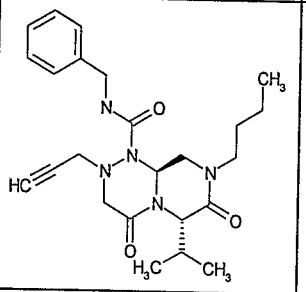
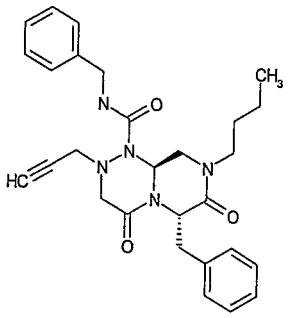
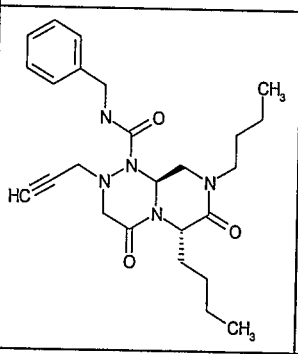
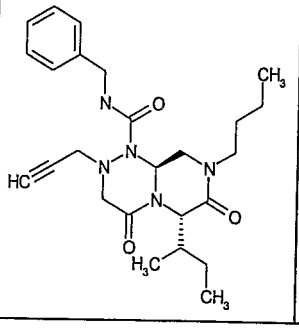
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1476		504	505
1477		552	553
1478		518	519
1479		518	519
1480		536	537

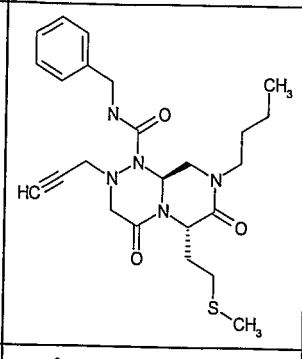
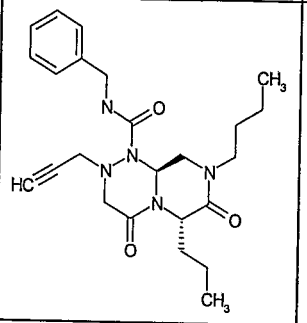
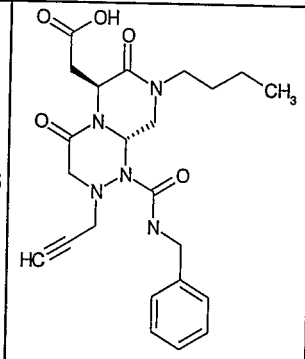
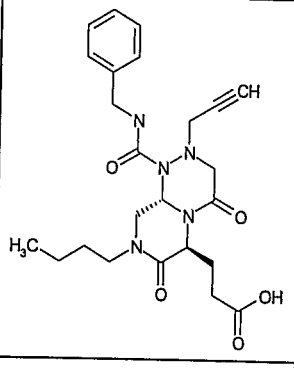
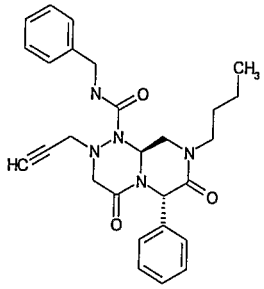
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1481		504	505
1482		520	521
1483		534	535
1484		538	539
1485		603	604

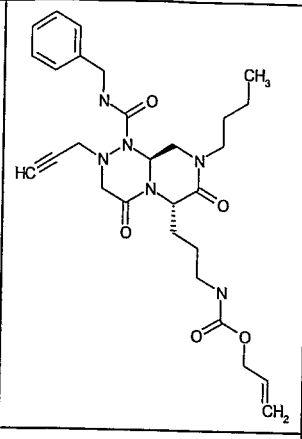
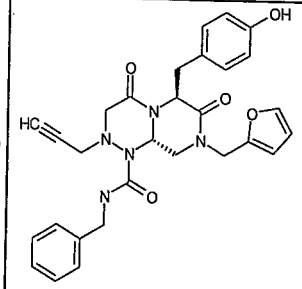
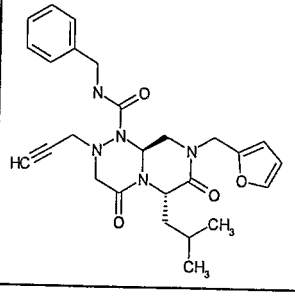
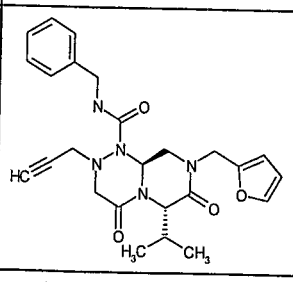
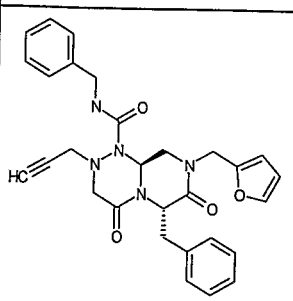
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1486		538	539
1487		488	489
1488		474	475
1489		522	523
1490		488	489

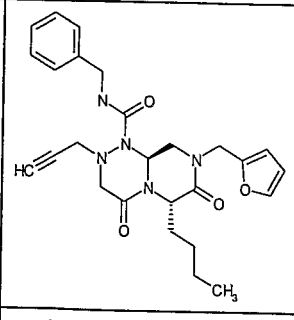
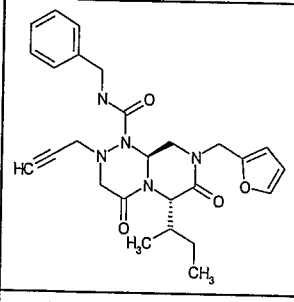
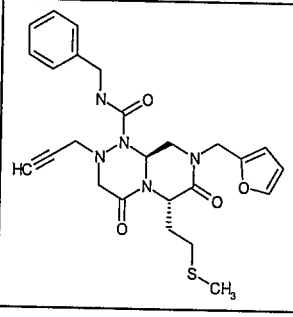
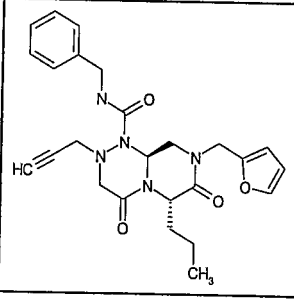
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1491		488	489
1492		506	507
1493		474	475
1494		490	491

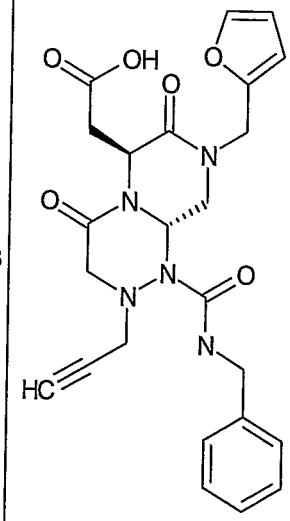
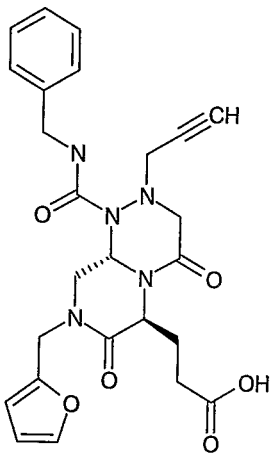
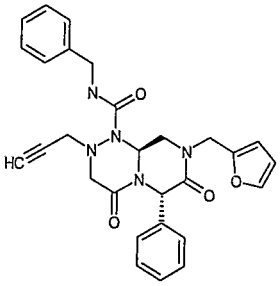
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1496		508	509
1497		573	574
1498		504	505

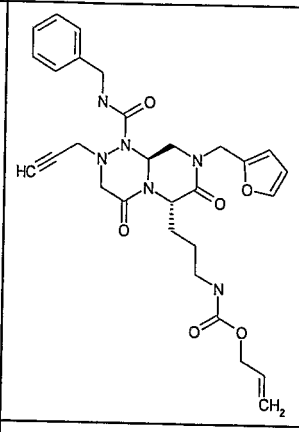
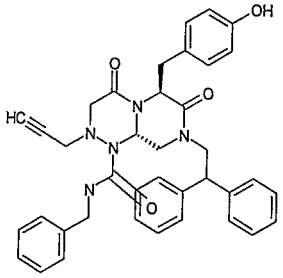
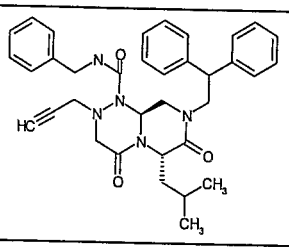
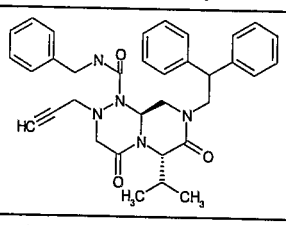
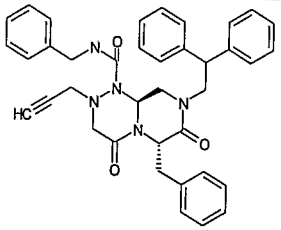
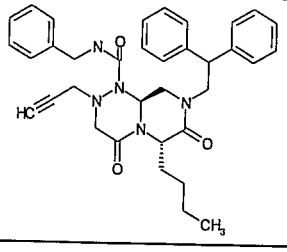
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1500		440	441
1501		488	489
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1503		454	455

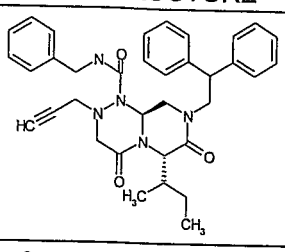
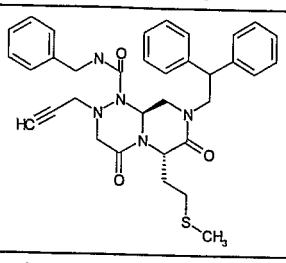
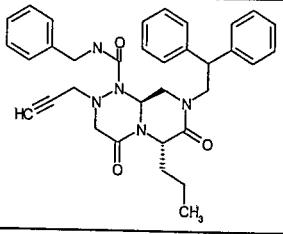
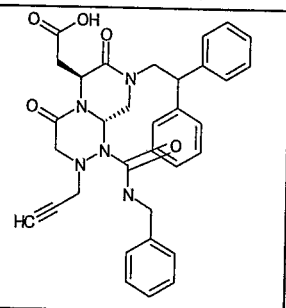
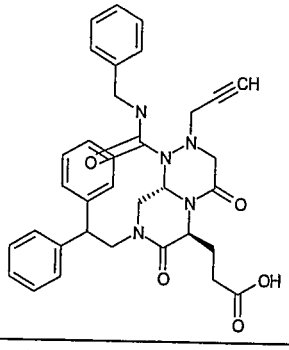
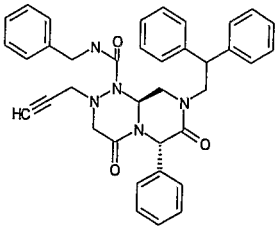
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1506		456	457
1507		470	471
1508		474	475

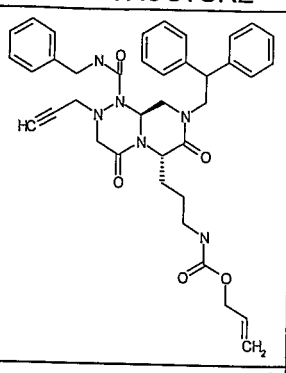
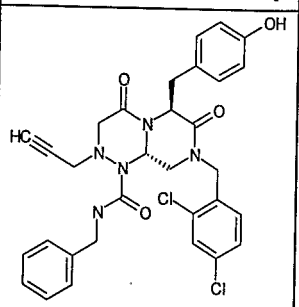
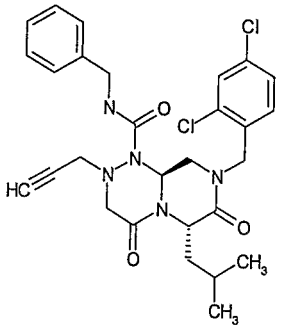
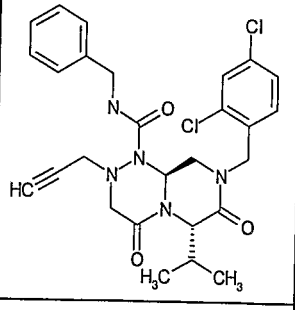
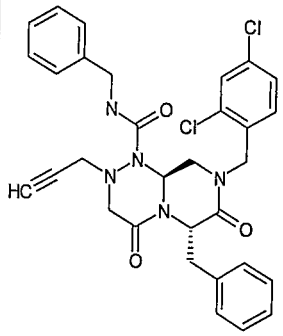
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1509		539	540
1510		528	529
1511		478	479
1512		464	465
1513		512	513

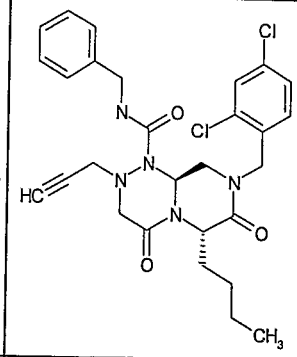
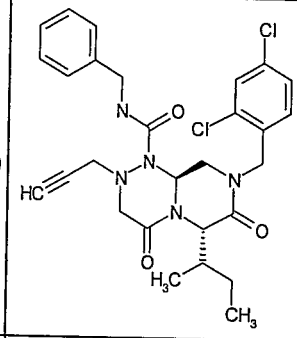
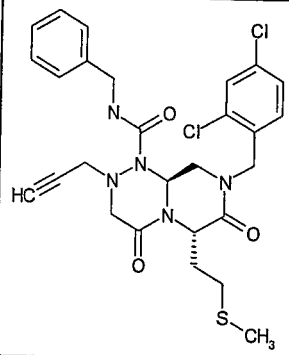
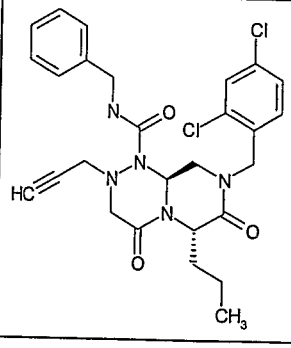
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1515		478	479
1516		496	497
1517		464	465

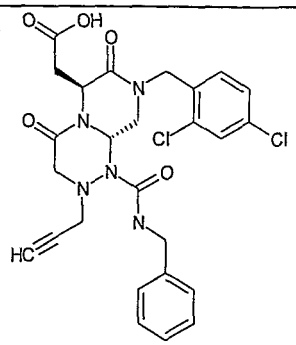
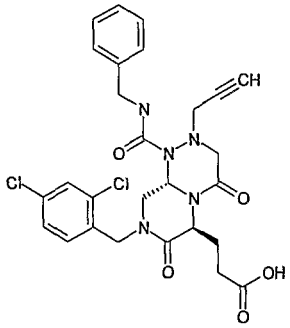
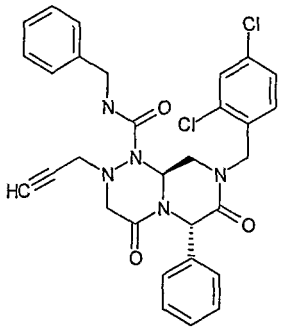
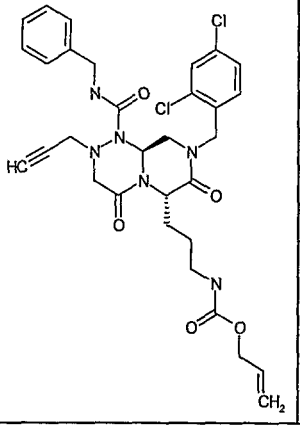
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1520		498	499

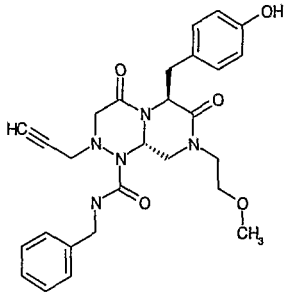
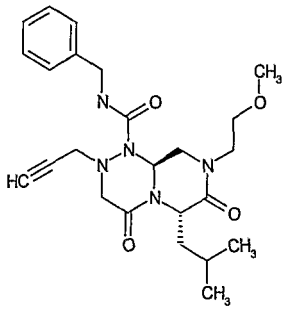
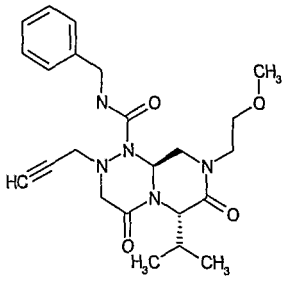
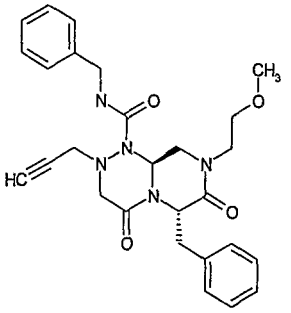
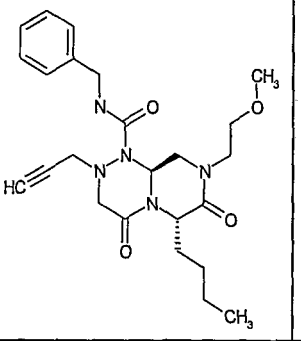
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1522		628	629
1523		578	579
1524		564	565
1525		612	613
1526		578	579

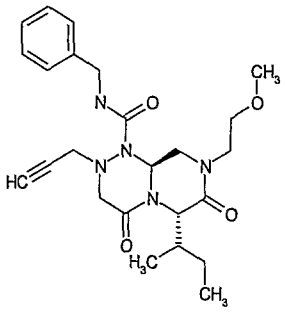
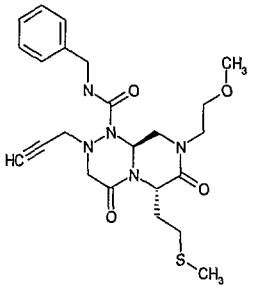
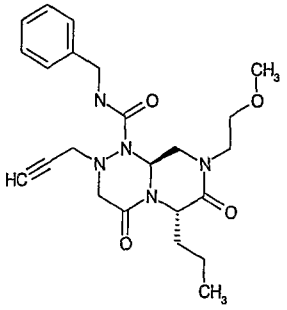
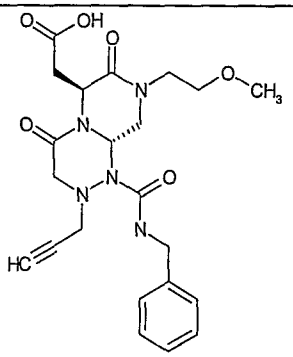
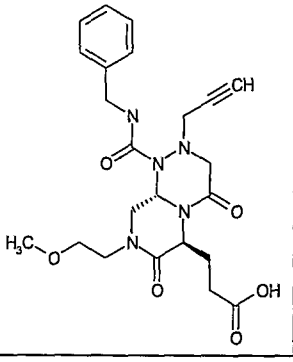
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1528		596	597
1529		564	565
1530		580	581
1531		594	595
1532		598	599

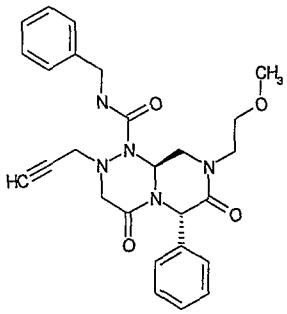
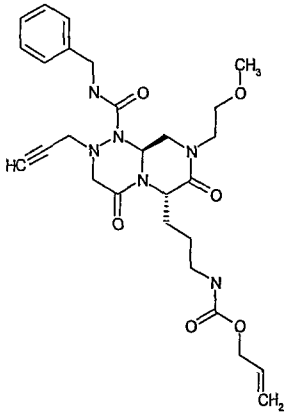
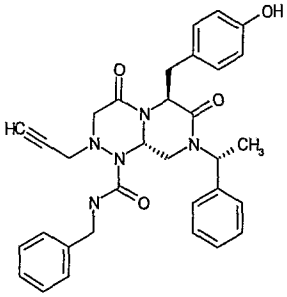
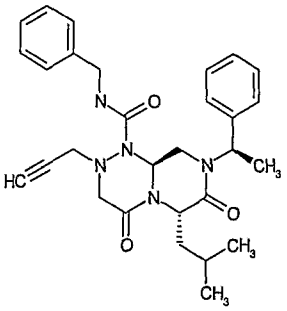
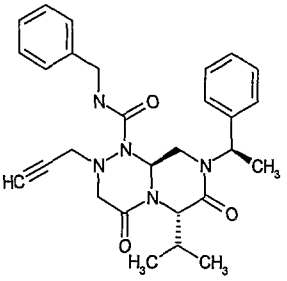
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1534		607	608
1535		556	557
1536		542	543
1537		591	592

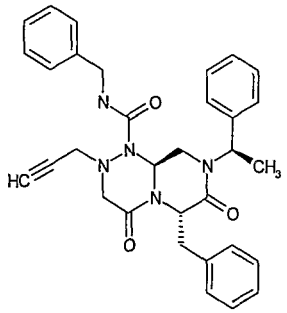
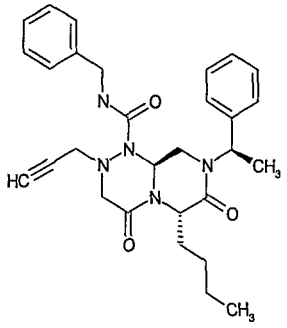
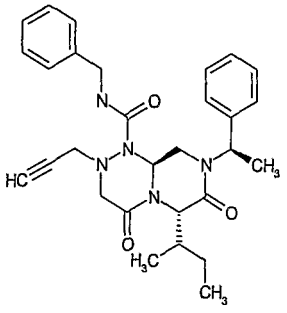
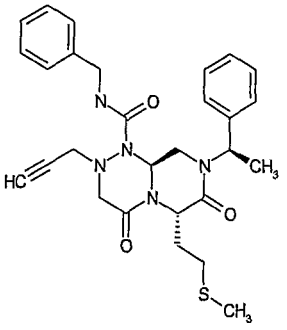
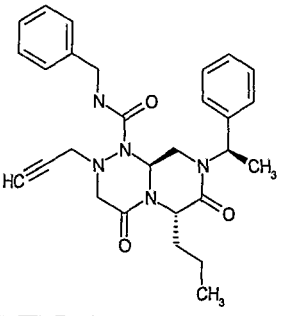
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1539		556	557
1540		575	576
1541		542	543

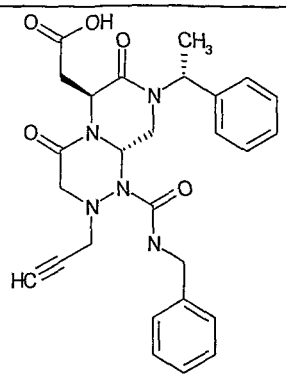
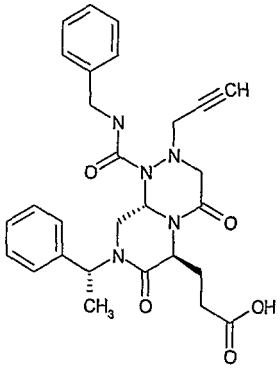
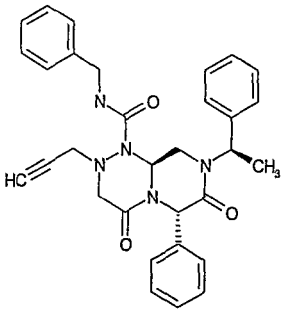
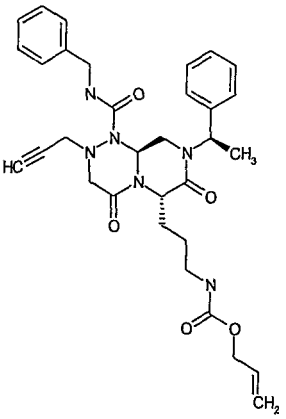
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1543		572	573
1544		576	577
1545		642	643

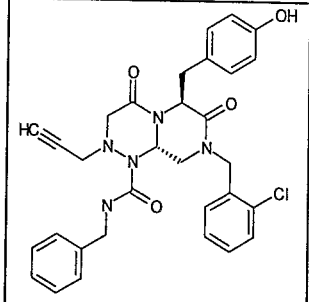
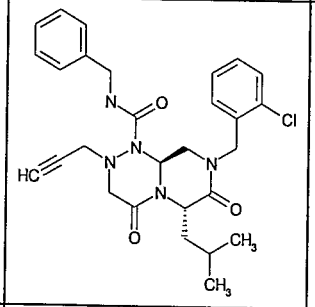
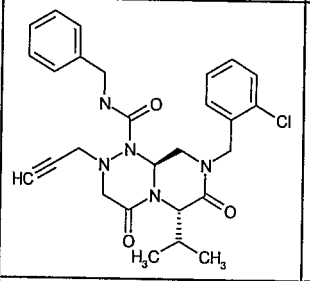
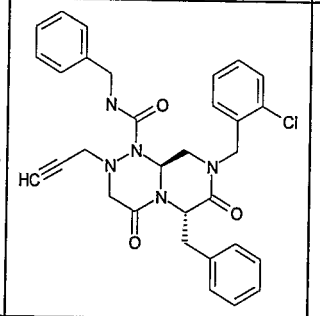
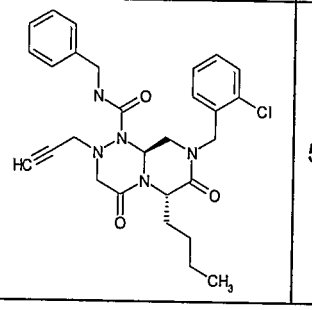
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1546		506	507
1547		456	457
1548		442	443
1549		490	491
1550		456	457

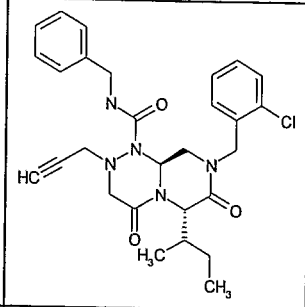
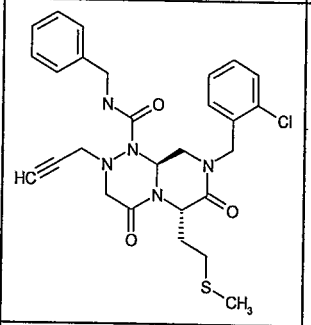
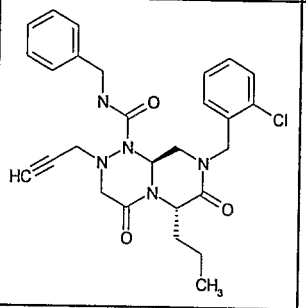
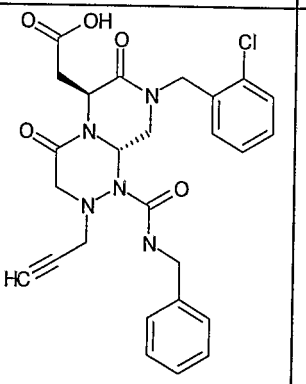
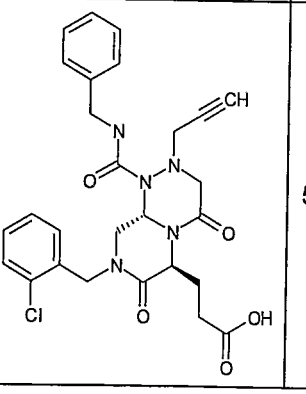
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1552		474	475
1553		442	443
1554		457	458
1555		472	473

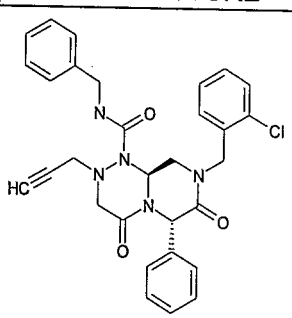
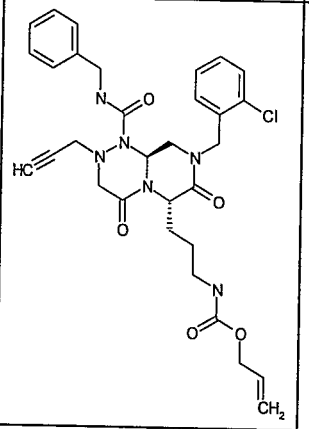
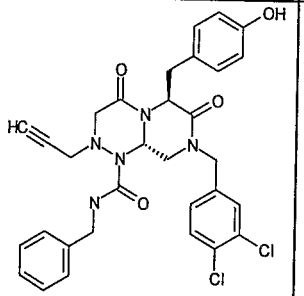
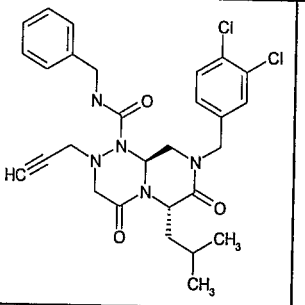
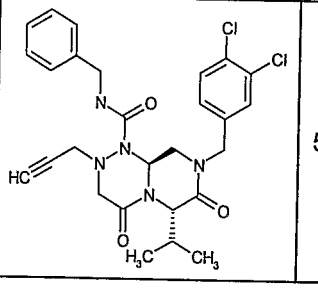
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1557		541	542
1558		552	553
1559		502	503
1560		488	489

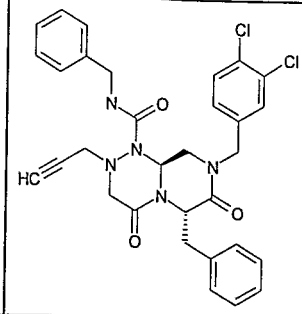
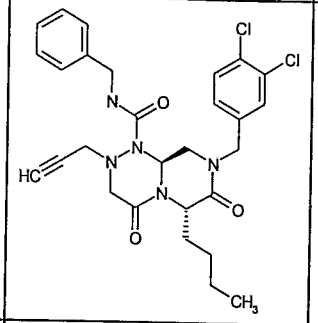
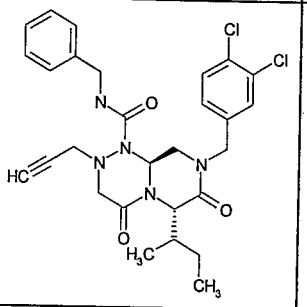
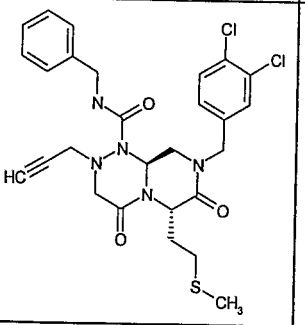
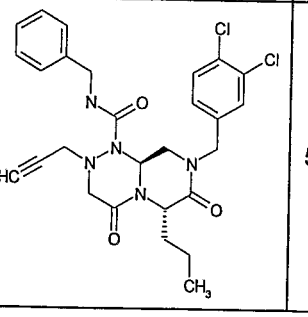
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1562		502	503
1563		502	503
1564		520	521
1565		488	489

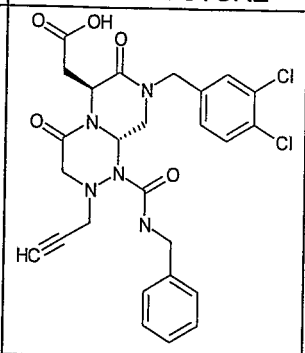
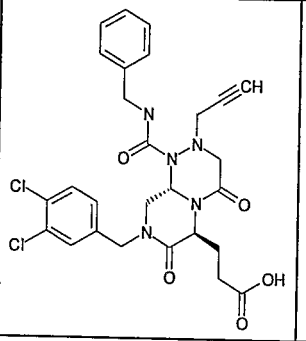
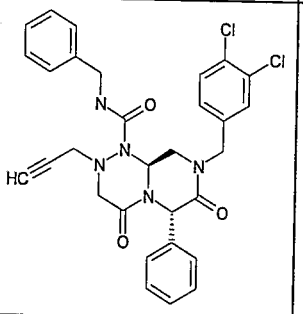
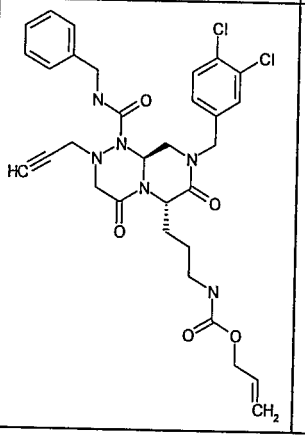
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1567		518	519
1568		522	523
1569		587	588

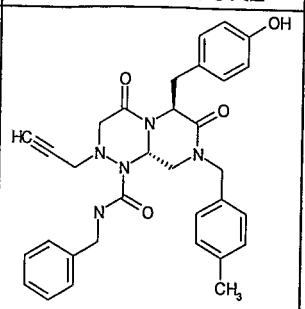
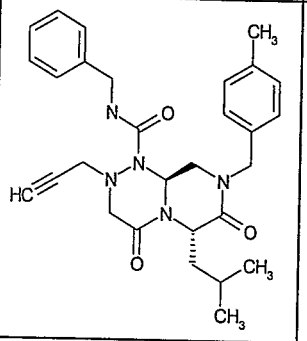
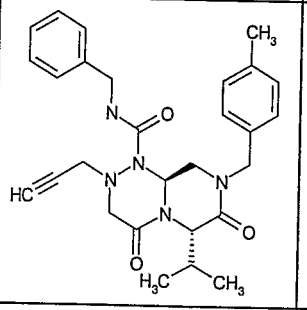
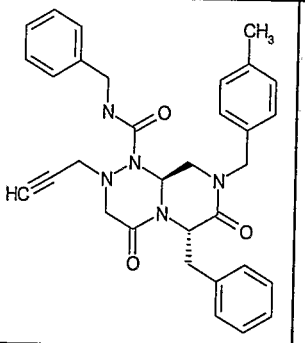
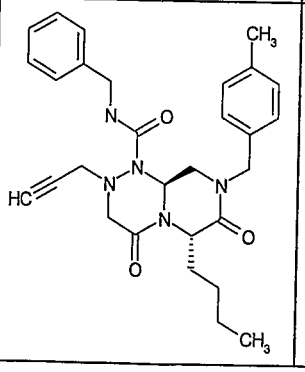
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1570		572	573
1571		522	523
1572		508	509
1573		556	557
1574		522	523

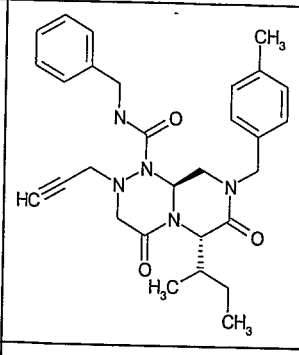
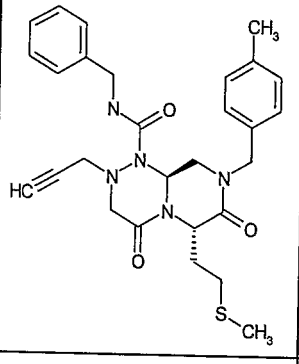
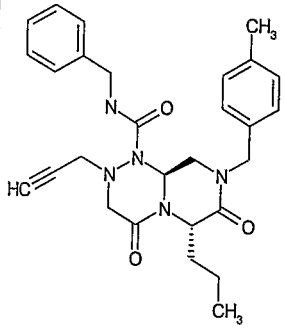
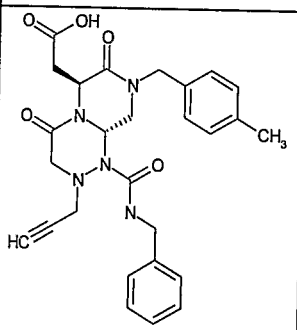
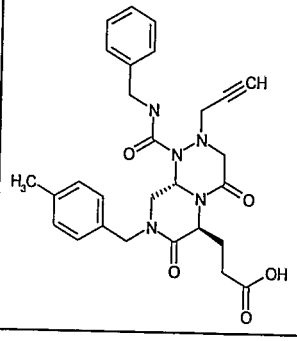
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1576		540	541
1577		508	509
1578		524	525
1579		538	539

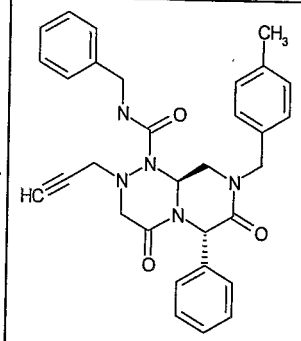
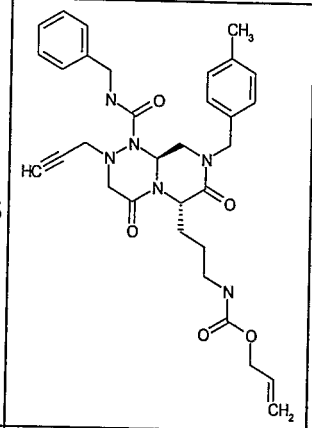
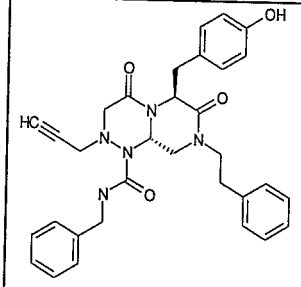
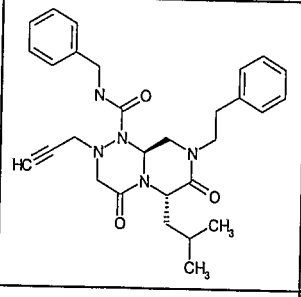
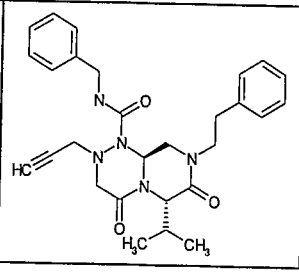
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1581		607	608
1582		607	608
1583		556	557
1584		542	543

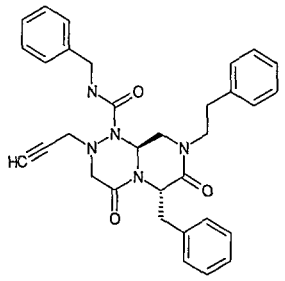
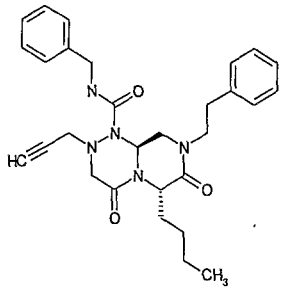
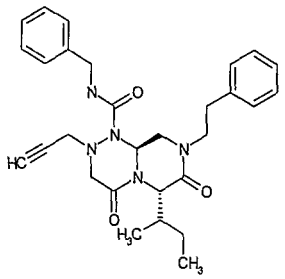
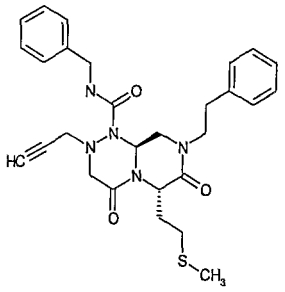
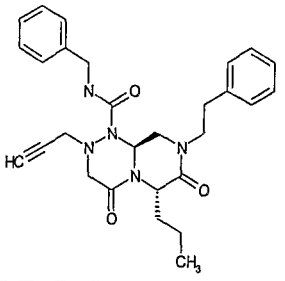
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1587		556	557
1588		575	576
1589		542	543

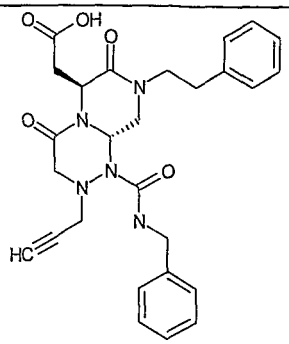
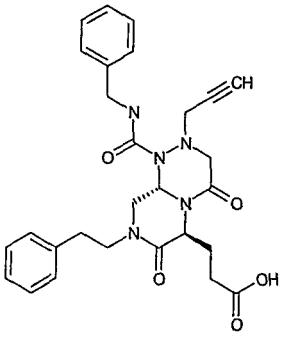
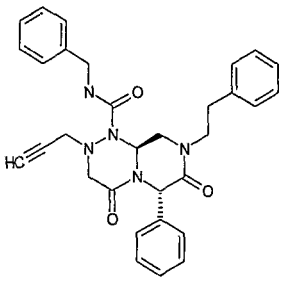
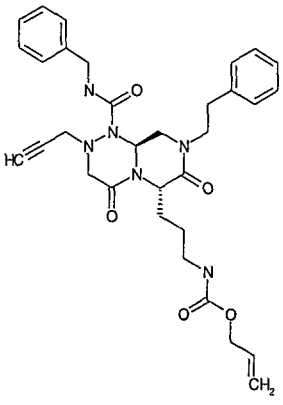
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1591		572	573
1592		576	577
1593		642	643

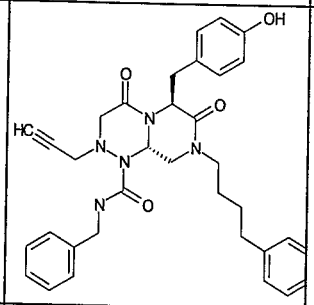
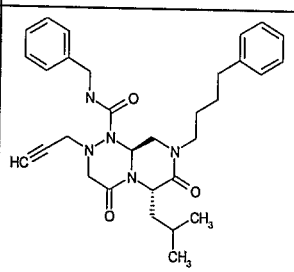
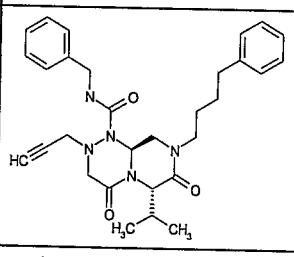
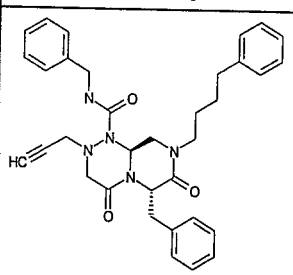
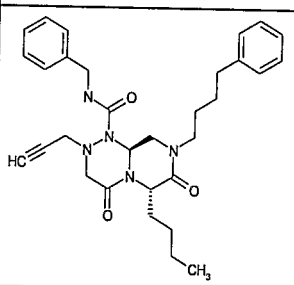
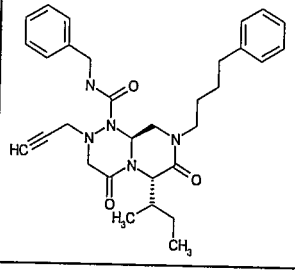
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1594		552	553
1595		502	503
1596		488	489
1597		536	537
1598		502	503

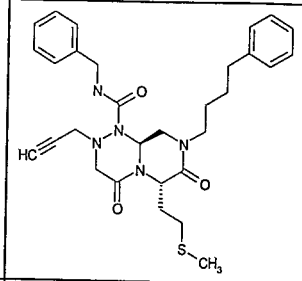
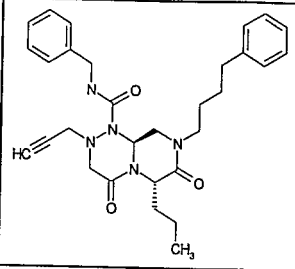
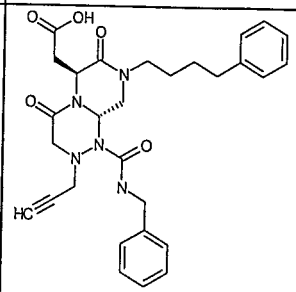
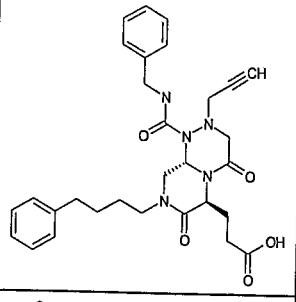
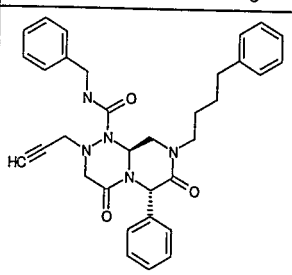
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1600		520	521
1601		488	489
1602		504	505
1603		518	519

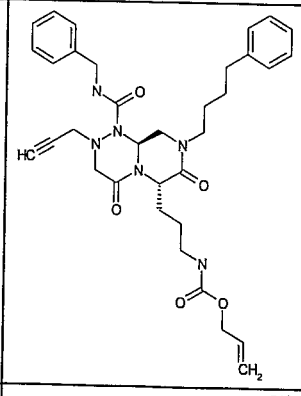
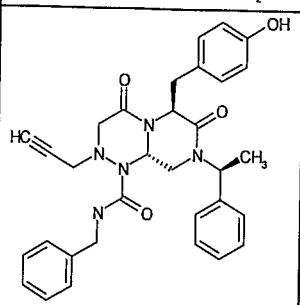
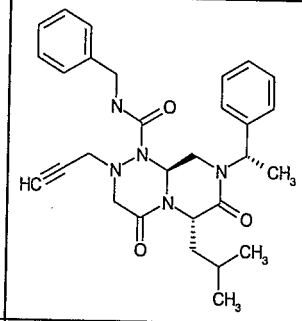
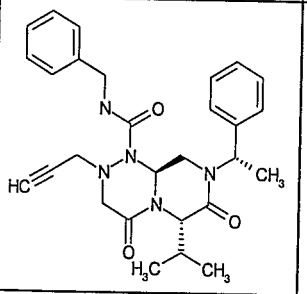
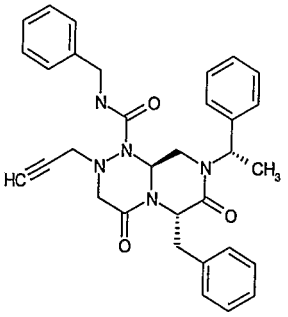
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1604		522	523
1605		587	588
1606		552	553
1607		502	503
1608		488	489

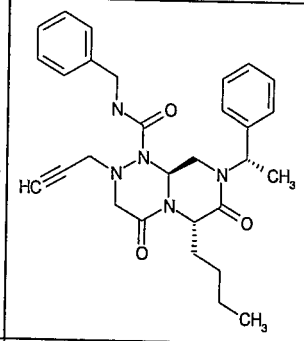
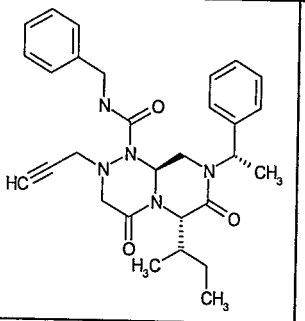
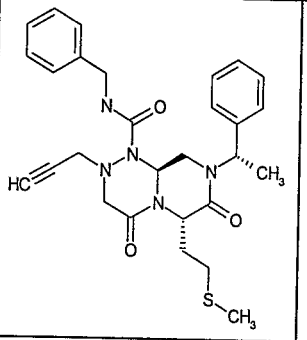
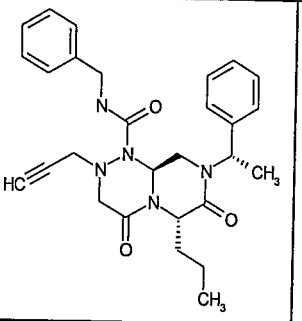
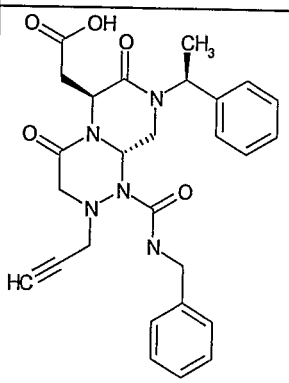
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1609		536	537
1610		502	503
1611		502	503
1612		520	521
1613		488	489

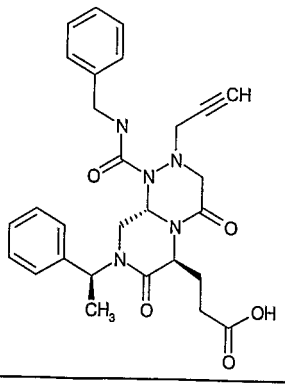
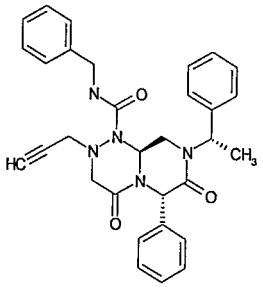
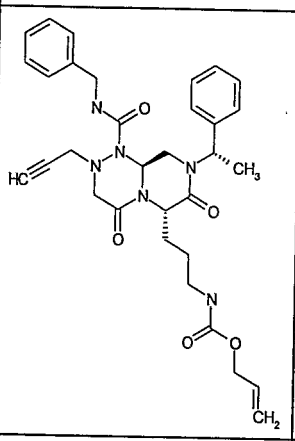
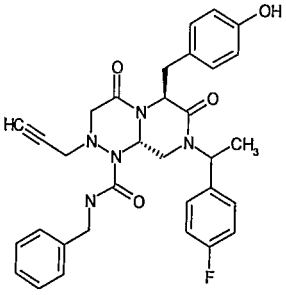
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1615		518	519
1616		522	523
1617		587	588

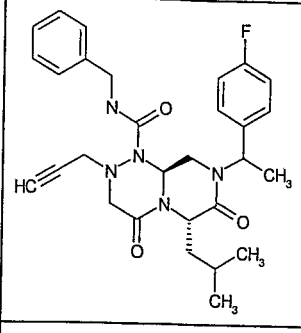
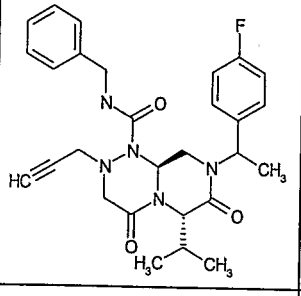
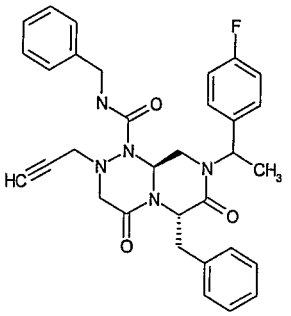
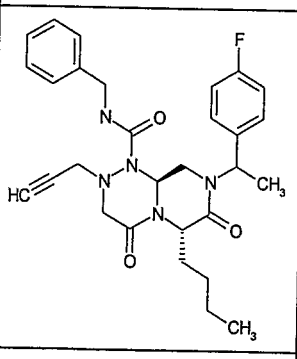
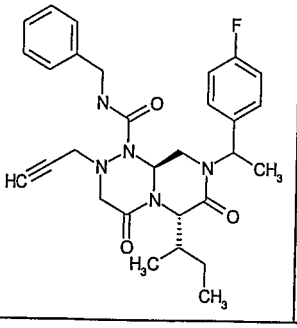
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1618		580	581
1619		530	531
1620		516	517
1621		564	565
1622		530	531
1623		530	531

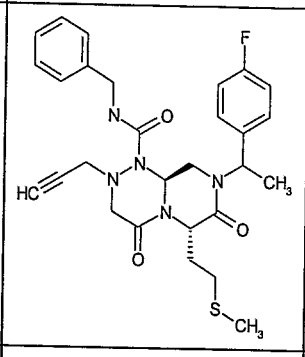
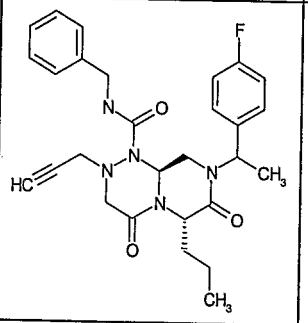
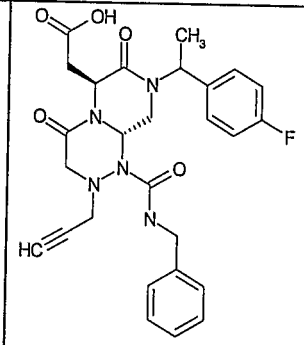
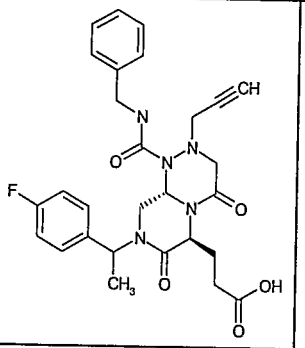
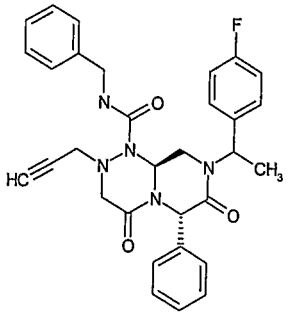
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1624		548	549
1625		516	517
1626		532	533
1627		546	547
1628		550	551

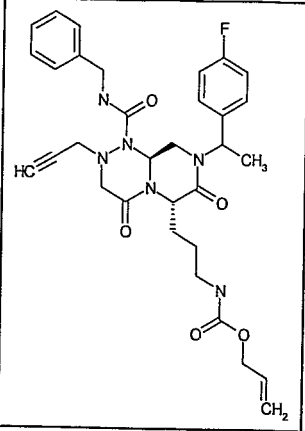
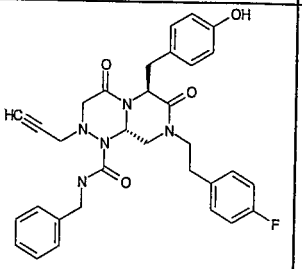
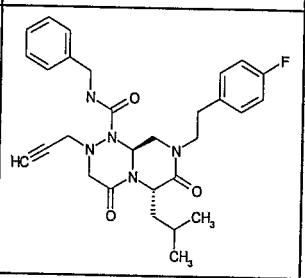
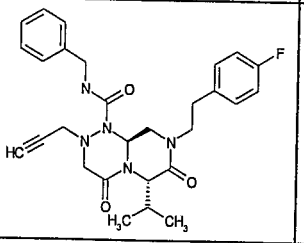
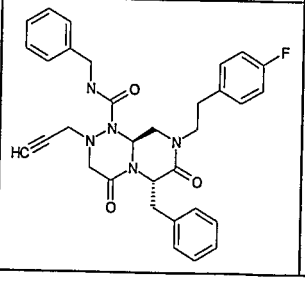
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1629		615	616
1630		552	553
1631		502	503
1632		488	489
1633		536	537

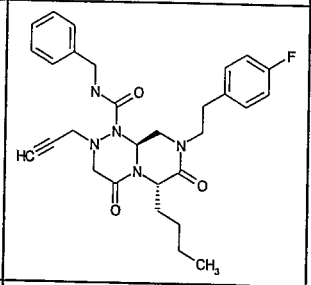
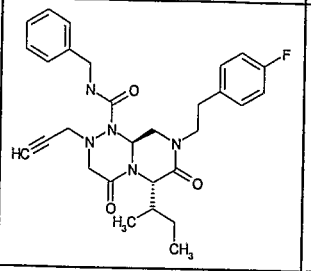
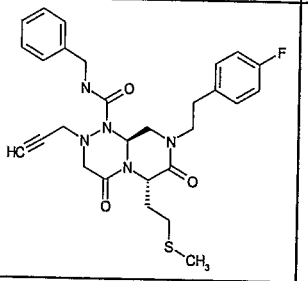
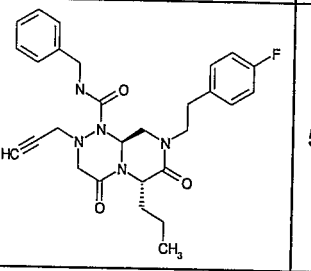
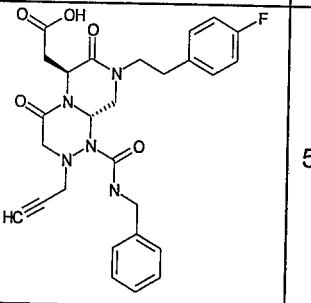
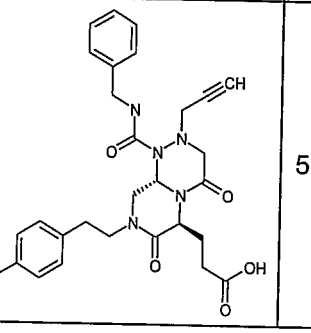
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1634		502	503
1635		502	503
1636		520	521
1637		488	489
1638		504	505

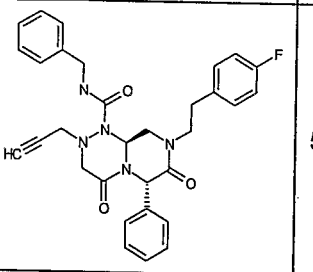
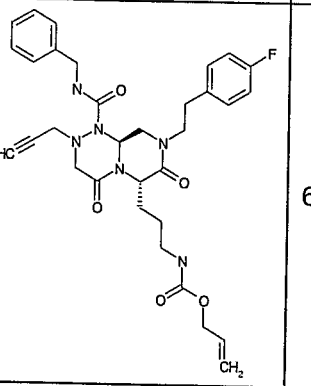
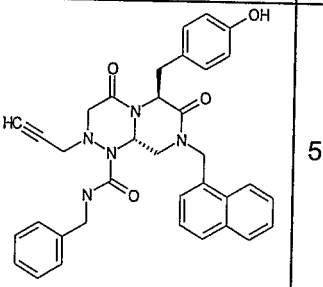
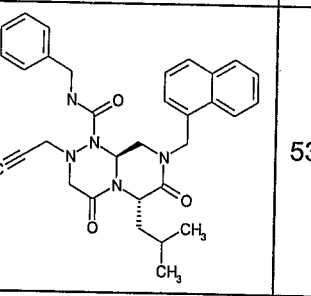
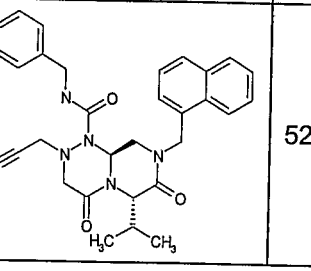
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1640		522	523
1641		587	588
1642		570	571

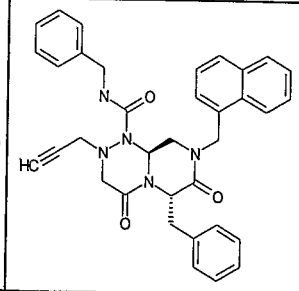
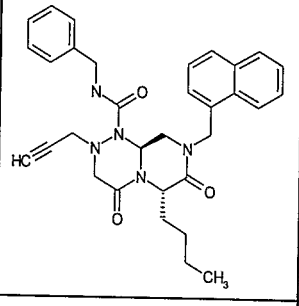
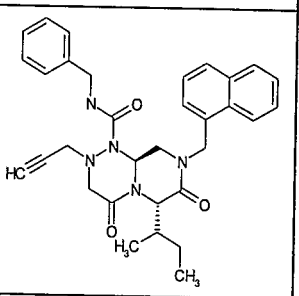
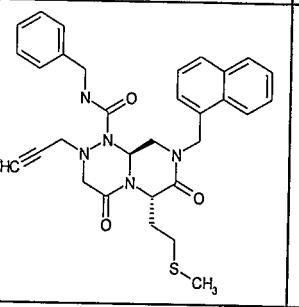
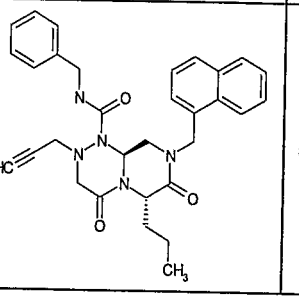
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1643		520	521
1644		506	507
1645		554	555
1646		520	521
1647		520	521

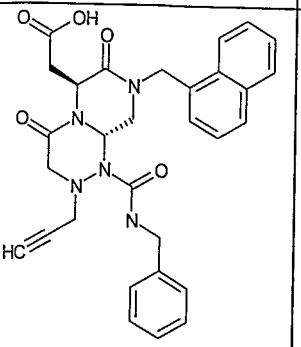
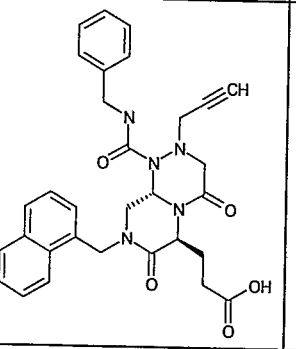
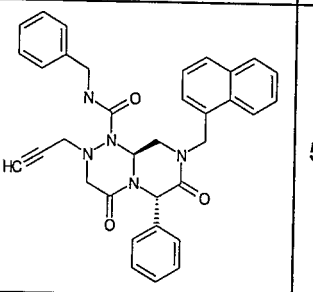
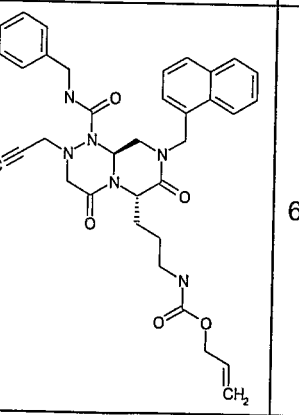
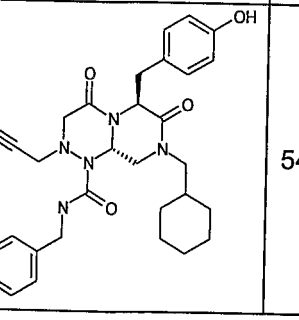
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1648		538	539
1649		506	507
1650		522	523
1651		536	537
1652		540	541

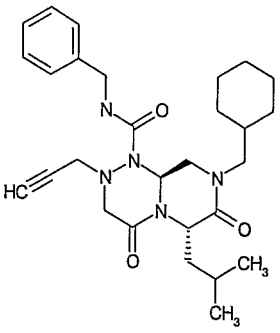
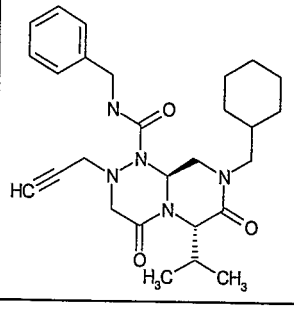
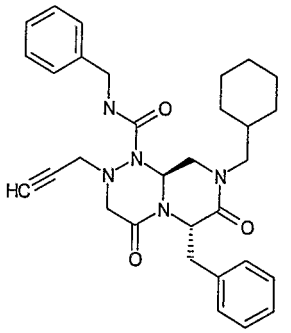
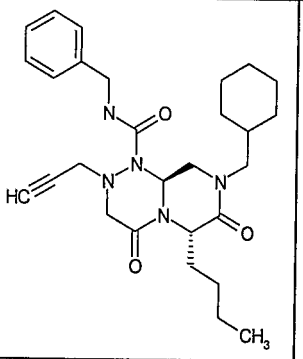
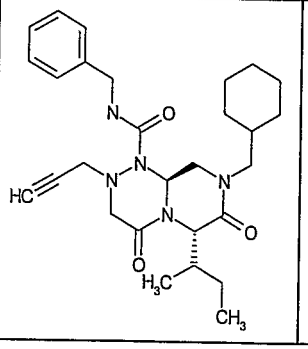
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1653		605	606
1654		570	571
1655		520	521
1656		506	507
1657		554	555

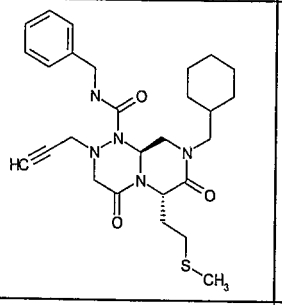
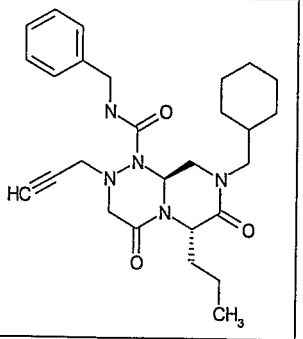
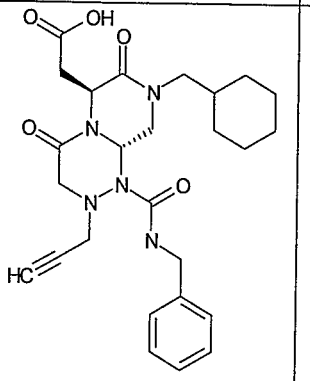
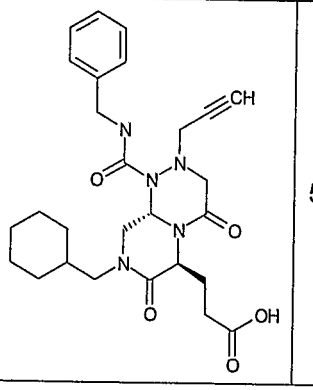
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1658		520	521
1659		520	521
1660		538	539
1661		506	507
1662		522	523
1663		536	537

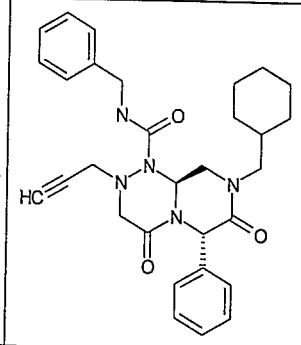
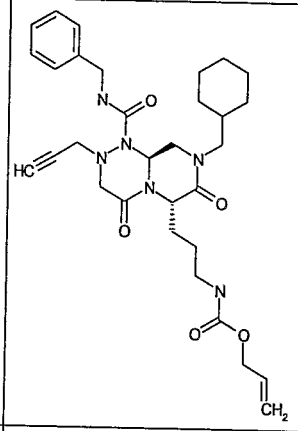
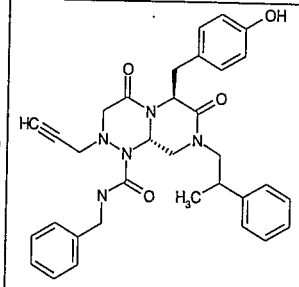
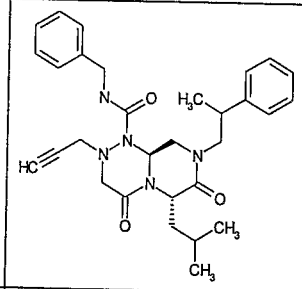
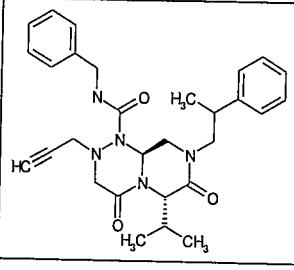
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1664		540	541
1665		605	606
1666		588	589
1667		538	539
1668		524	525

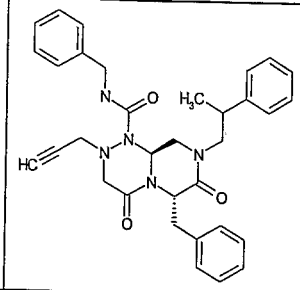
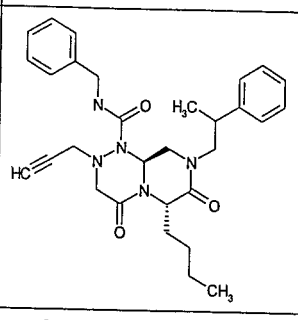
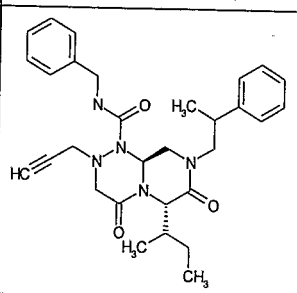
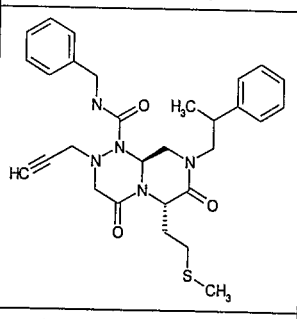
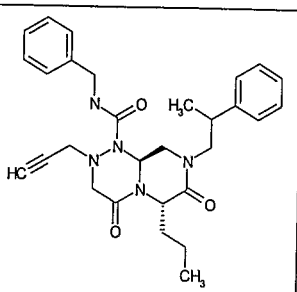
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1669		572	573
1670		538	539
1671		538	539
1672		556	557
1673		524	525

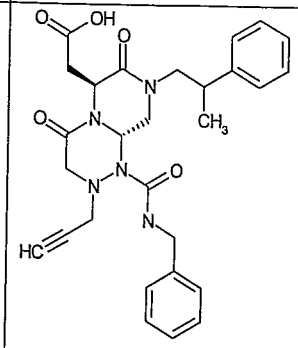
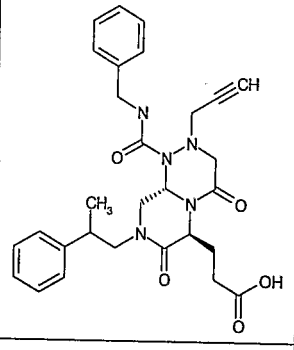
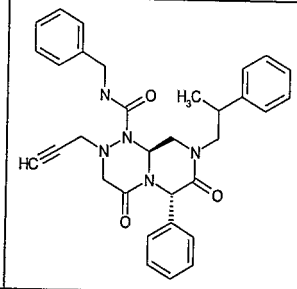
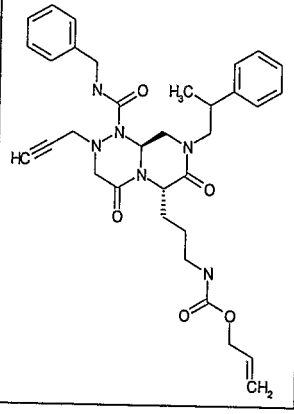
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1674		540	541
1675		554	555
1676		558	559
1677		623	624
1678		544	545

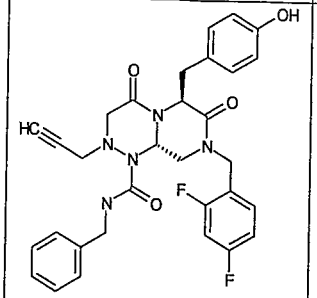
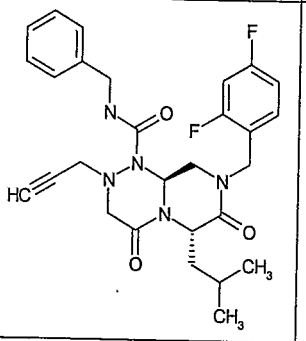
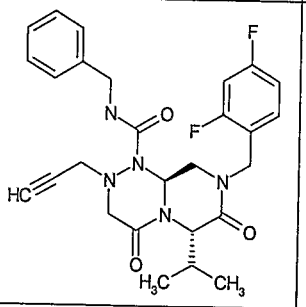
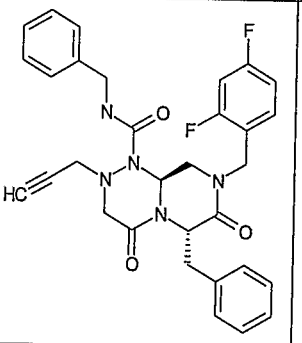
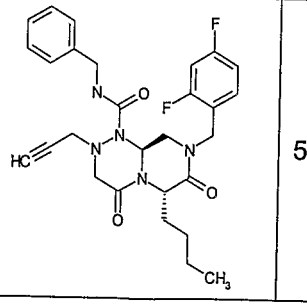
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
1679		494	495
1680		480	481
1681		528	529
1682		494	495
1683		494	495

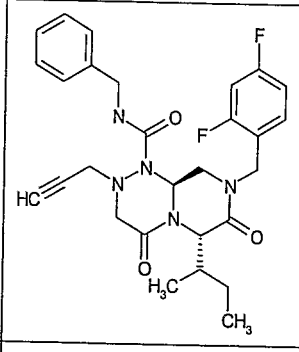
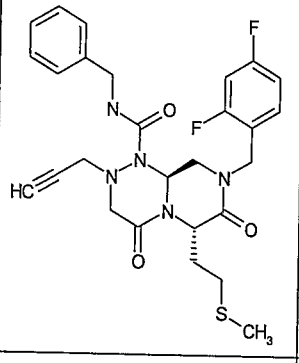
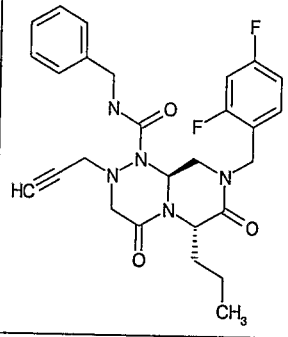
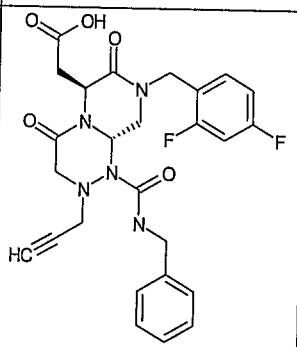
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1685		480	481
1686		496	497
1687		510	511

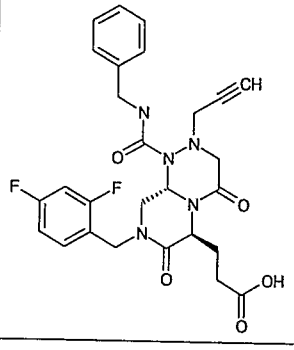
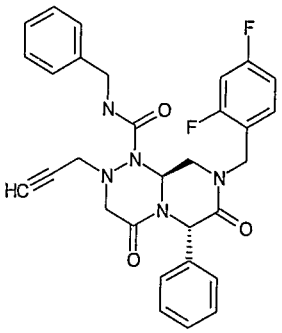
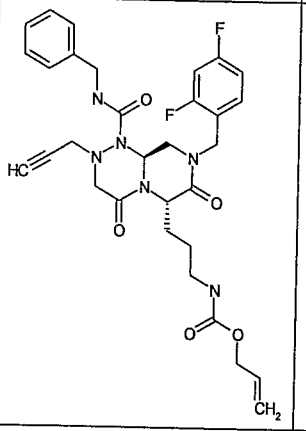
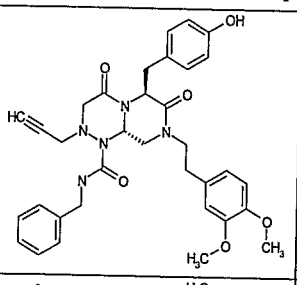
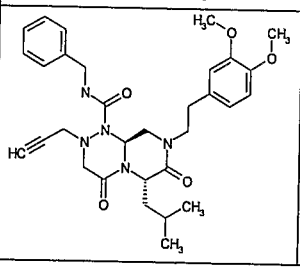
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1689		579	580
1690		566	567
1691		516	517
1692		502	503

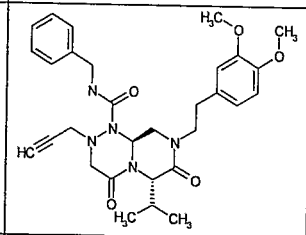
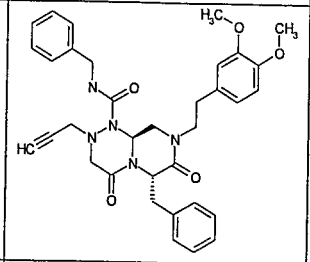
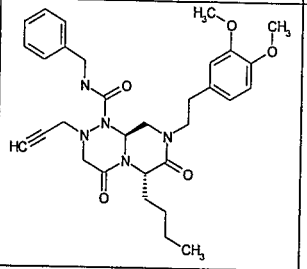
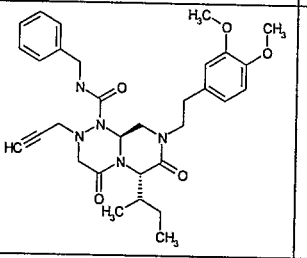
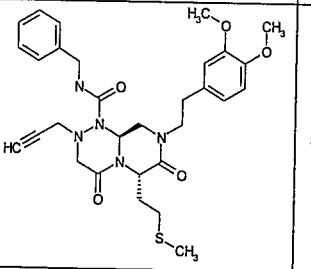
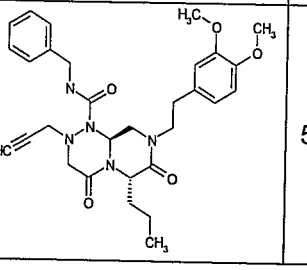
No	MOLSTRUCTURE	Mol. Weight	M+H(MS)
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1694		516	517
1695		516	517
1696		534	535
1697		502	503

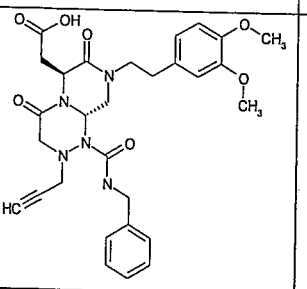
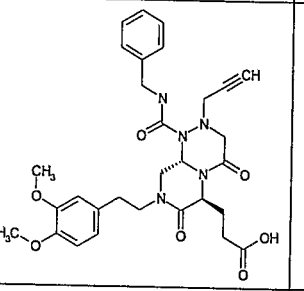
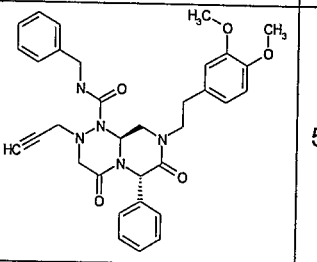
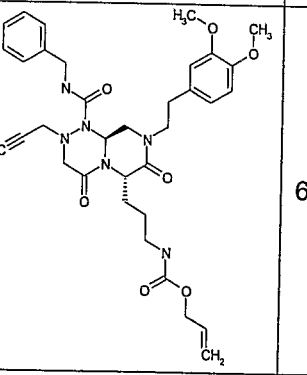
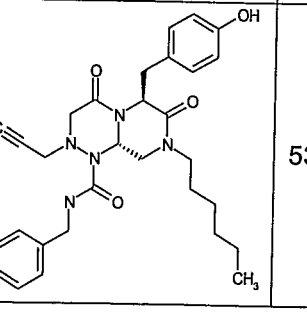
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1698		518	519
1699		532	533
1700		536	537
1701		601	602

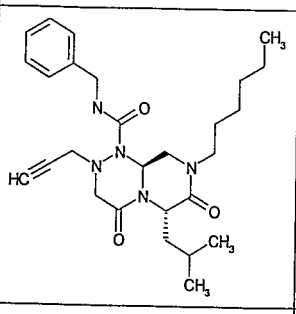
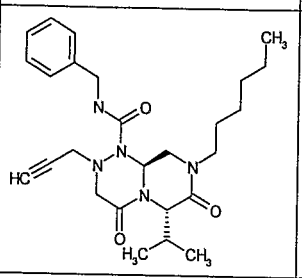
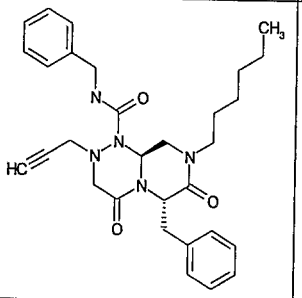
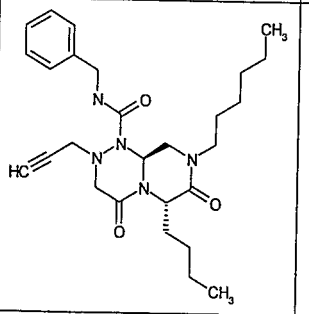
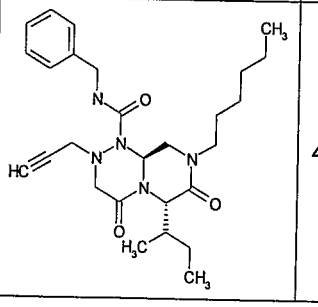
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1702		574	575
1703		524	525
1704		510	511
1705		558	559
1706		524	525

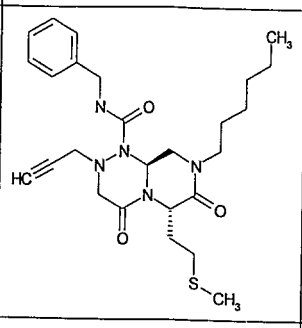
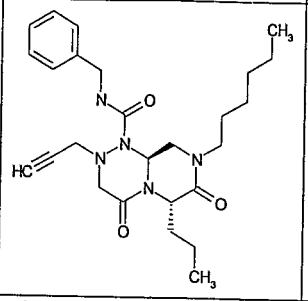
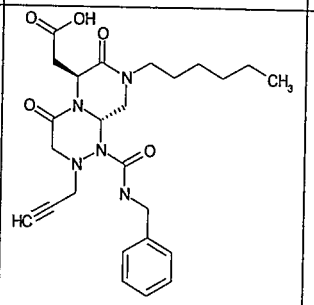
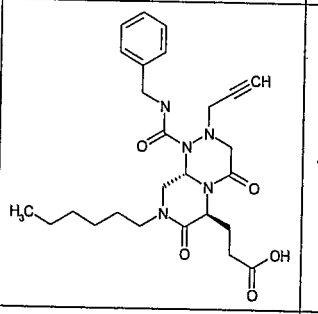
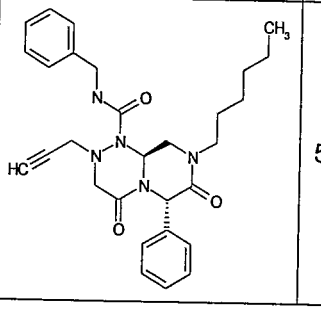
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1707		524	525
1708		542	543
1709		510	511
1710		526	527

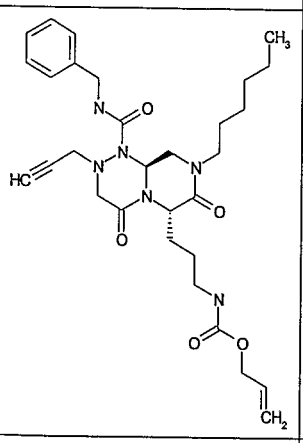
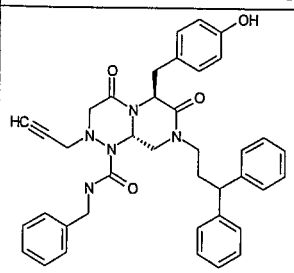
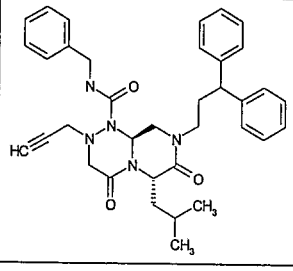
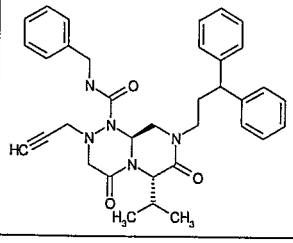
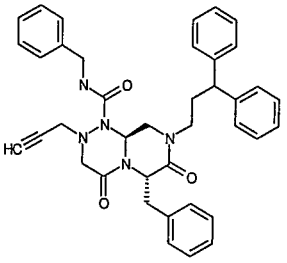
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1711		540	541
1712		544	545
1713		609	610
1714		612	613
1715		562	563

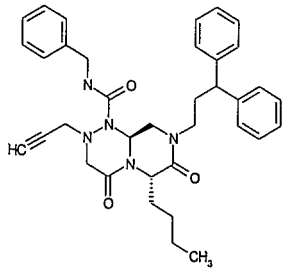
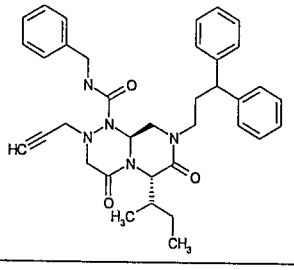
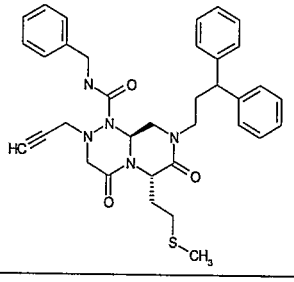
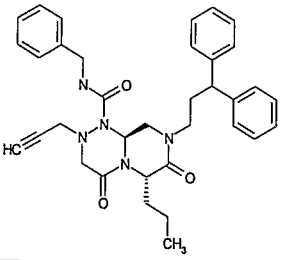
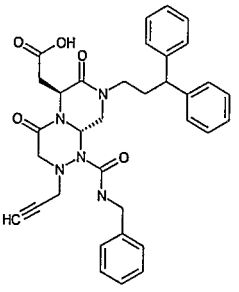
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1716		548	549
1717		596	597
1718		562	563
1719		562	563
1720		580	581
1721		548	549

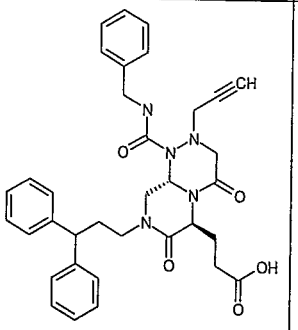
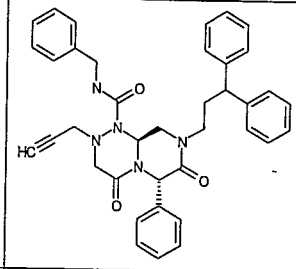
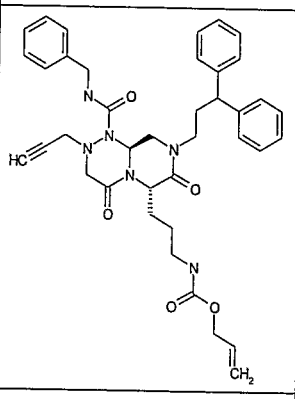
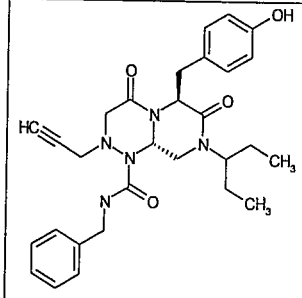
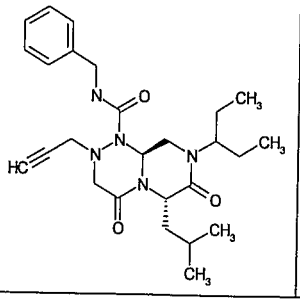
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1722		564	565
1723		578	579
1724		582	583
1725		647	648
1726		532	533

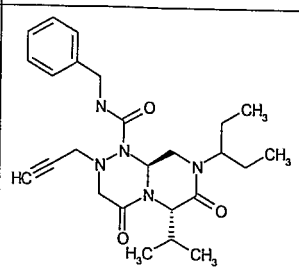
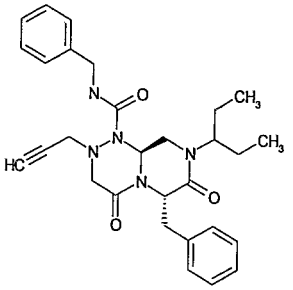
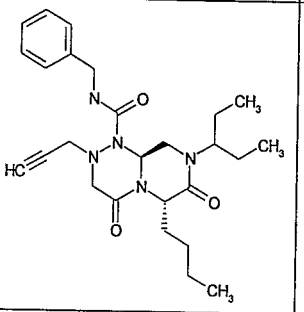
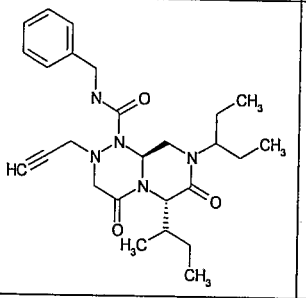
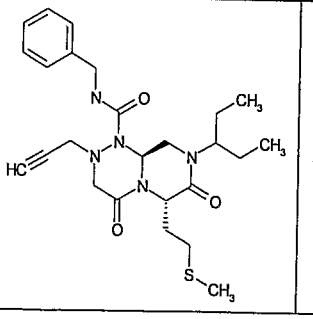
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1727		482	483
1728		468	469
1729		516	517
1730		482	483
1731		482	483

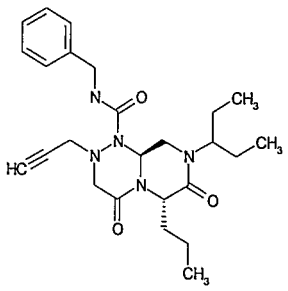
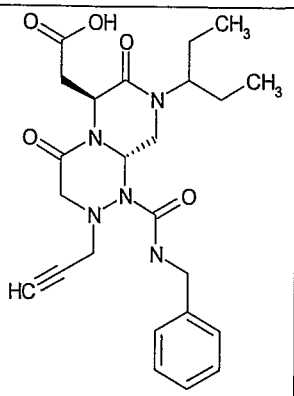
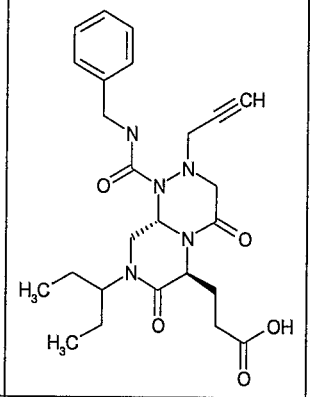
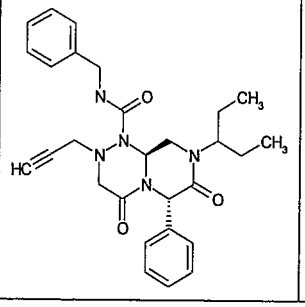
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1732		500	501
1733		468	469
1734		484	485
1735		498	499
1736		502	503

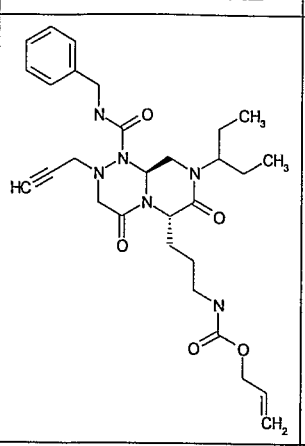
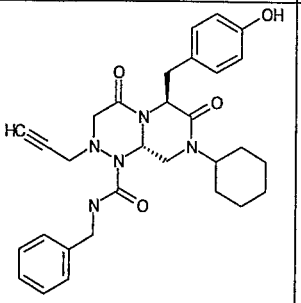
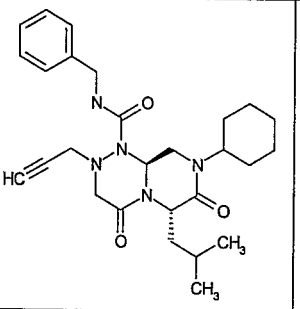
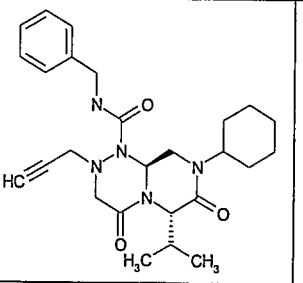
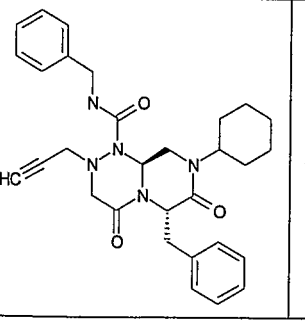
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1737		567	568
1738		642	643
1739		592	593
1740		578	579
1741		626	627

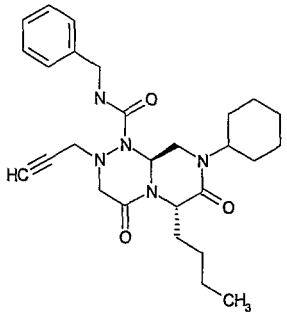
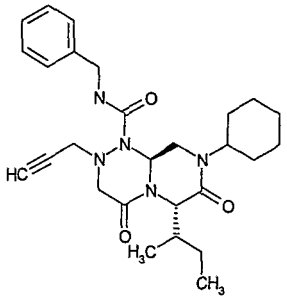
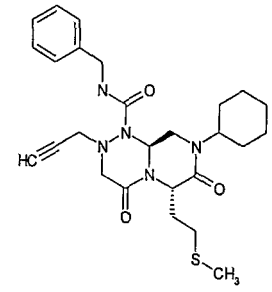
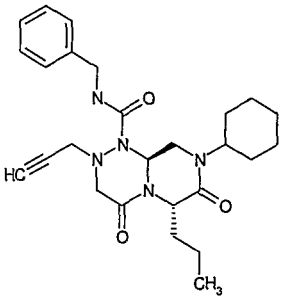
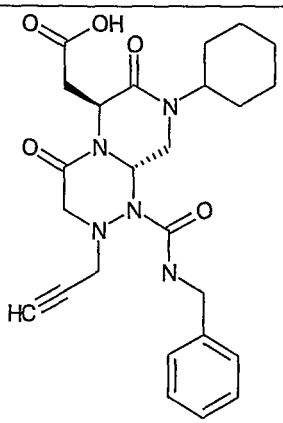
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1742		592	593
1743		592	593
1744		610	611
1745		578	579
1746		594	595

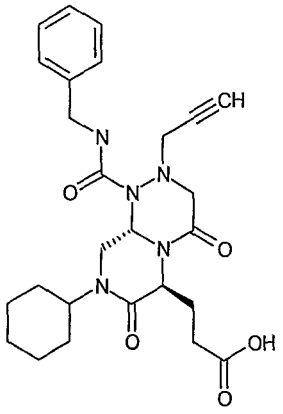
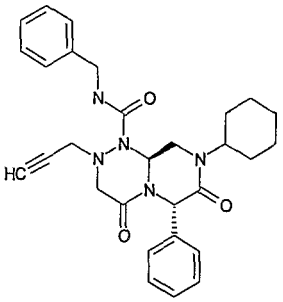
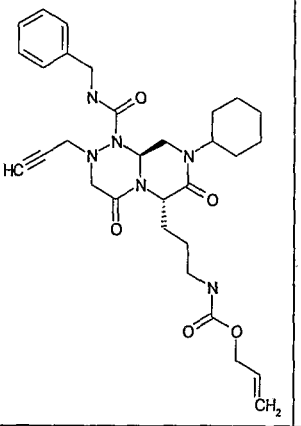
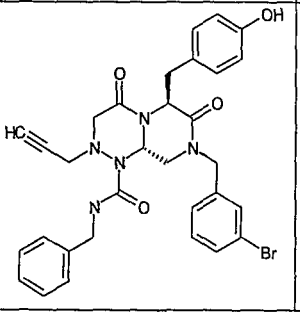
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1747		608	609
1748		612	613
1749		677	678
1750		518	519
1751		468	469

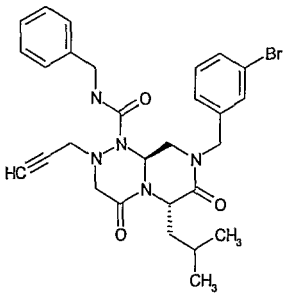
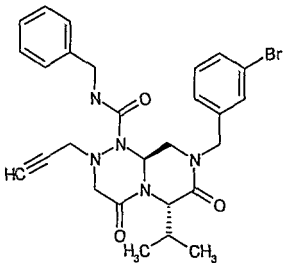
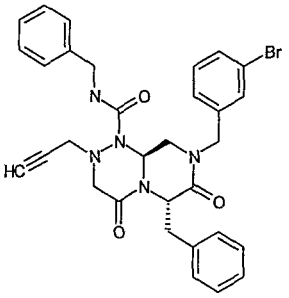
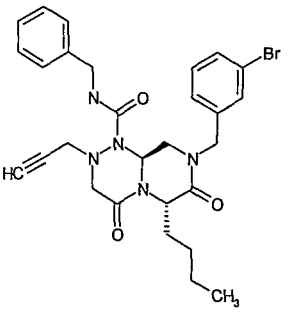
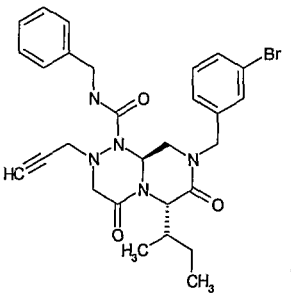
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1752		454	455
1753		502	503
1754		468	469
1755		468	469
1756		486	487

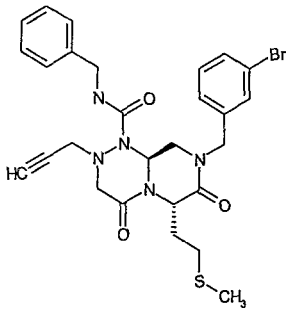
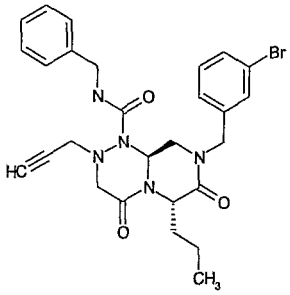
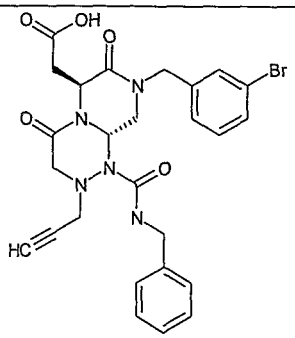
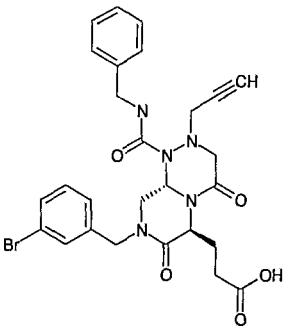
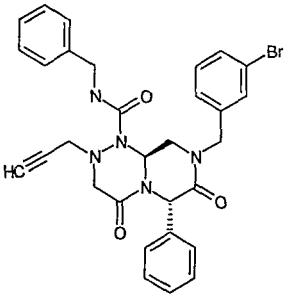
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1757		454	455
1758		470	471
1759		484	485
1760		488	489

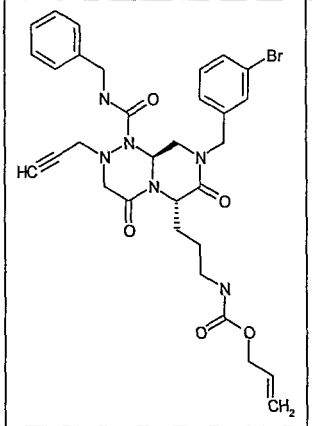
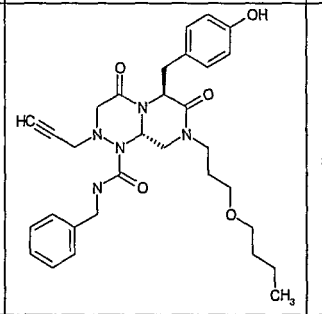
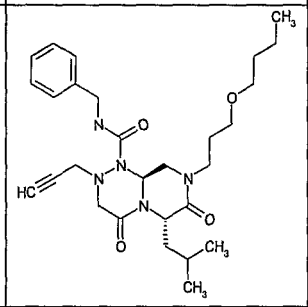
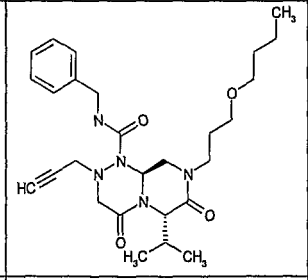
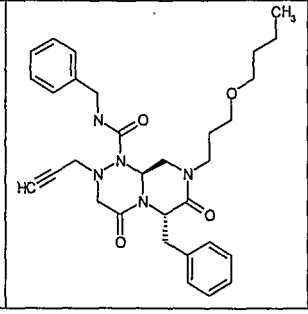
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1761		553	554
1762		530	531
1763		480	481
1764		466	467
1765		514	515

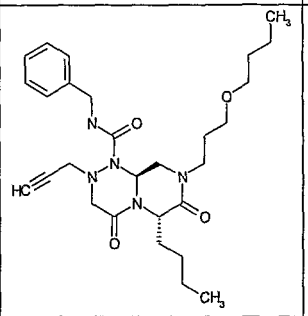
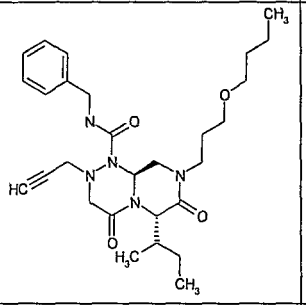
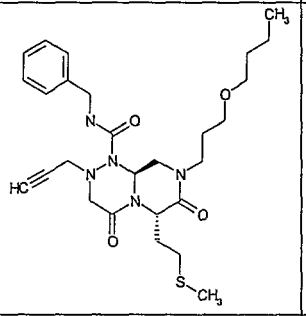
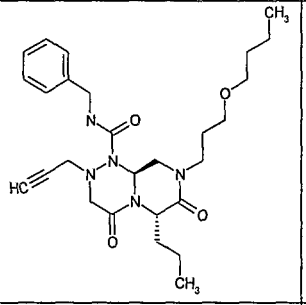
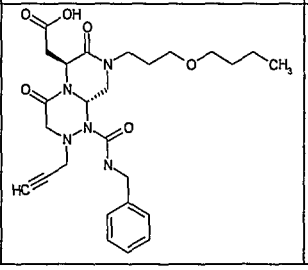
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1766		480	481
1767		480	481
1768		498	499
1769		466	467
1770		482	483

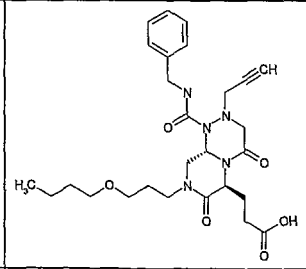
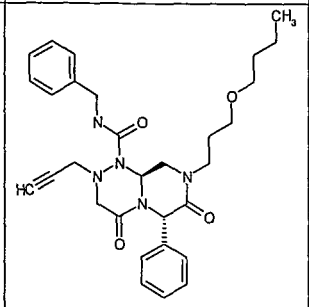
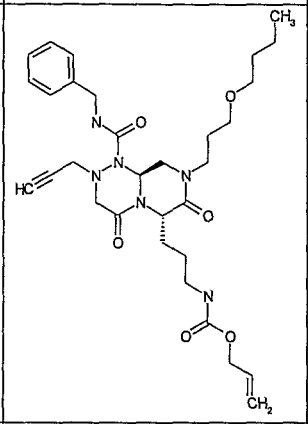
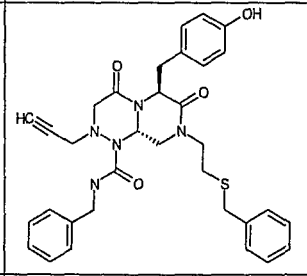
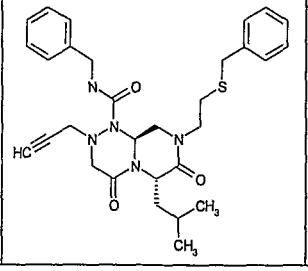
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1771		496	497
1772		500	501
1773		565	566
1774		617	618

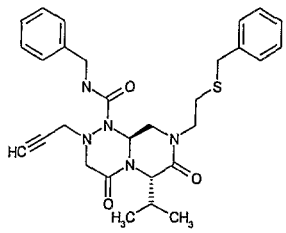
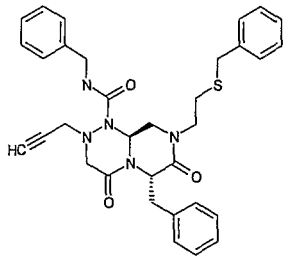
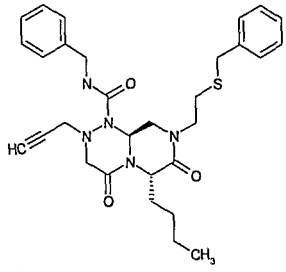
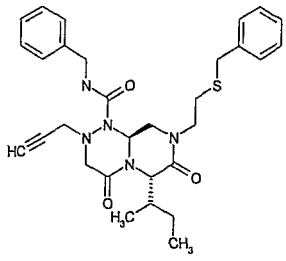
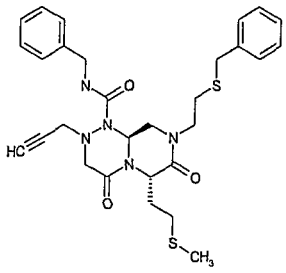
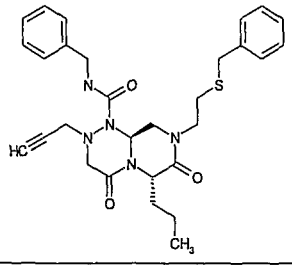
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1775		567	568
1776		552	553
1777		601	602
1778		567	568
1779		567	568

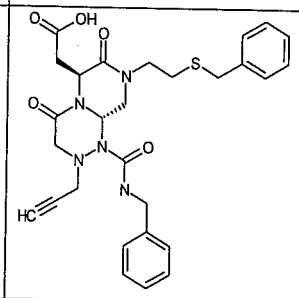
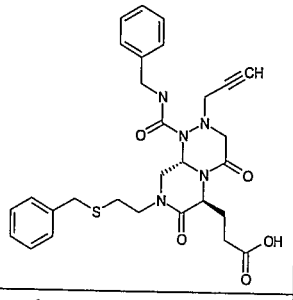
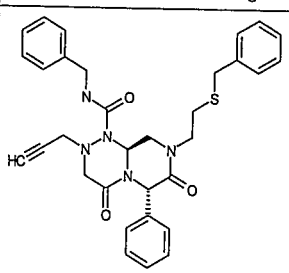
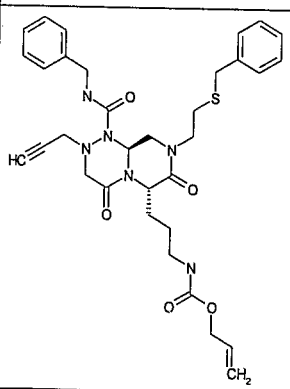
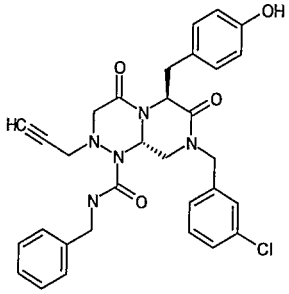
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1780		585	586
1781		552	553
1782		568	569
1783		582	583
1784		586	587

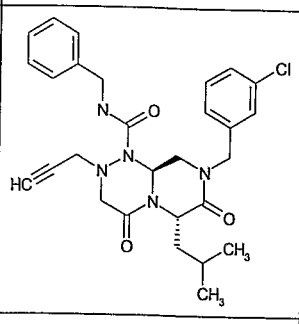
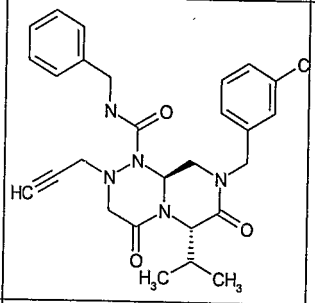
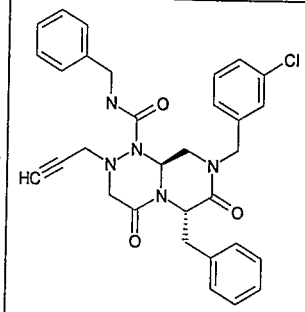
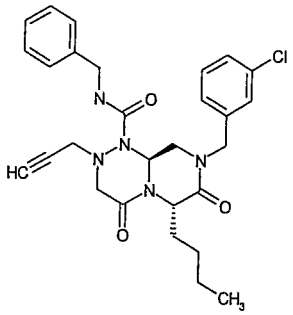
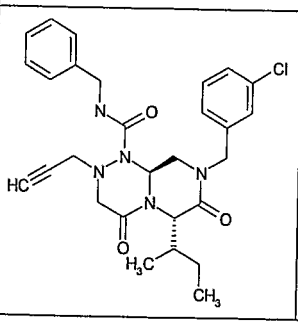
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1785		652	653
1786		562	563
1787		512	513
1788		498	499
1789		546	547

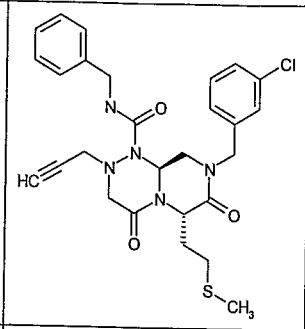
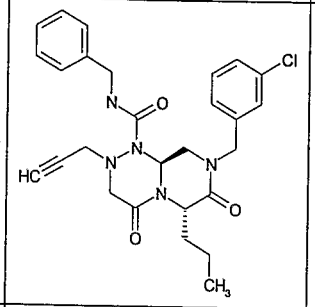
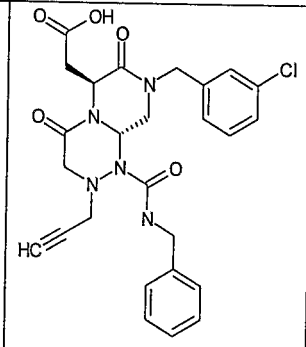
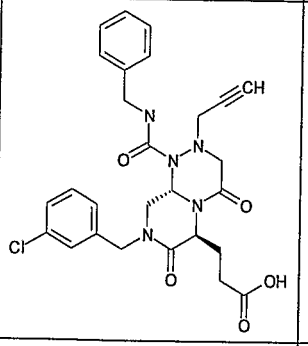
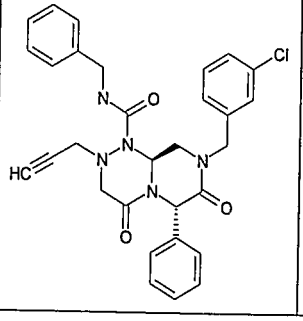
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1790		512	513
1791		512	513
1792		530	531
1793		498	499
1794		514	515

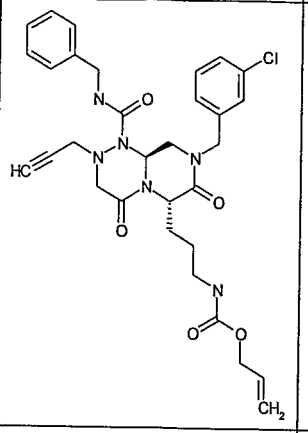
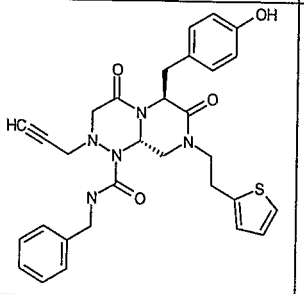
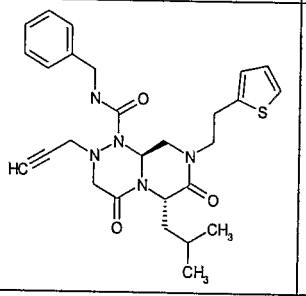
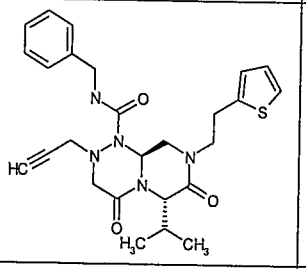
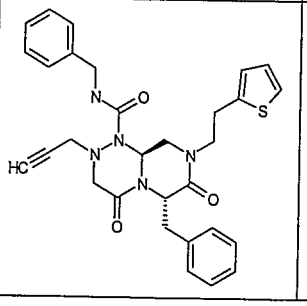
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1795		528	529
1796		532	533
1797		597	598
1798		598	599
1799		548	549

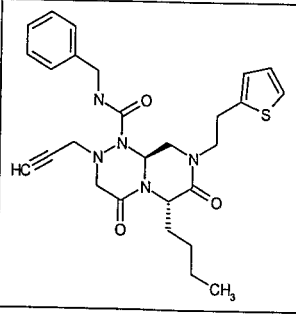
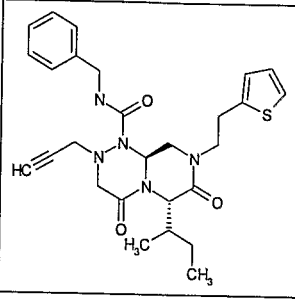
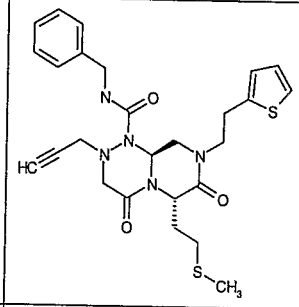
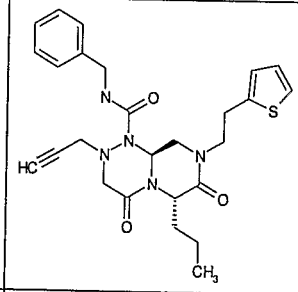
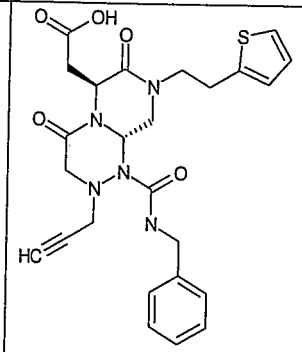
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1800		534	535
1801		582	583
1802		548	549
1803		548	549
1804		566	567
1805		534	535

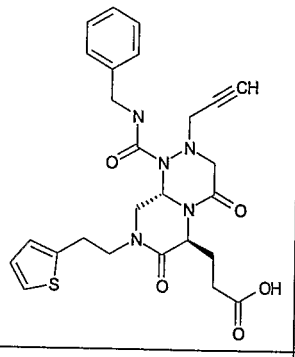
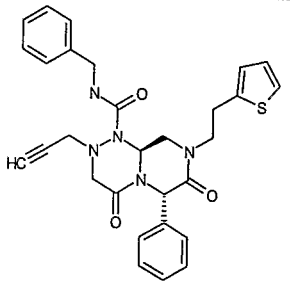
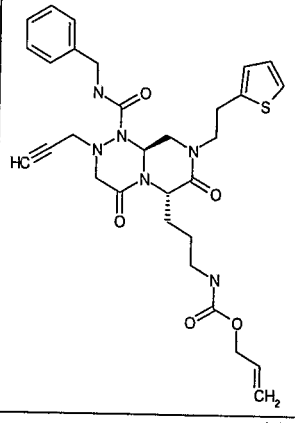
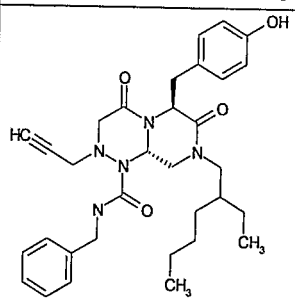
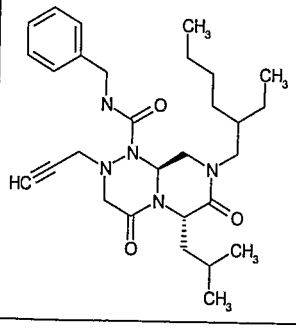
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1806		550	551
1807		564	565
1808		568	569
1809		633	634
1810		572	573

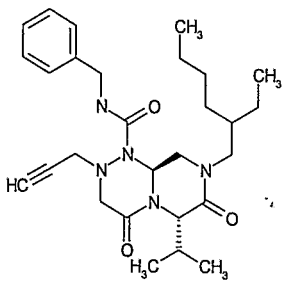
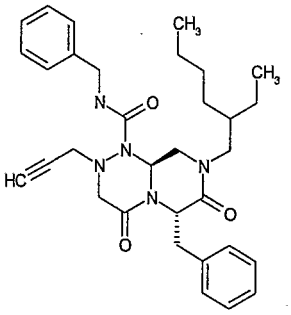
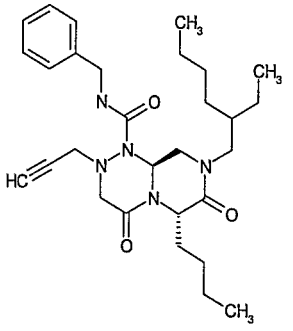
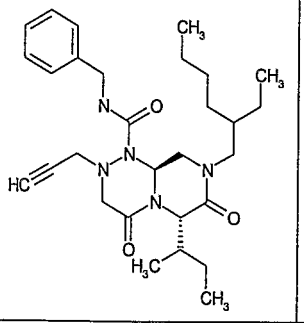
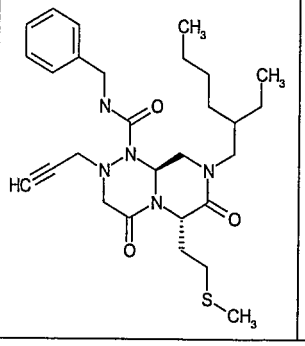
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1811		522	523
1812		508	509
1813		556	557
1814		522	523
1815		522	523

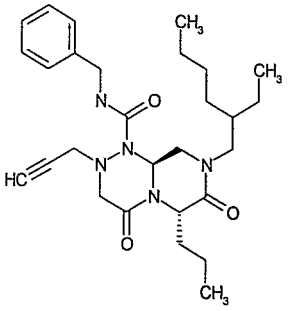
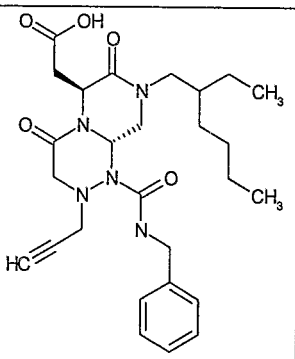
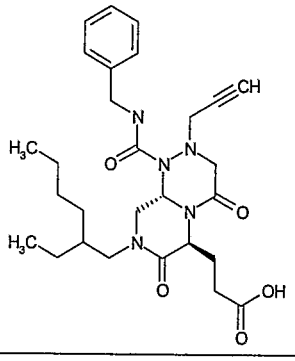
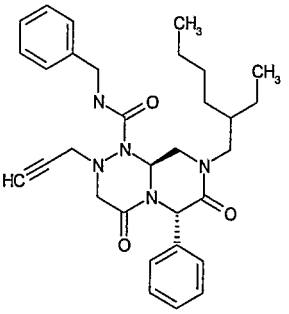
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1816		540	541
1817		508	509
1818		524	525
1819		538	539
1820		542	543

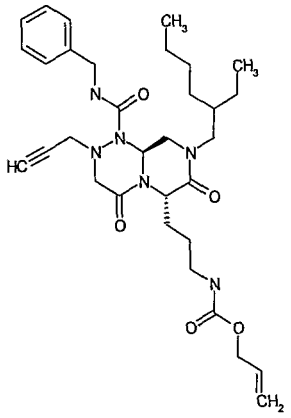
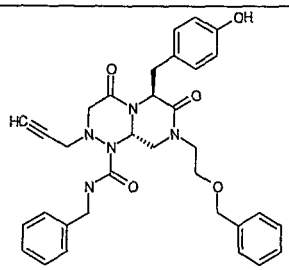
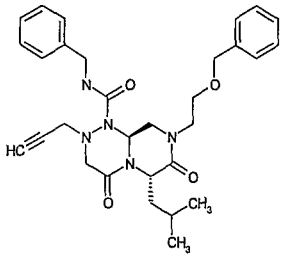
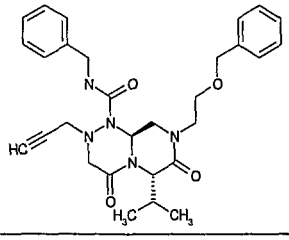
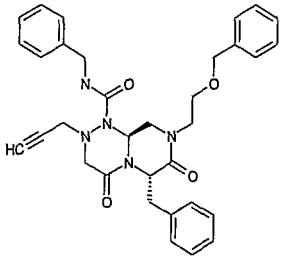
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1821		607	608
1822		558	559
1823		508	509
1824		494	495
1825		542	543

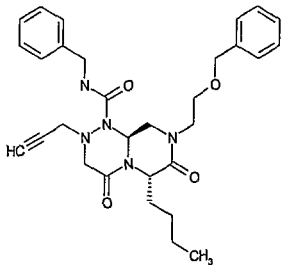
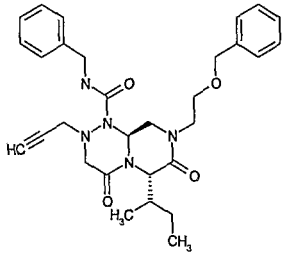
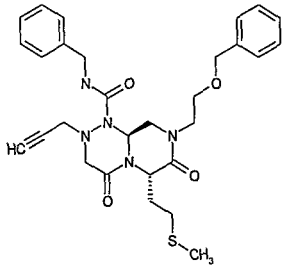
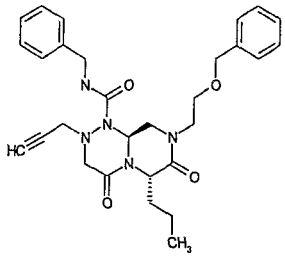
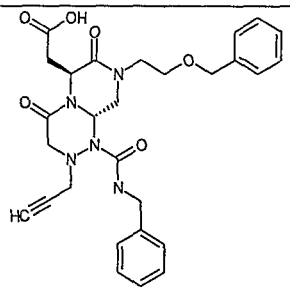
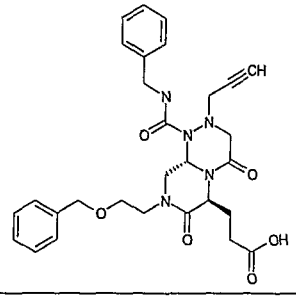
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1826		508	509
1827		508	509
1828		526	527
1829		494	495
1830		510	511

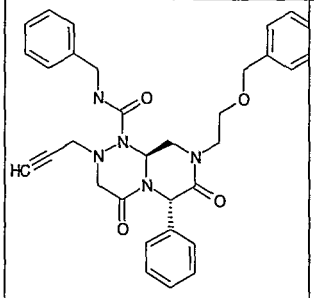
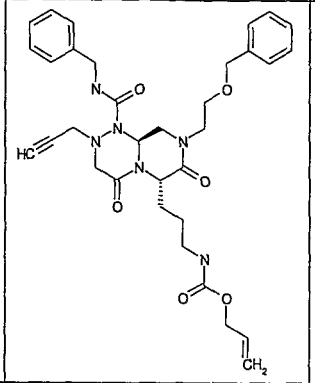
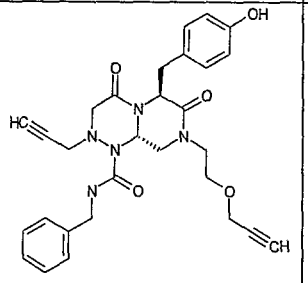
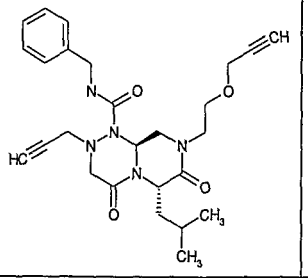
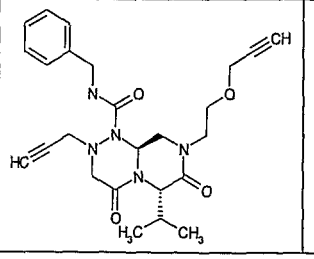
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1831		524	525
1832		528	529
1833		593	594
1834		560	561
1835		510	511

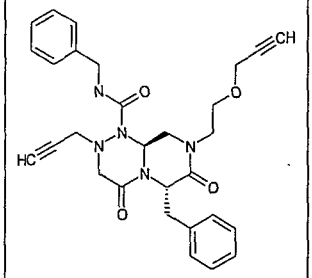
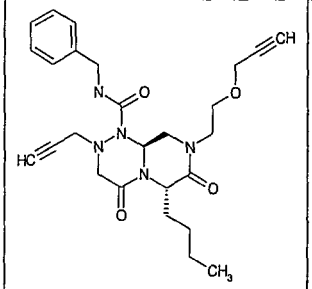
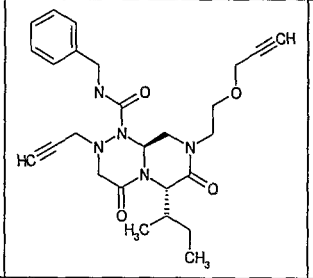
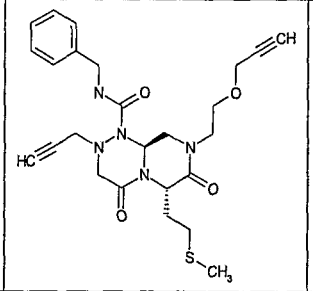
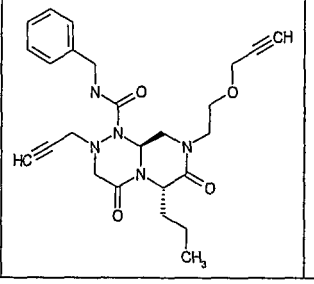
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1836		496	497
1837		544	545
1838		510	511
1839		510	511
1840		528	529

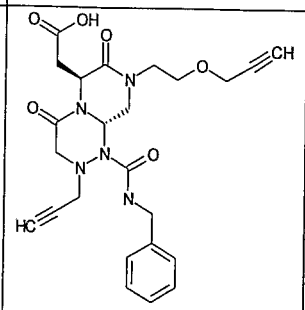
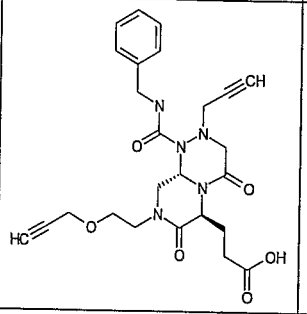
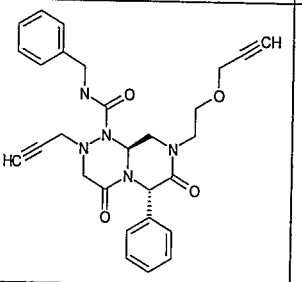
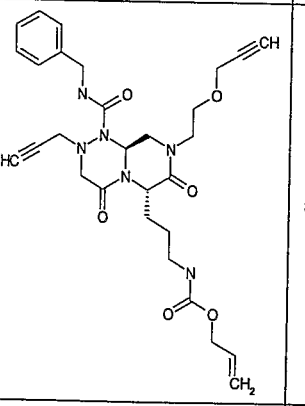
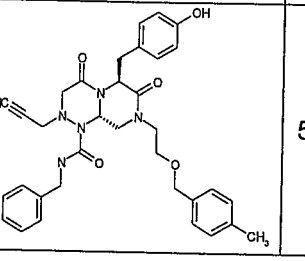
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1841		496	497
1842		512	513
1843		526	527
1844		530	531

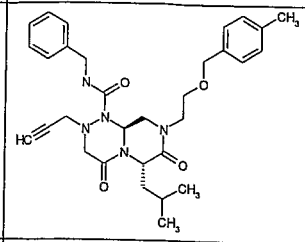
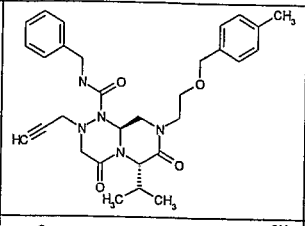
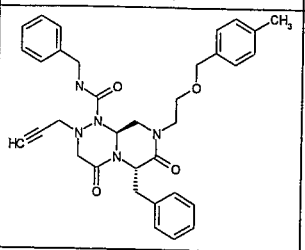
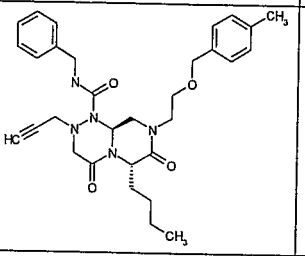
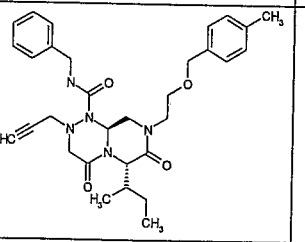
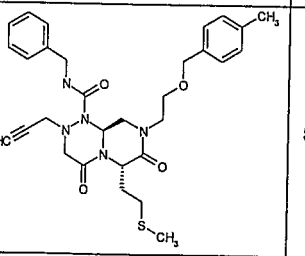
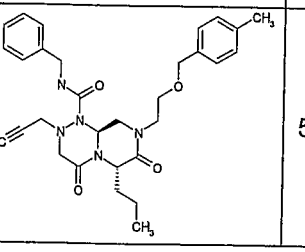
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1845		595	596
1846		582	583
1847		532	533
1848		518	519
1849		566	567

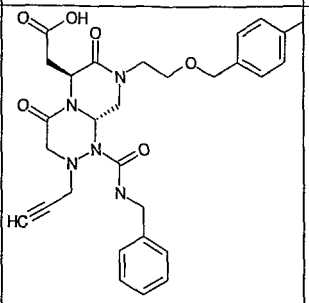
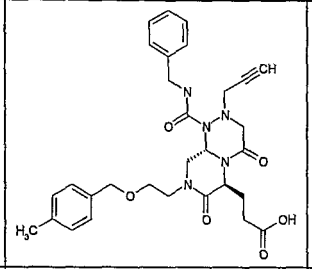
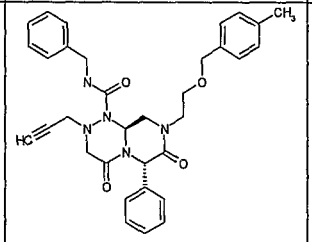
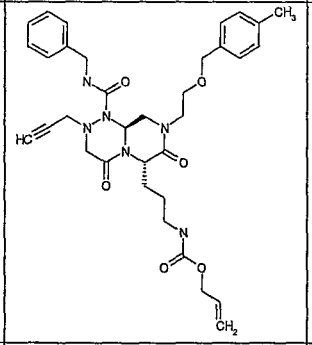
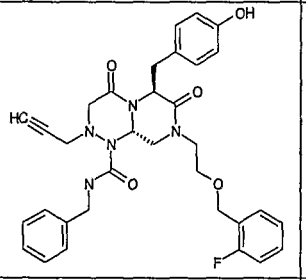
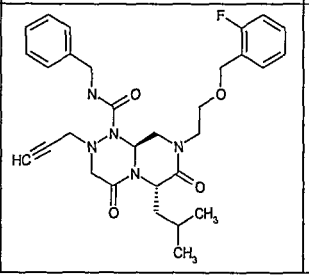
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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1851		532	533
1852		550	551
1853		518	519
1854		534	535
1855		548	549

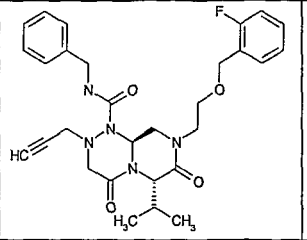
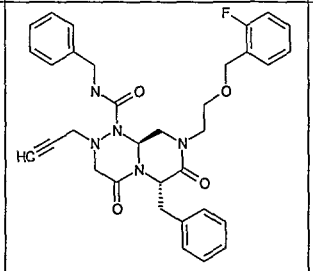
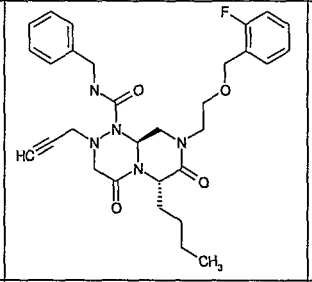
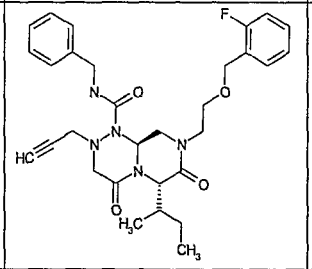
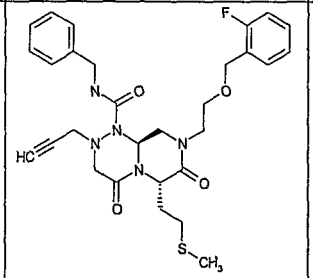
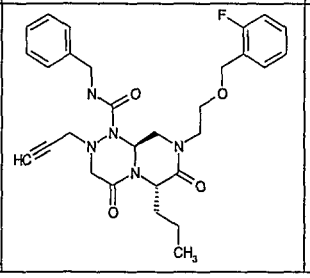
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1856		552	553
1857		617	618
1858		530	531
1859		480	481
1860		466	467

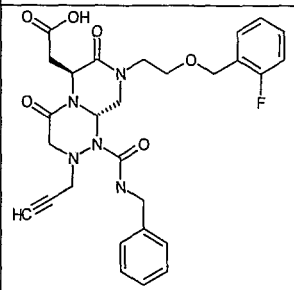
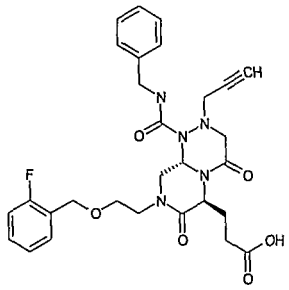
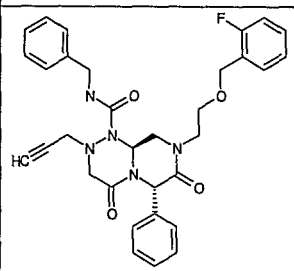
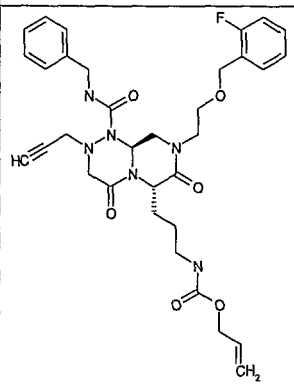
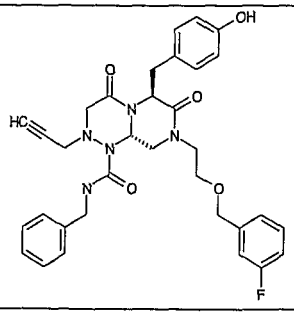
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1861		514	515
1862		480	481
1863		480	481
1864		498	499
1865		466	467

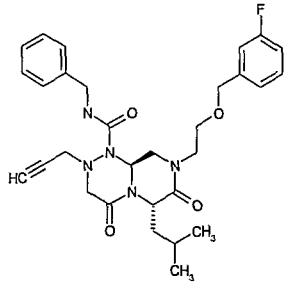
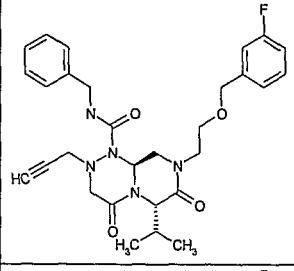
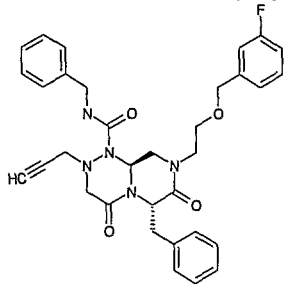
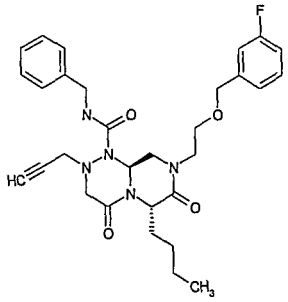
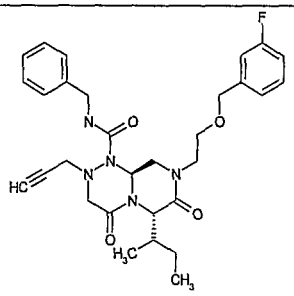
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1866		482	483
1867		496	497
1868		500	501
1869		565	566
1870		596	597

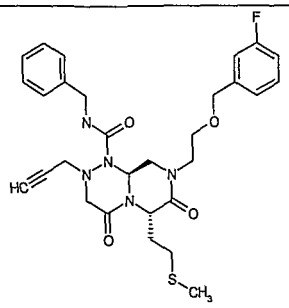
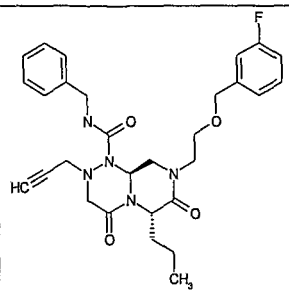
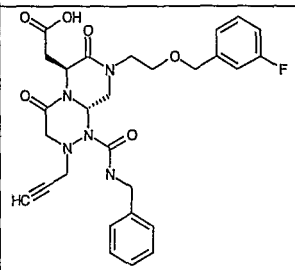
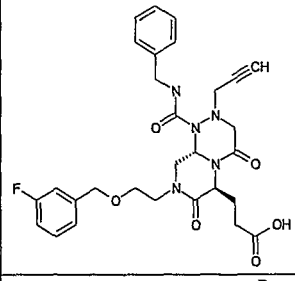
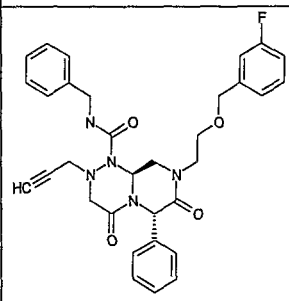
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1871		546	547
1872		532	533
1873		580	581
1874		546	547
1875		546	547
1876		564	565
1877		532	533

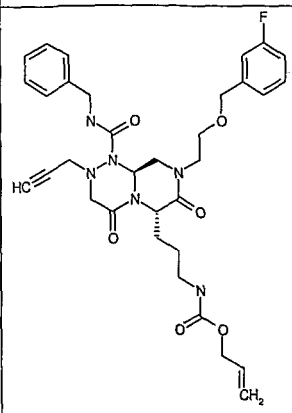
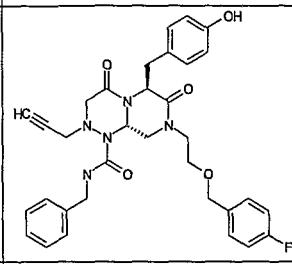
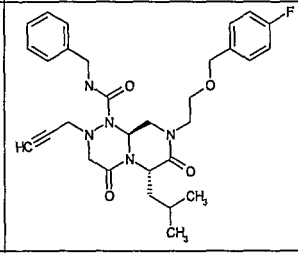
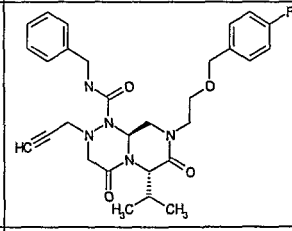
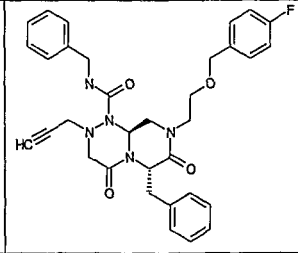
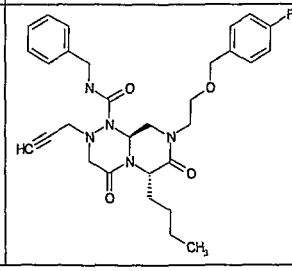
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1878		548	549
1879		562	563
1880		566	567
1881		631	632
1882		600	601
1883		550	551

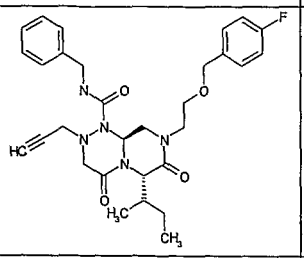
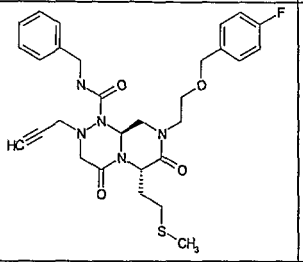
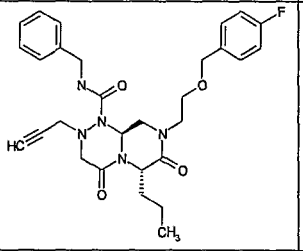
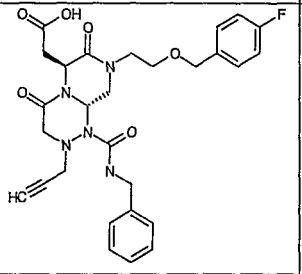
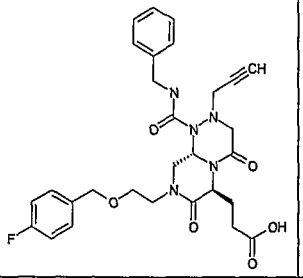
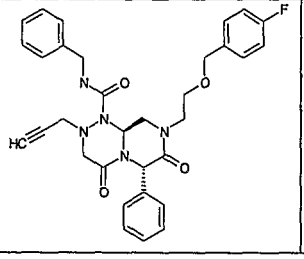
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1884		536	537
1885		584	585
1886		550	551
1887		550	551
1888		568	569
1889		536	537

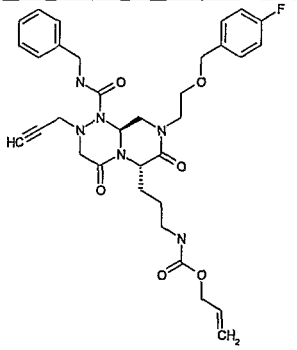
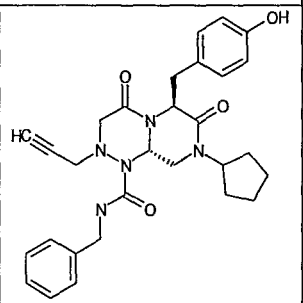
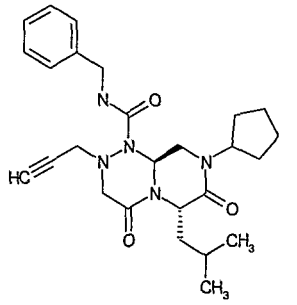
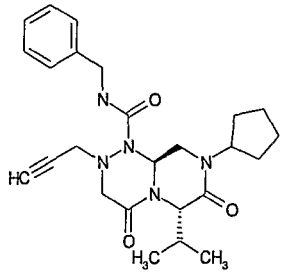
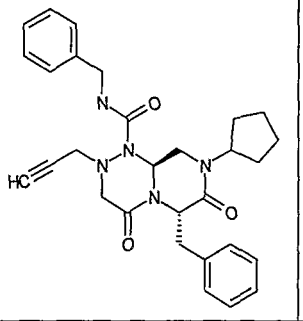
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1890		552	553
1891		566	567
1892		570	571
1893		635	636
1894		600	601

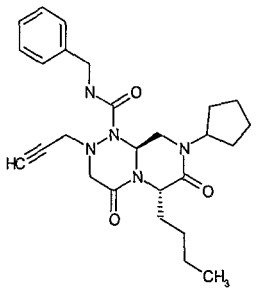
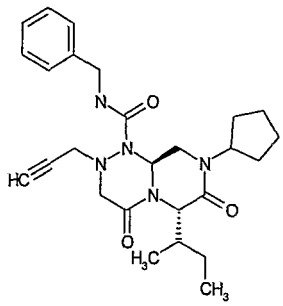
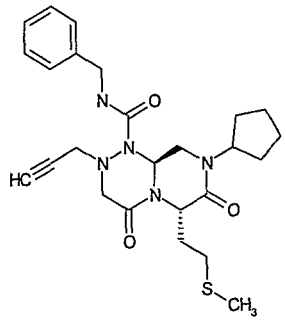
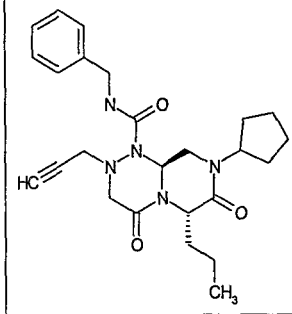
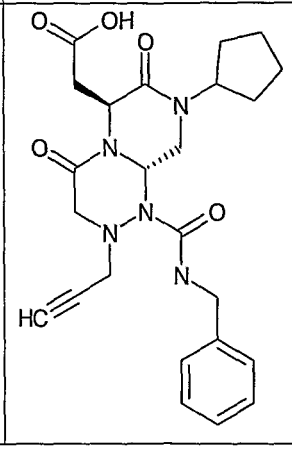
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1895		550	551
1896		536	537
1897		584	585
1898		550	551
1899		550	551

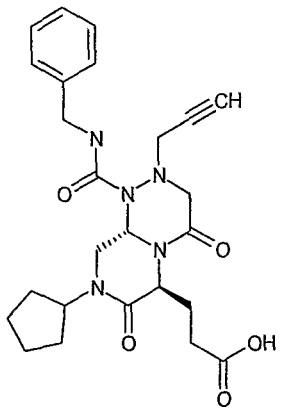
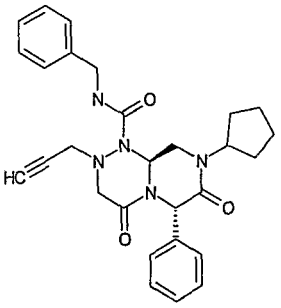
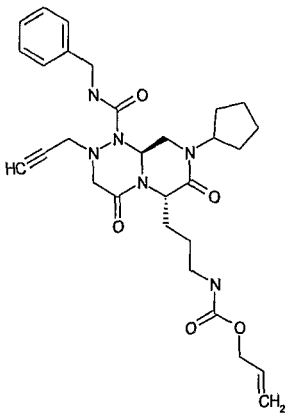
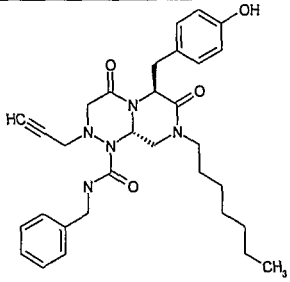
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1900		568	569
1901		536	537
1902		552	553
1903		566	567
1904		570	571

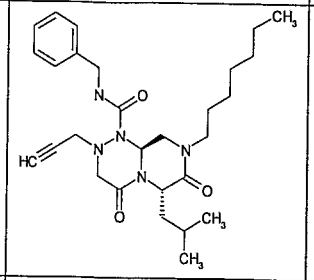
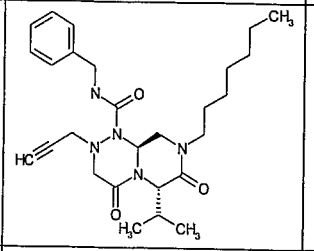
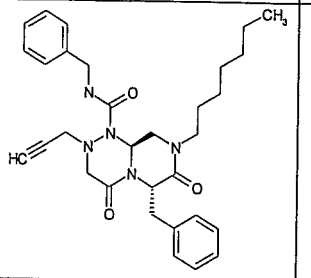
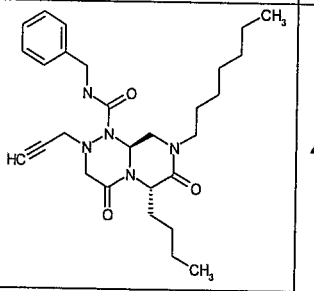
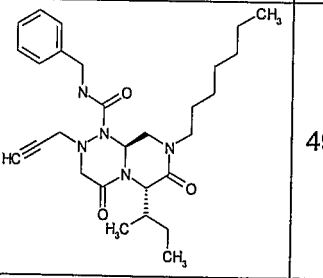
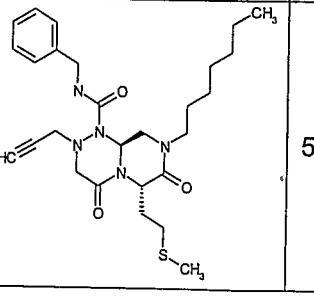
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1905		635	636
1906		600	601
1907		550	551
1908		536	537
1909		584	585
1910		550	551

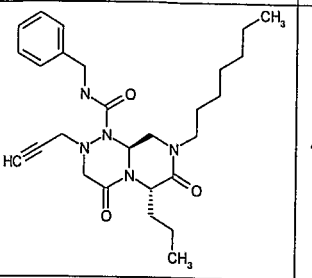
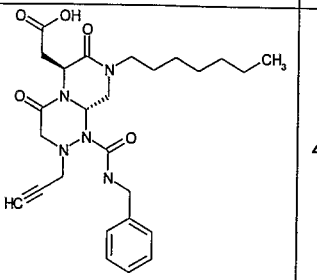
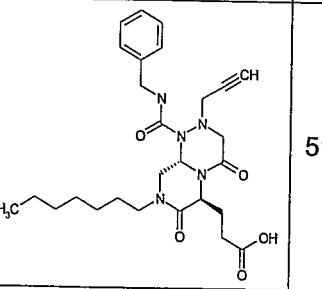
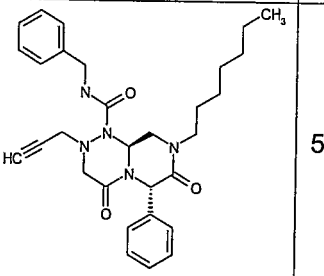
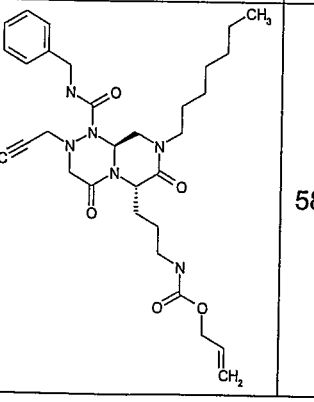
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1911		550	551
1912		568	569
1913		536	537
1914		552	553
1915		566	567
1916		570	571

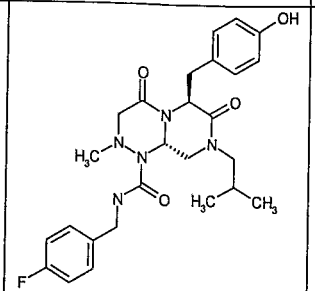
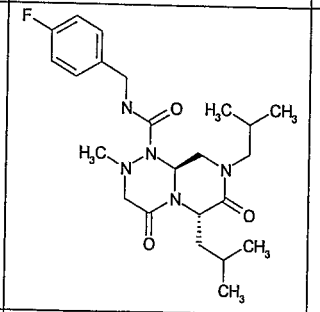
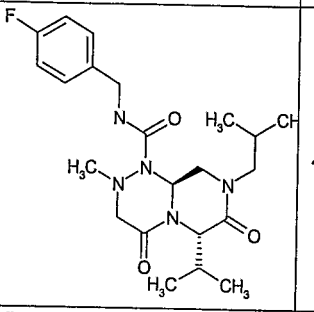
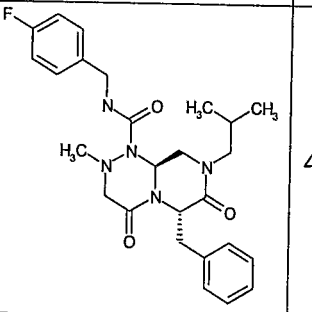
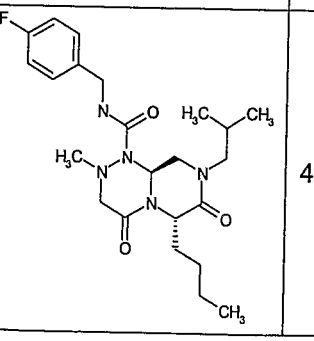
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1917		635	636
1918		516	517
1919		466	467
1920		452	453
1921		500	501

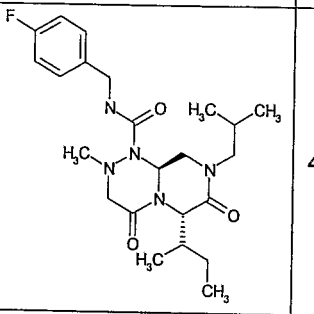
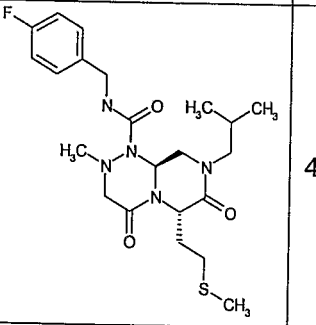
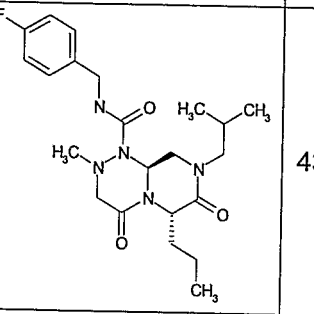
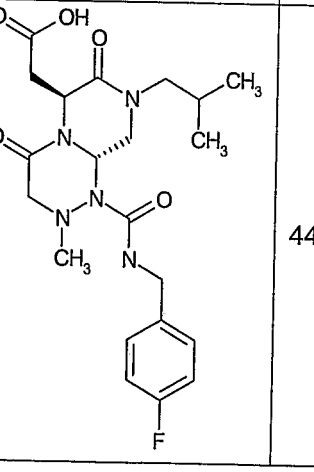
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1922		466	467
1923		466	467
1924		484	485
1925		452	453
1926		468	469

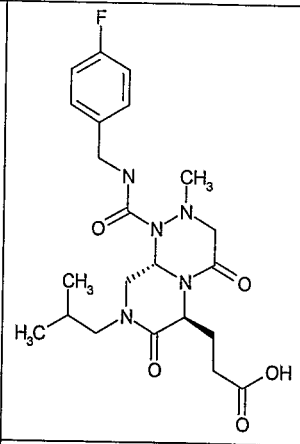
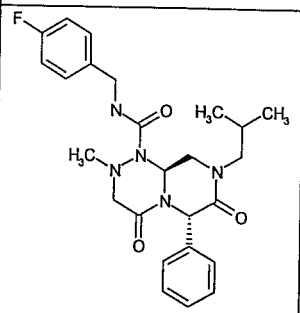
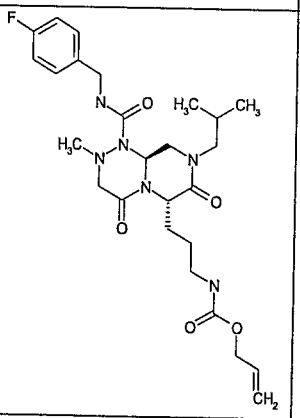
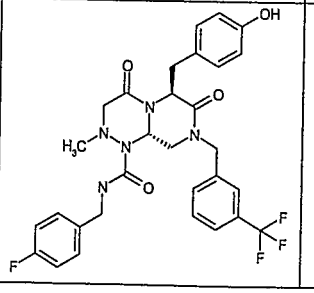
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1927		482	483
1928		486	487
1929		551	552
1930		546	547

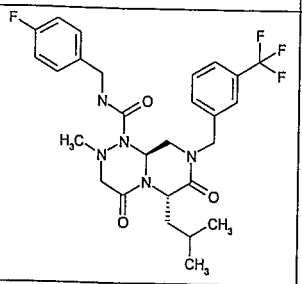
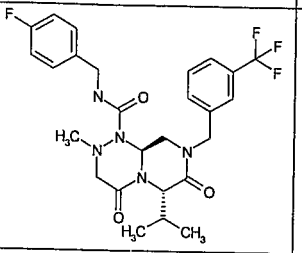
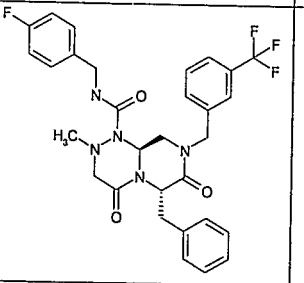
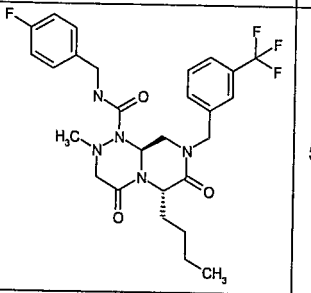
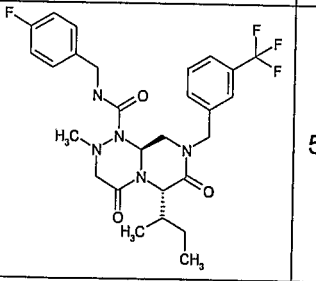
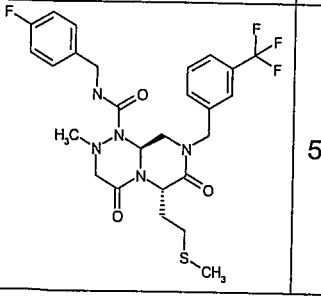
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1931		496	497
1932		482	483
1933		530	531
1934		496	497
1935		496	497
1936		514	515

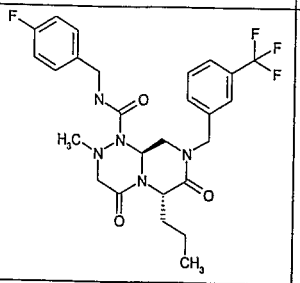
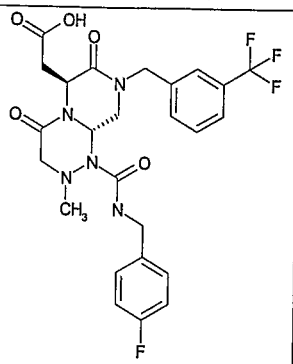
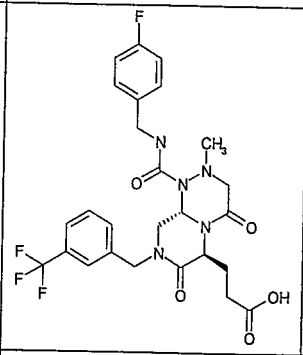
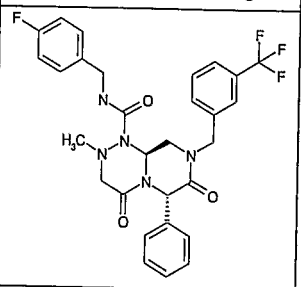
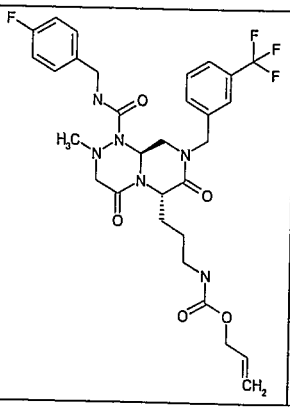
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1937		482	483
1938		498	499
1939		512	513
1940		516	517
1941		581	582

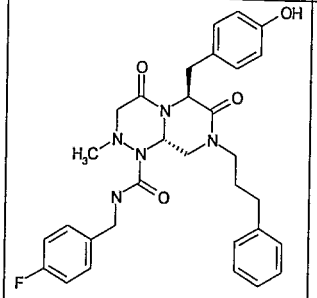
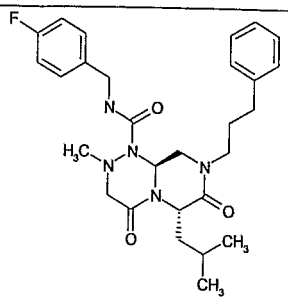
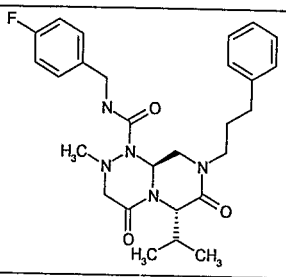
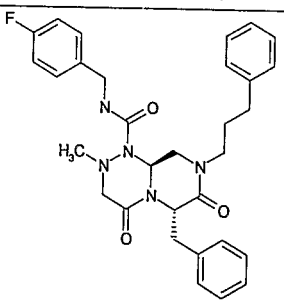
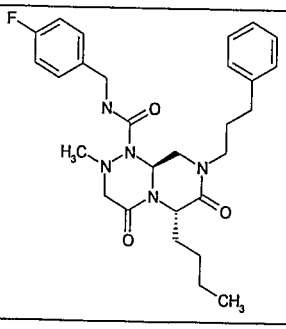
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1942		498	499
1943		448	449
1944		434	435
1945		482	483
1946		448	449

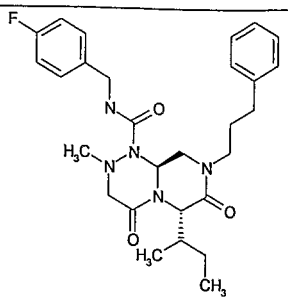
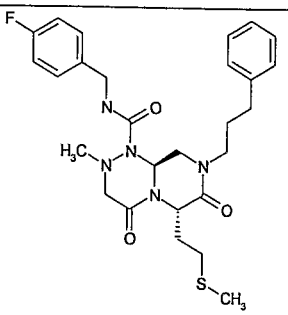
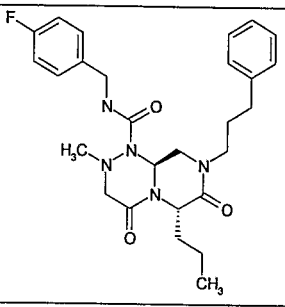
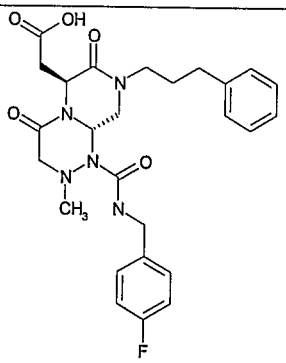
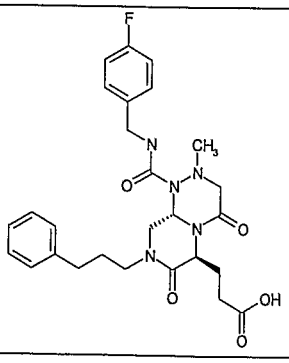
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1947		448	449
1948		466	467
1949		434	435
1950		449	450

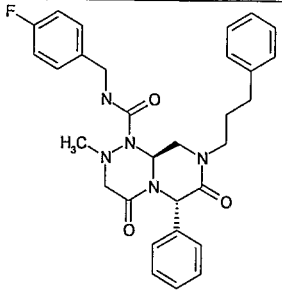
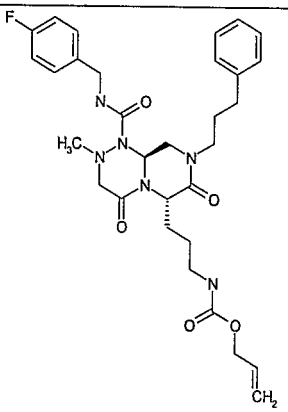
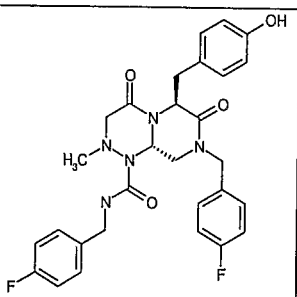
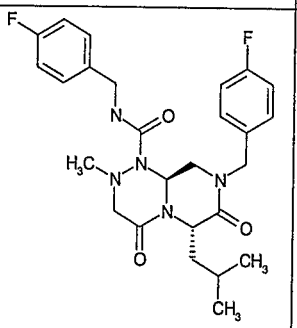
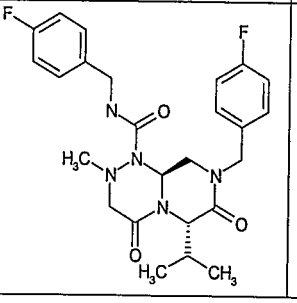
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1951		464	465
1952		468	469
1953		533	534
1954		600	601

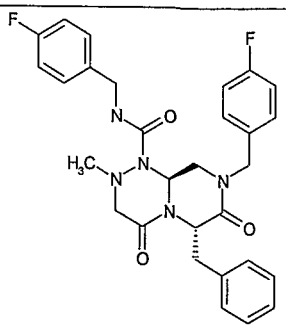
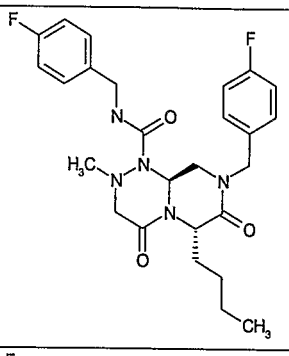
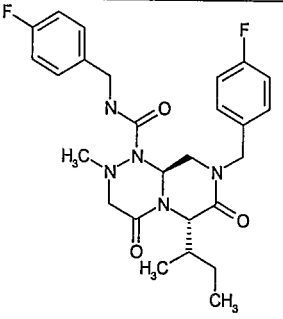
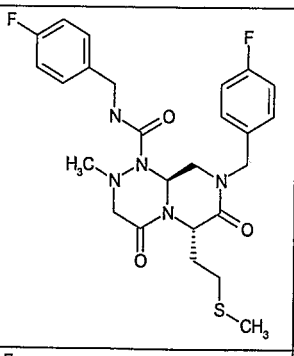
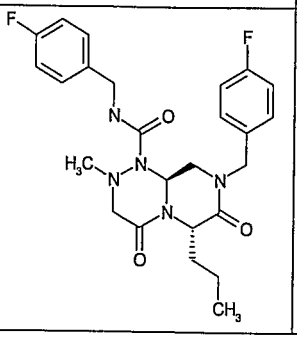
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1955		550	551
1956		536	537
1957		584	585
1958		550	551
1959		550	551
1960		568	569

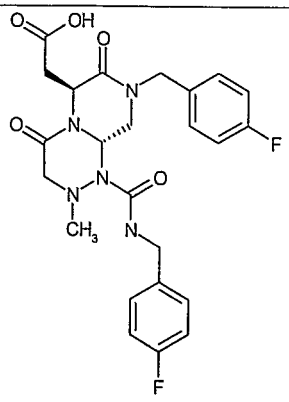
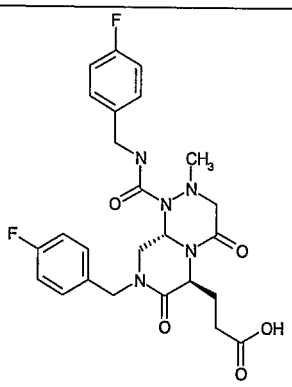
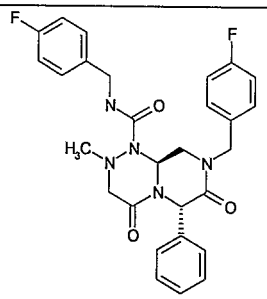
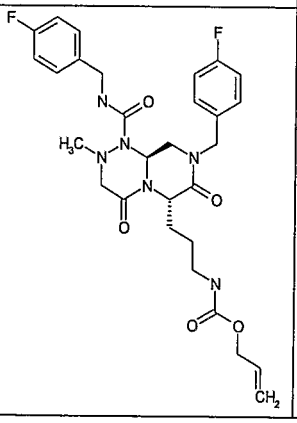
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1961		536	537
1962		552	553
1963		566	567
1964		570	571
1965		635	636

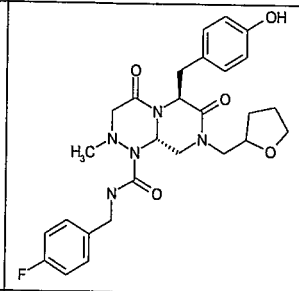
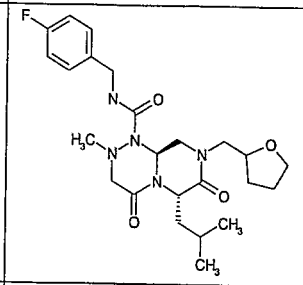
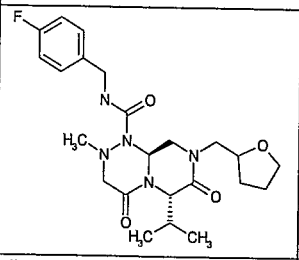
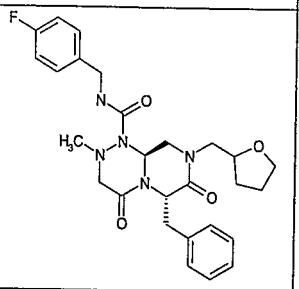
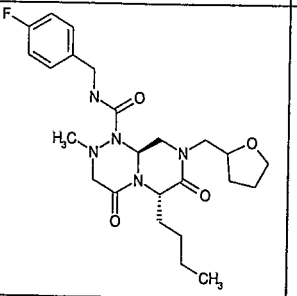
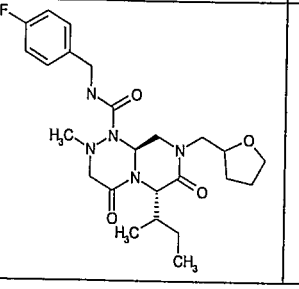
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1966		560	561
1967		510	511
1968		496	497
1969		544	545
1970		510	511

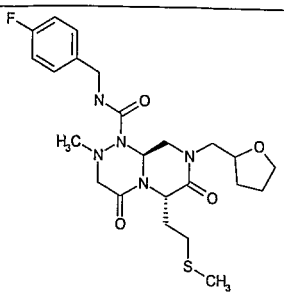
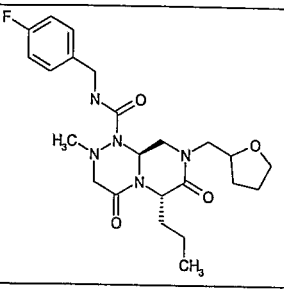
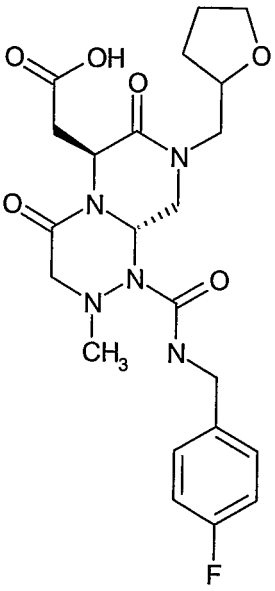
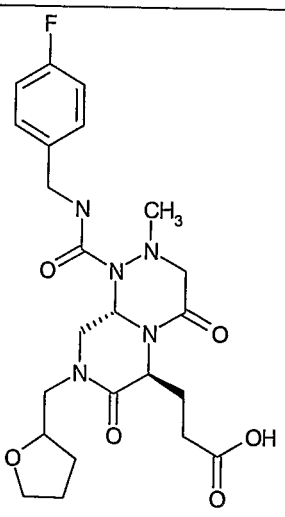
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1971		510	511
1972		528	529
1973		496	497
1974		512	513
1975		526	527

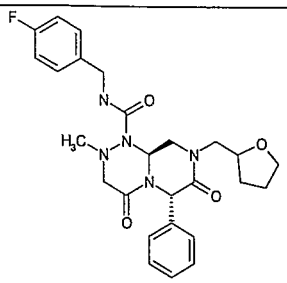
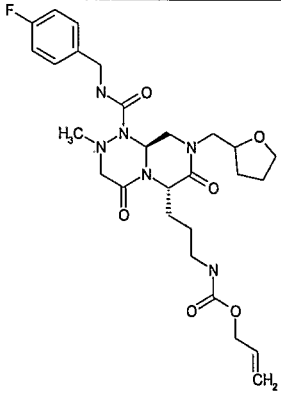
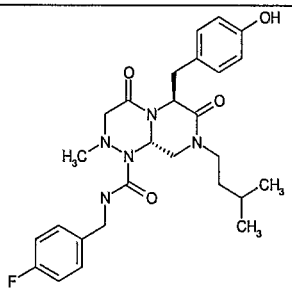
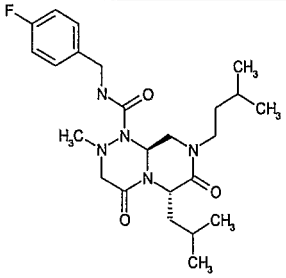
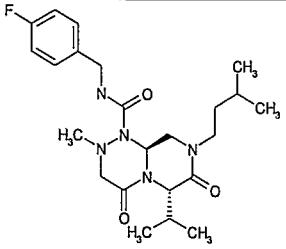
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1976		530	531
1977		595	596
1978		550	551
1979		500	501
1980		486	487

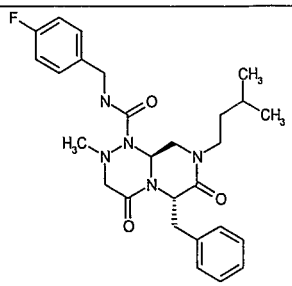
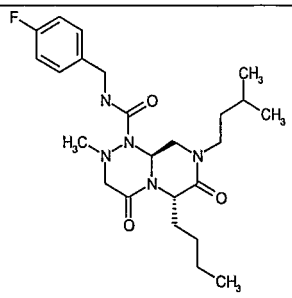
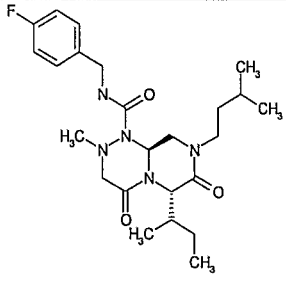
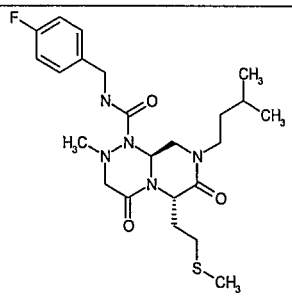
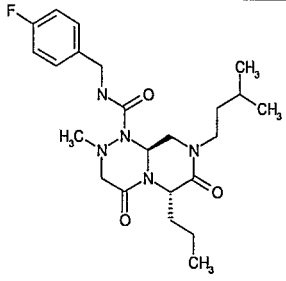
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1981		534	535
1982		500	501
1983		500	501
1984		518	519
1985		486	487

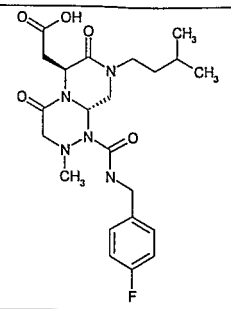
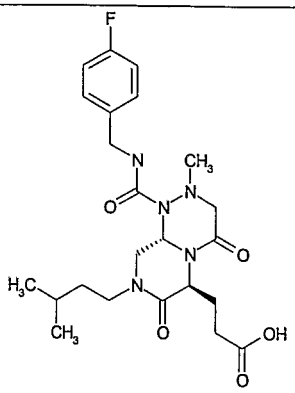
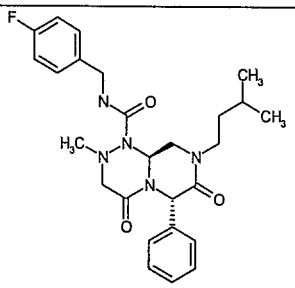
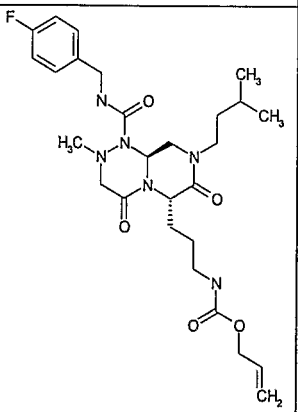
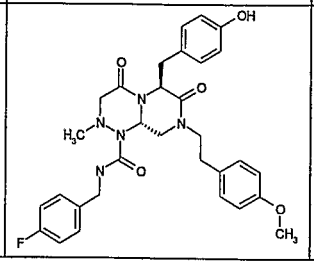
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1986		501	502
1987		516	517
1988		520	521
1989		585	586

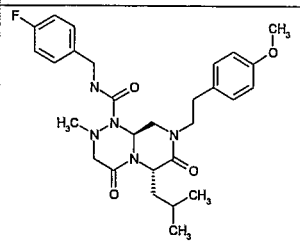
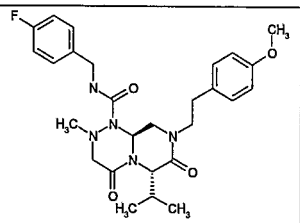
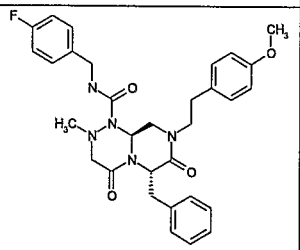
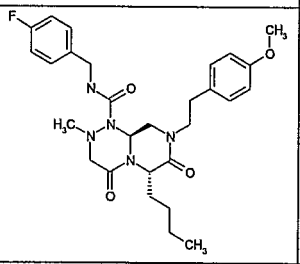
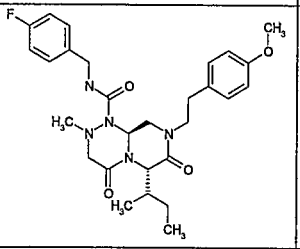
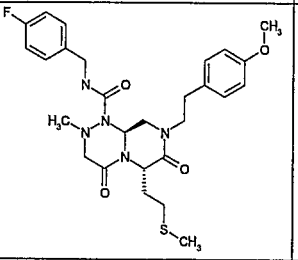
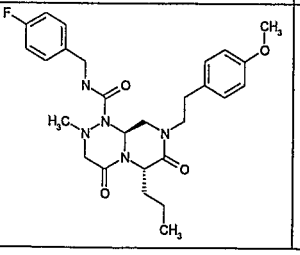
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1990		526	527
1991		476	477
1992		462	463
1993		510	511
1994		476	477
1995		476	477

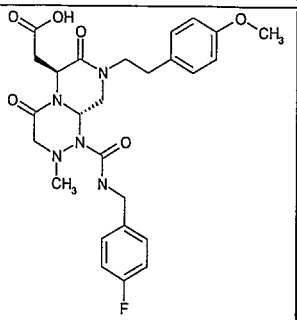
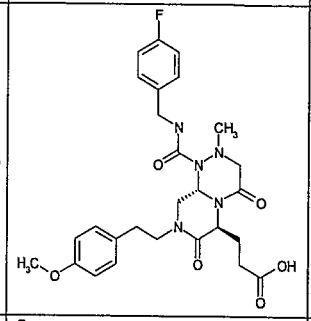
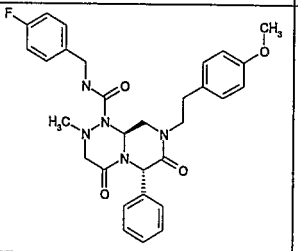
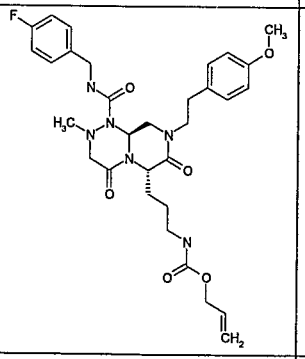
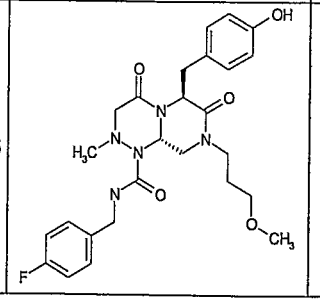
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
1996		494	495
1997		462	463
1998		477	478
1999		492	493

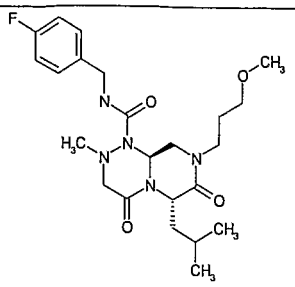
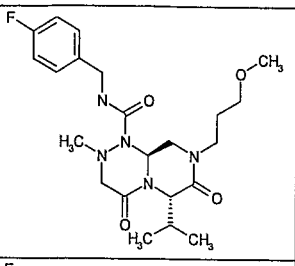
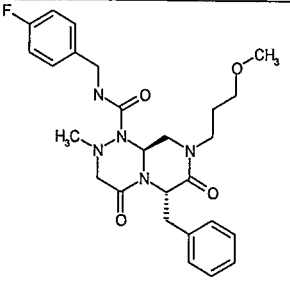
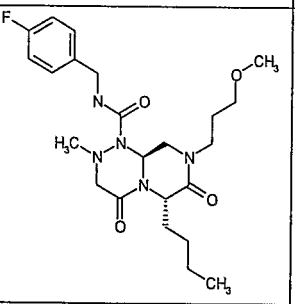
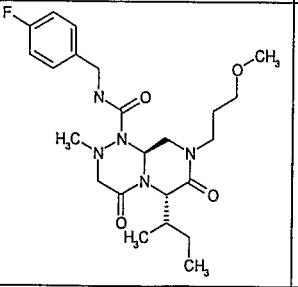
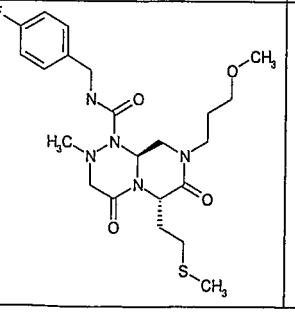
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2000		496	497
2001		561	562
2002		512	513
2003		462	463
2004		448	449

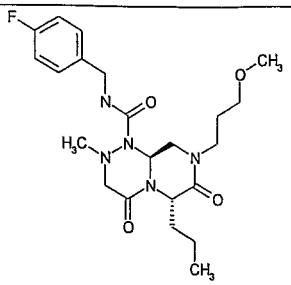
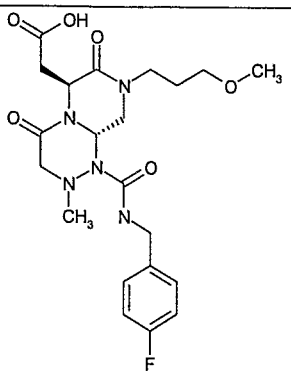
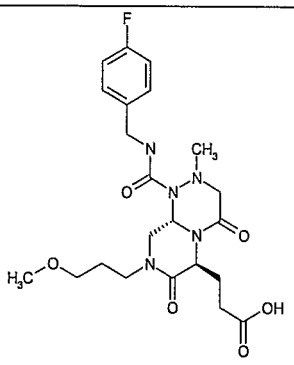
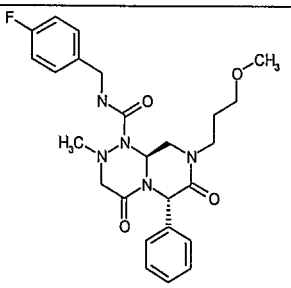
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2005		496	497
2006		462	463
2007		462	463
2008		480	481
2009		448	449

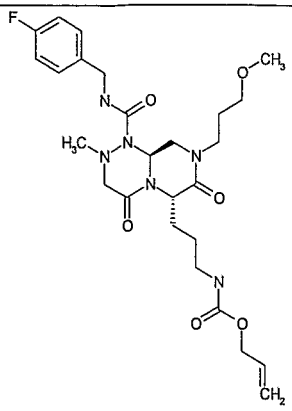
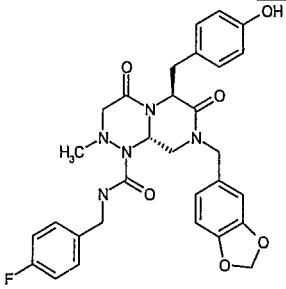
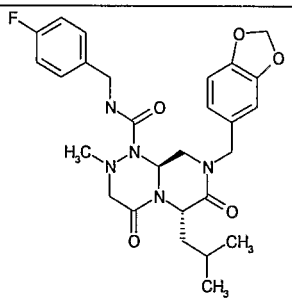
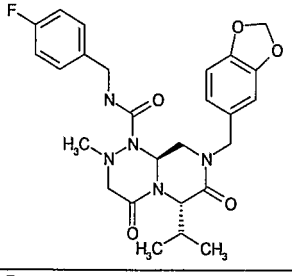
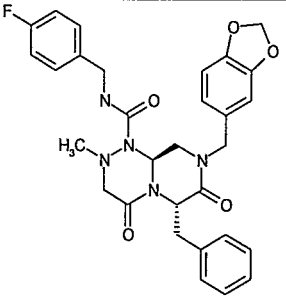
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2010		464	465
2011		478	479
2012		482	483
2013		547	548
2014		576	577

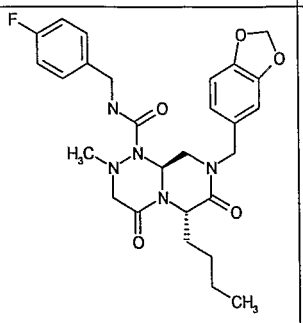
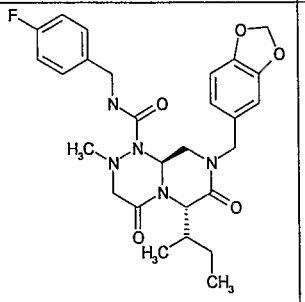
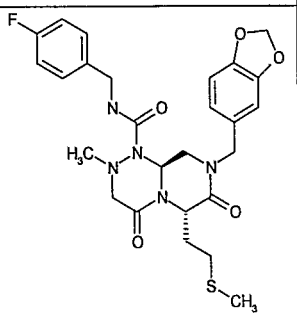
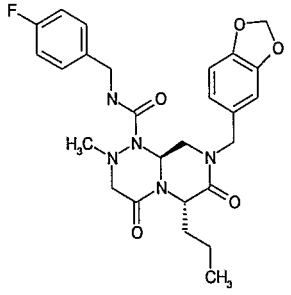
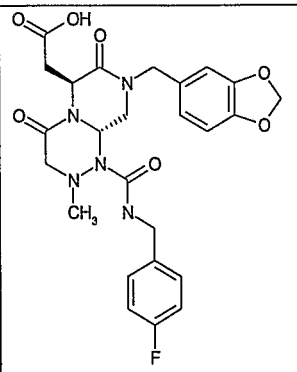
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2015		526	527
2016		512	513
2017		560	561
2018		526	527
2019		526	527
2020		544	545
2021		512	513

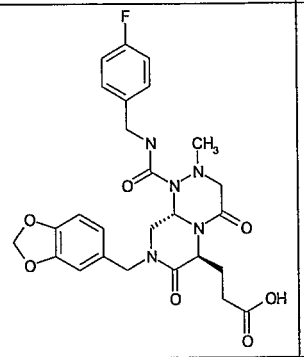
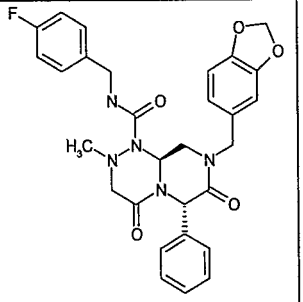
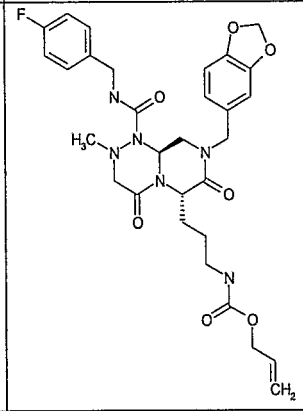
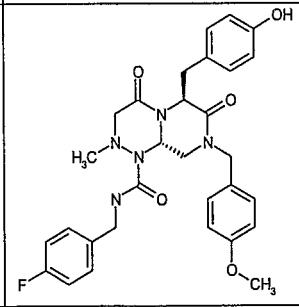
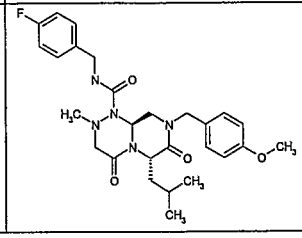
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2022		528	529
2023		542	543
2024		546	547
2025		611	612
2026		514	515

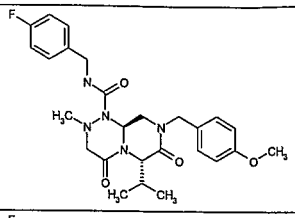
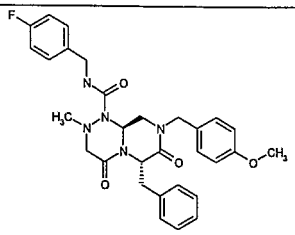
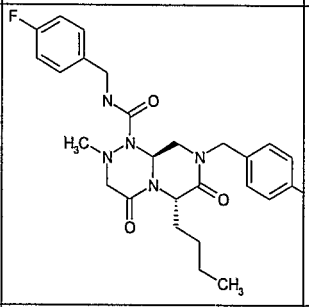
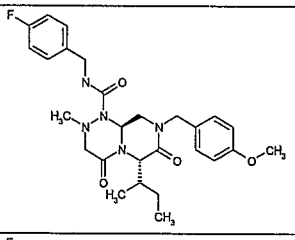
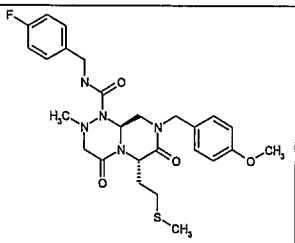
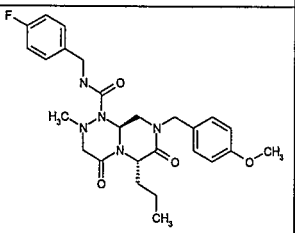
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2027		464	465
2028		450	451
2029		498	499
2030		464	465
2031		464	465
2032		482	483

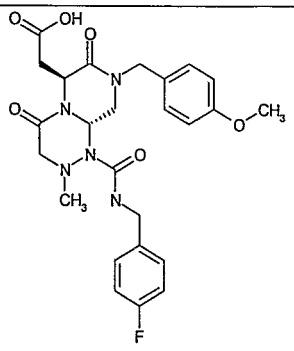
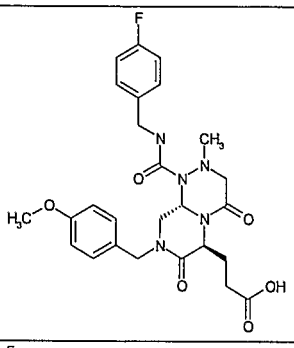
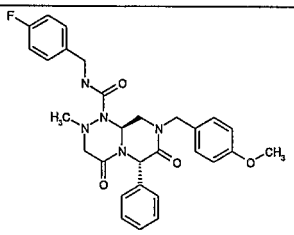
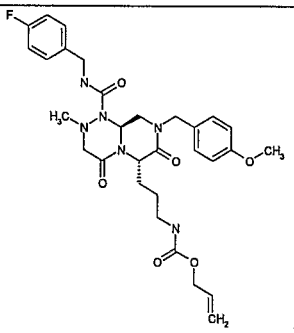
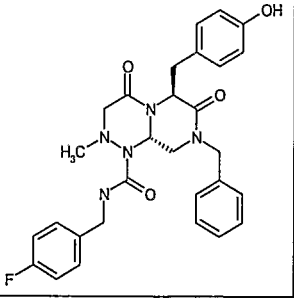
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2033		450	451
2034		465	466
2035		480	481
2036		484	485

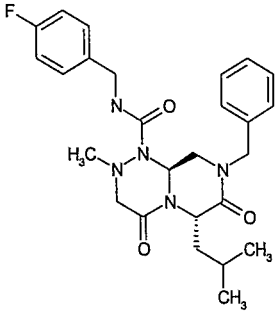
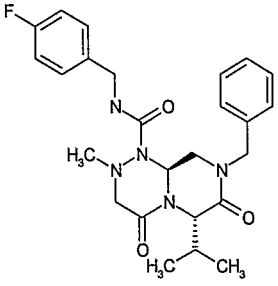
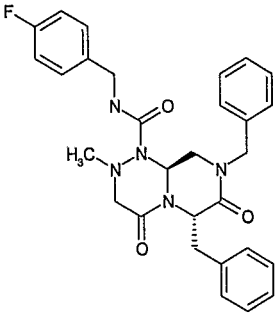
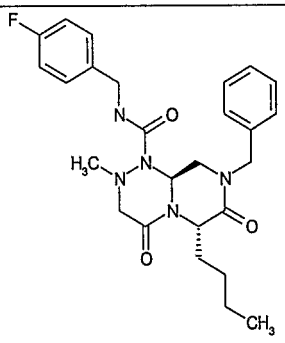
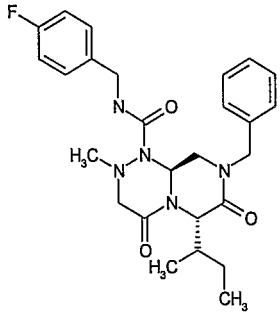
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2037		549	550
2038		576	577
2039		526	527
2040		512	513
2041		560	561

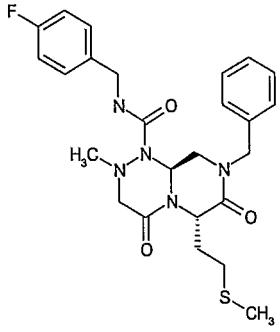
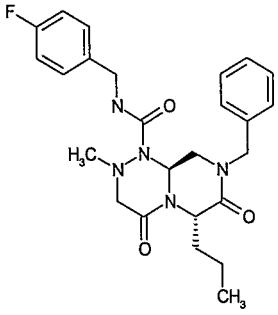
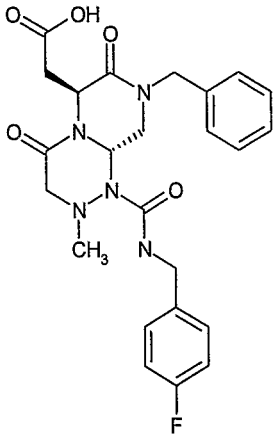
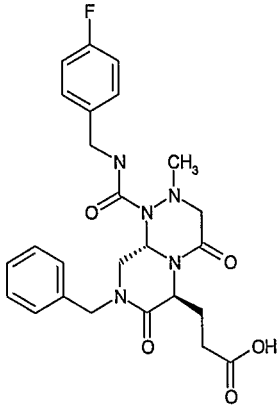
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2042		526	527
2043		526	527
2044		544	545
2045		512	513
2046		528	529

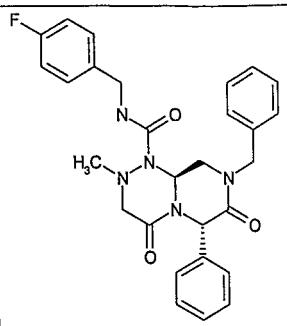
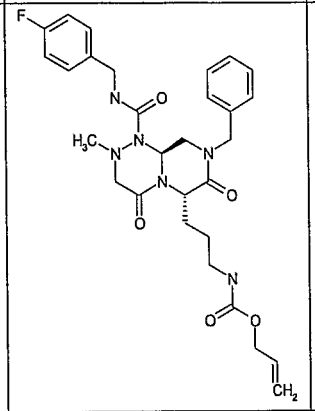
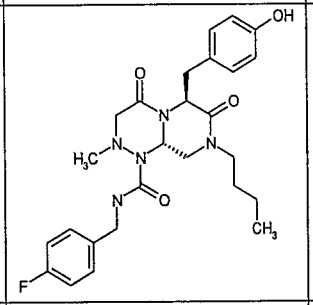
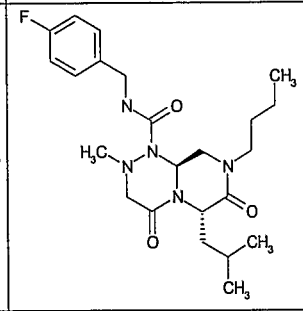
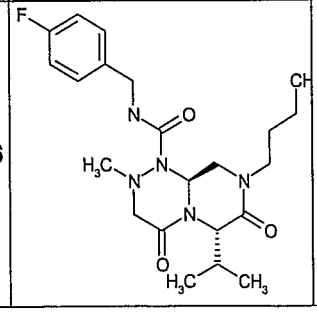
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2047		542	543
2048		546	547
2049		611	612
2050		562	563
2051		512	513

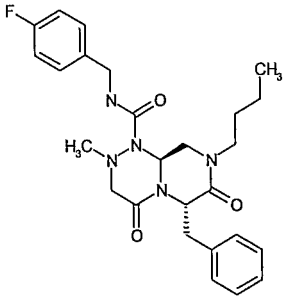
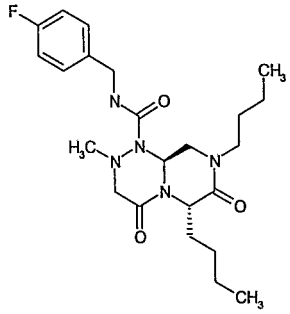
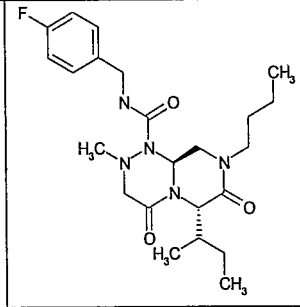
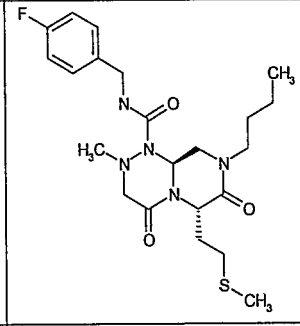
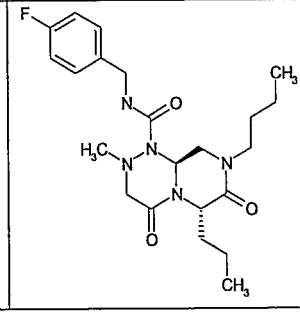
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2052		498	499
2053		546	547
2054		512	513
2055		512	513
2056		530	531
2057		498	499

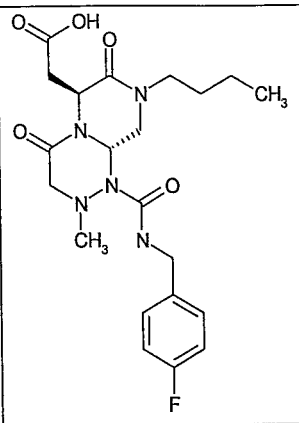
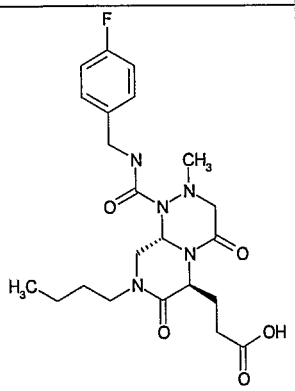
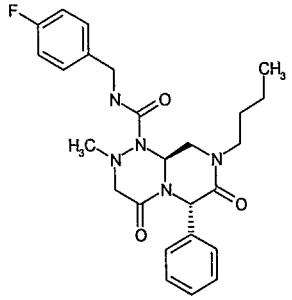
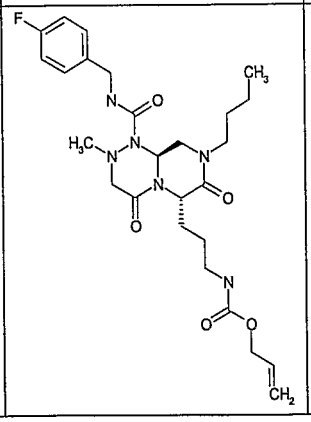
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2058		514	515
2059		528	529
2060		532	533
2061		597	598
2062		532	533

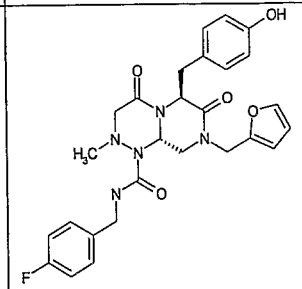
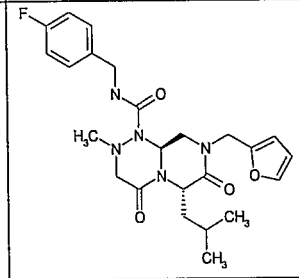
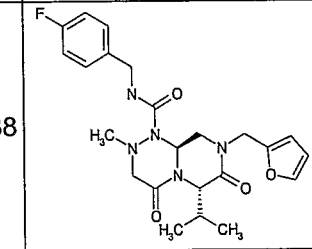
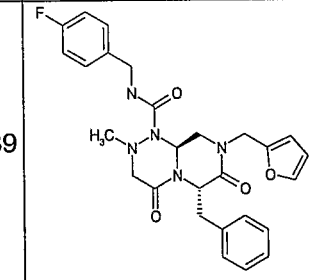
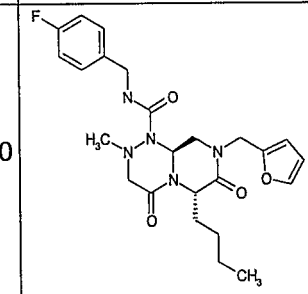
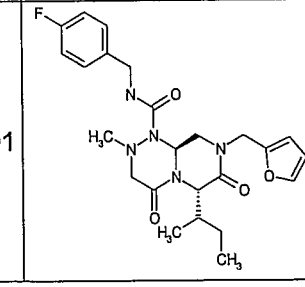
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2063		482	483
2064		468	469
2065		516	517
2066		482	483
2067		482	483

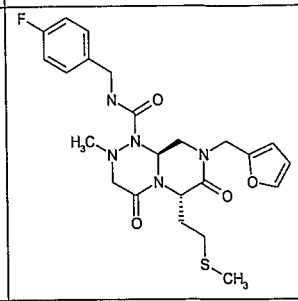
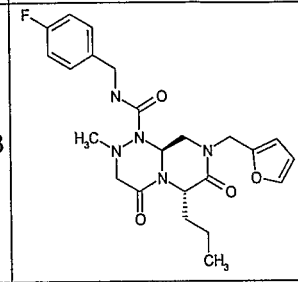
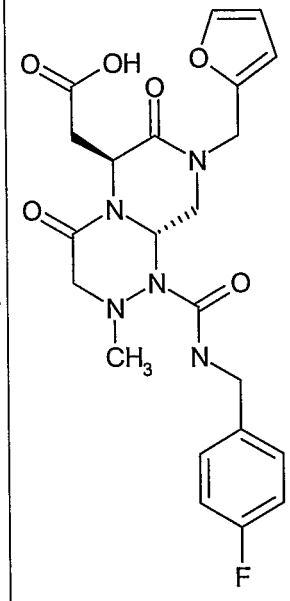
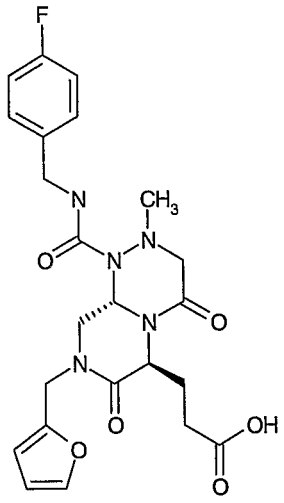
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2068		500	501
2069		468	469
2070		484	485
2071		498	499

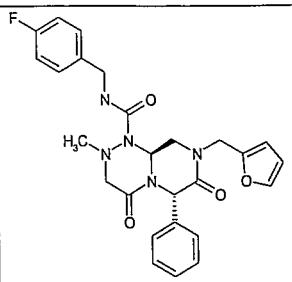
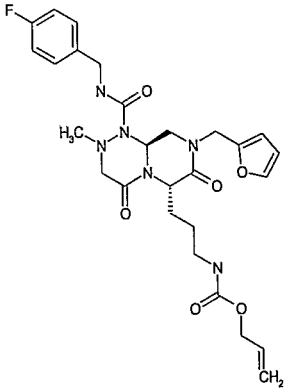
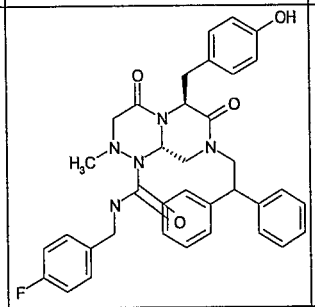
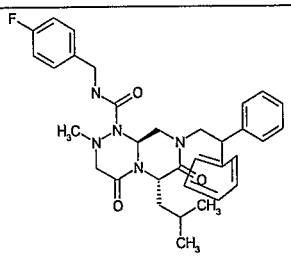
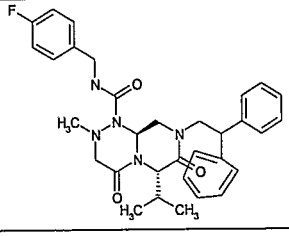
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2072		502	503
2073		567	568
2074		498	499
2075		448	449
2076		434	435

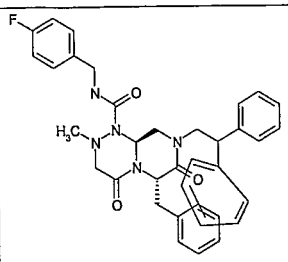
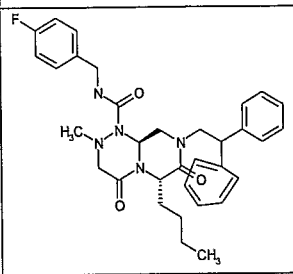
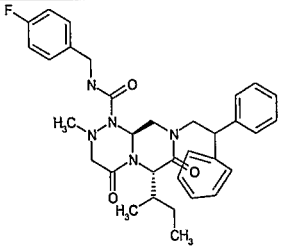
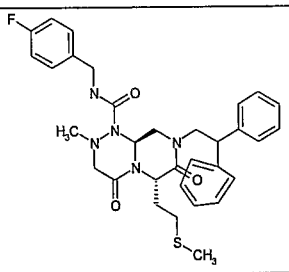
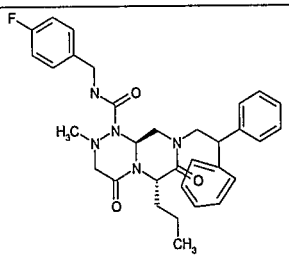
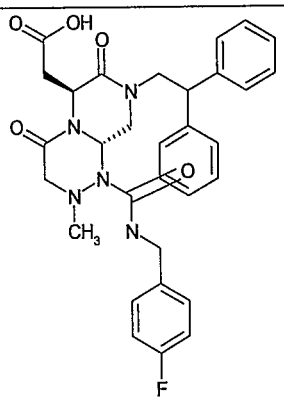
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2077		482	483
2078		448	449
2079		448	449
2080		466	467
2081		434	435

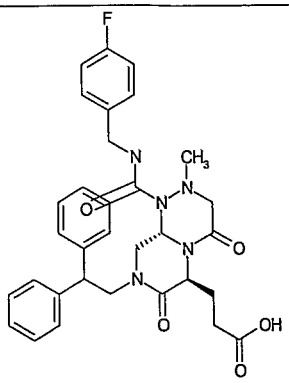
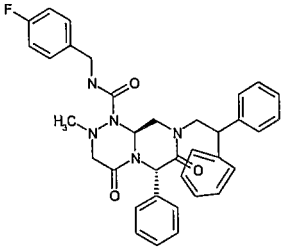
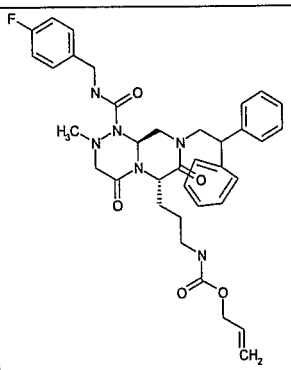
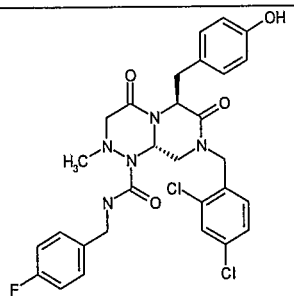
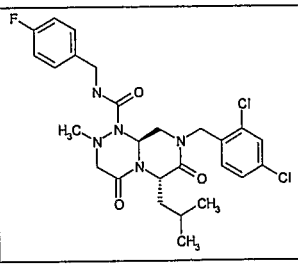
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2082		449	450
2083		464	465
2084		468	469
2085		533	534

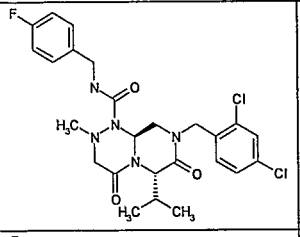
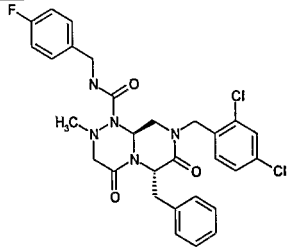
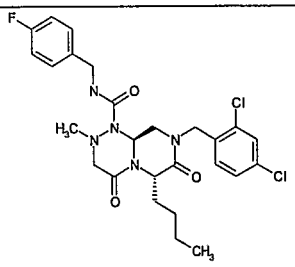
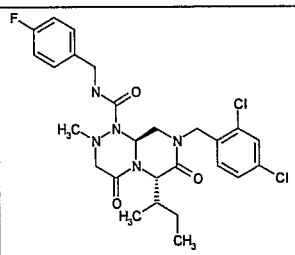
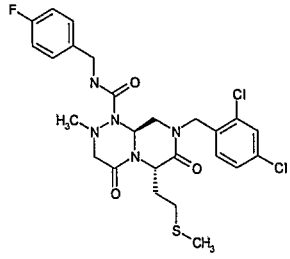
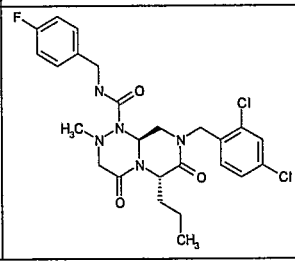
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2086		522	523
2087		472	473
2088		458	459
2089		506	507
2090		472	473
2091		472	473

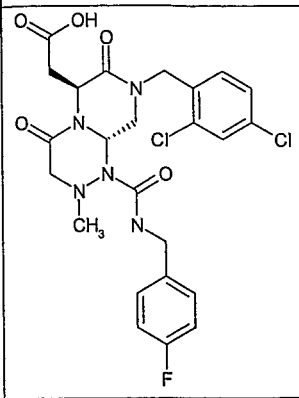
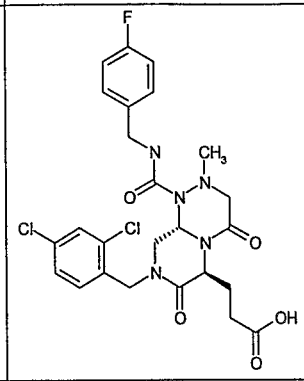
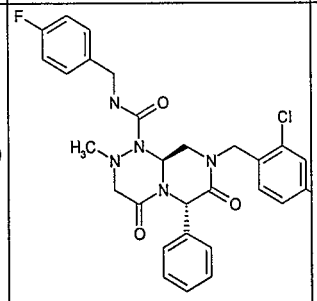
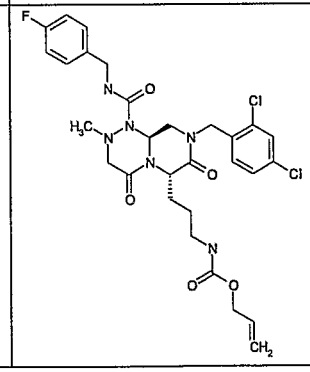
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2092		490	491
2093		458	459
2094		473	474
2095		487	488

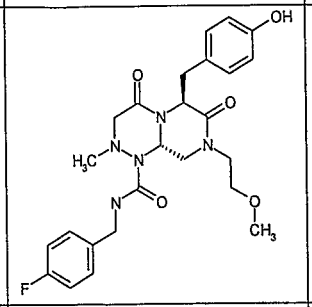
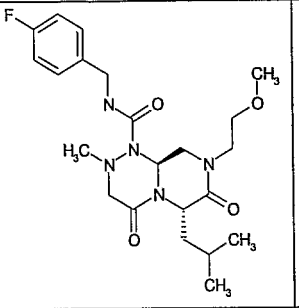
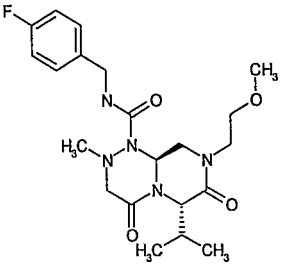
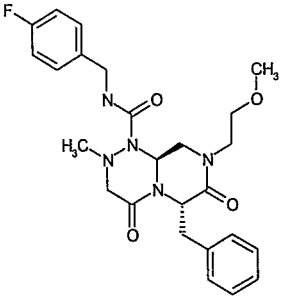
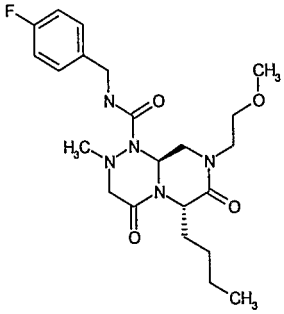
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2096		492	493
2097		557	558
2098		622	623
2099		572	573
2100		558	559

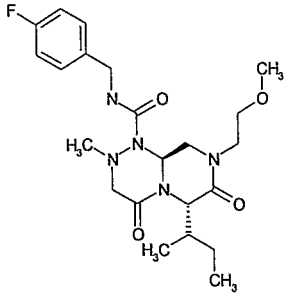
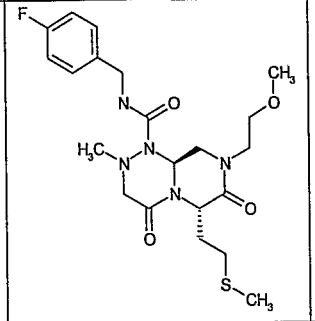
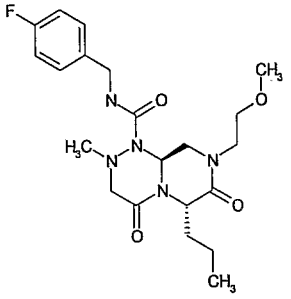
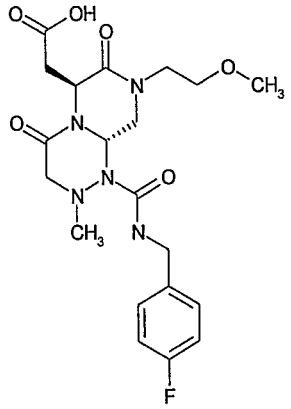
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2101		606	607
2102		572	573
2103		572	573
2104		590	591
2105		558	559
2106		574	575

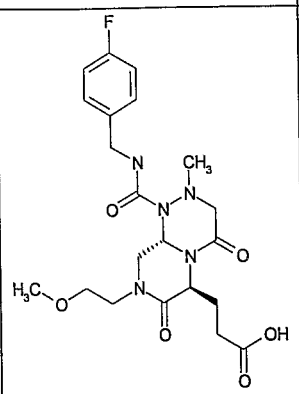
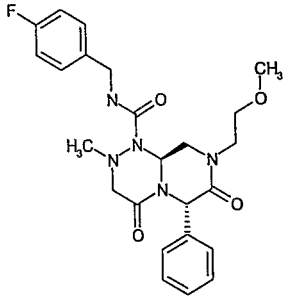
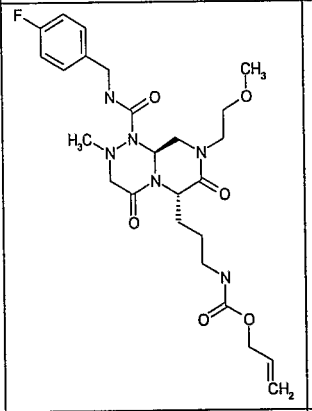
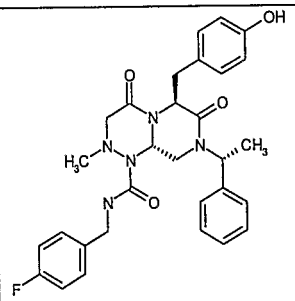
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2107		588	589
2108		592	593
2109		657	658
2110		600	601
2111		550	551

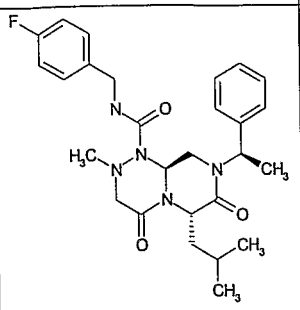
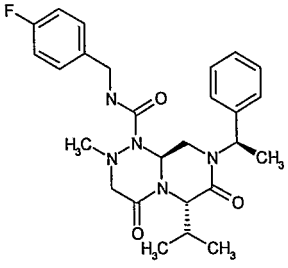
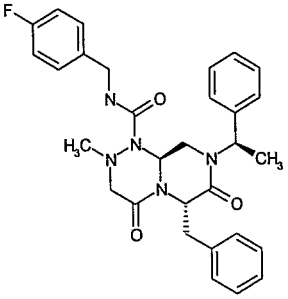
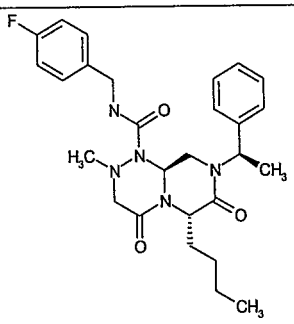
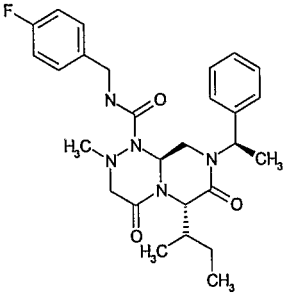
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2112		536	537
2113		584	585
2114		550	551
2115		550	551
2116		569	570
2117		536	537

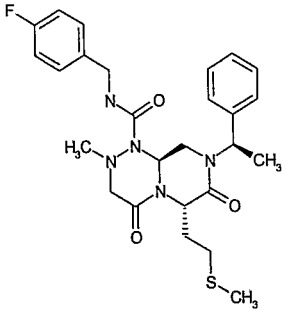
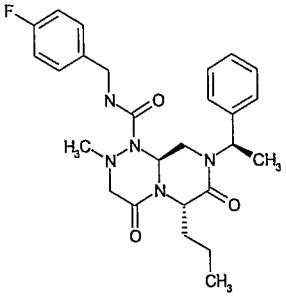
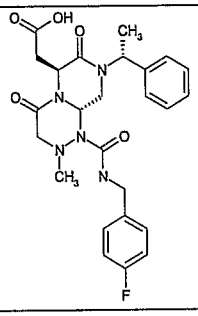
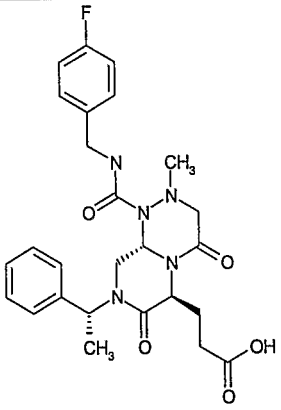
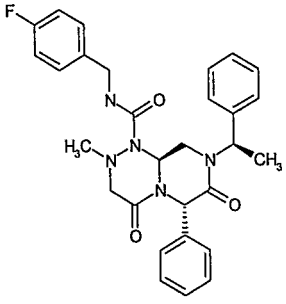
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2118		552	553
2119		566	567
2120		570	571
2121		636	637

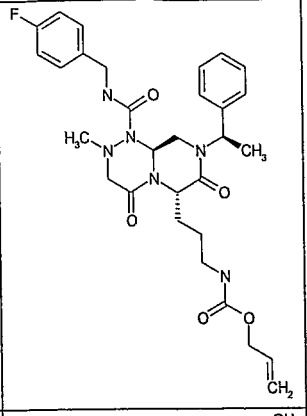
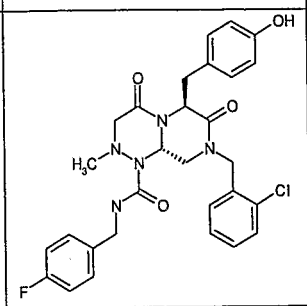
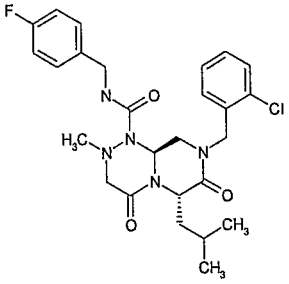
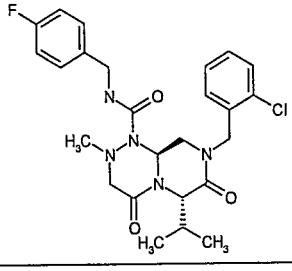
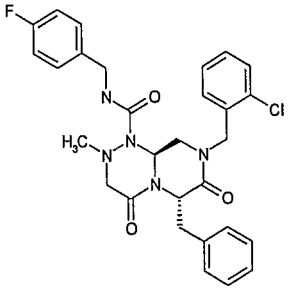
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2122		500	501
2123		450	451
2124		436	437
2125		484	485
2126		450	451

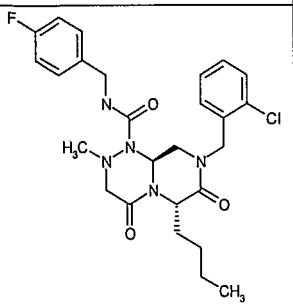
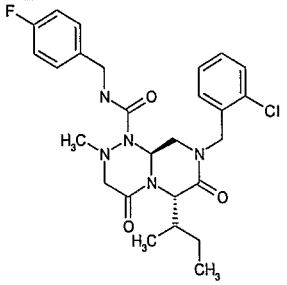
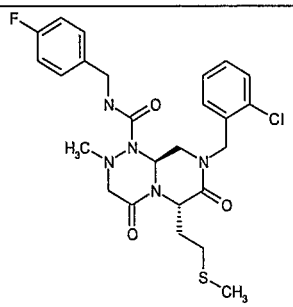
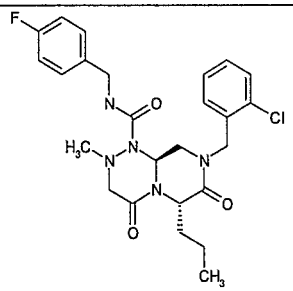
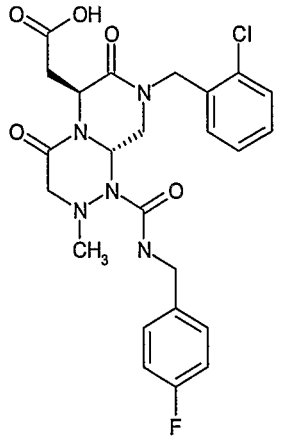
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2127		450	451
2128		468	469
2129		436	437
2130		451	452

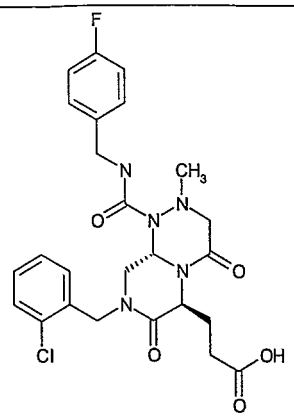
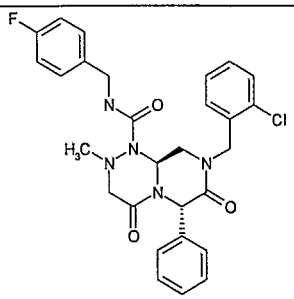
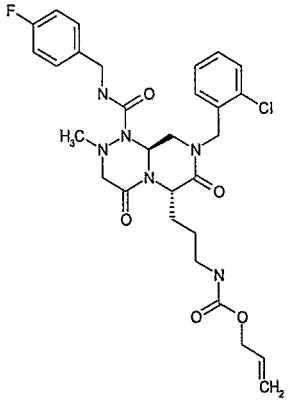
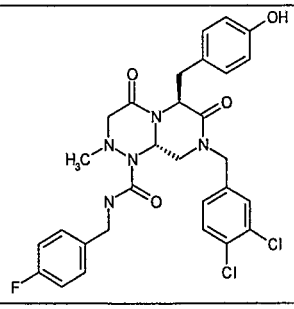
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2131		465	466
2132		470	471
2133		535	536
2134		546	547

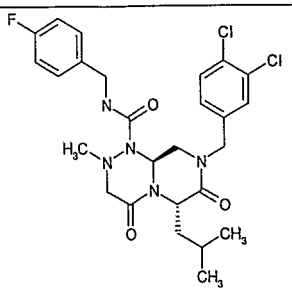
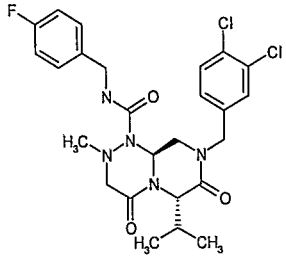
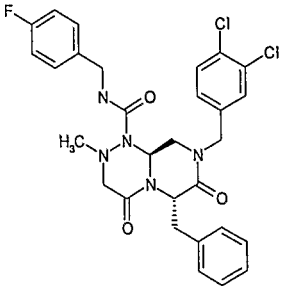
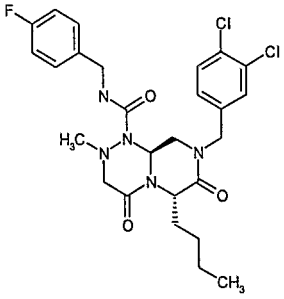
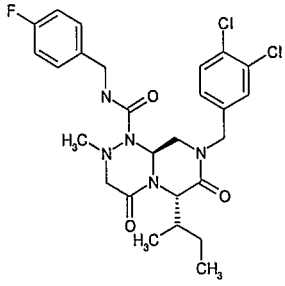
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2135		496	497
2136		482	483
2137		530	531
2138		496	497
2139		496	497

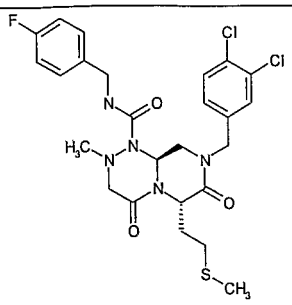
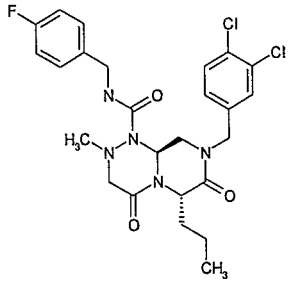
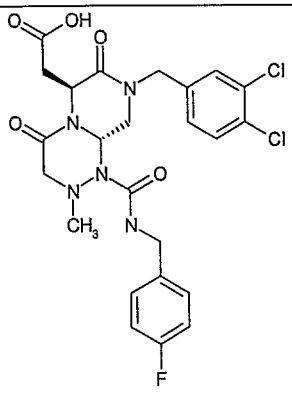
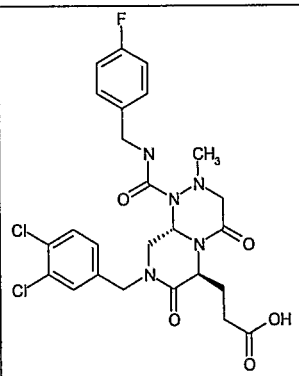
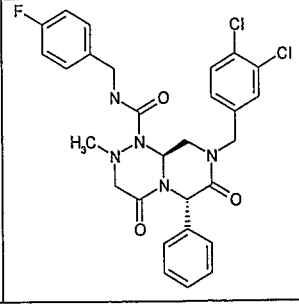
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2140		514	515
2141		482	483
2142		498	499
2143		512	513
2144		516	517

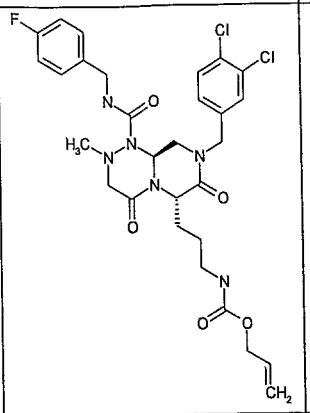
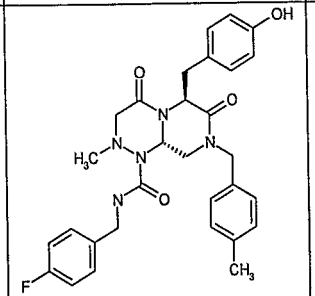
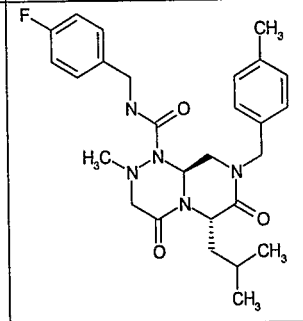
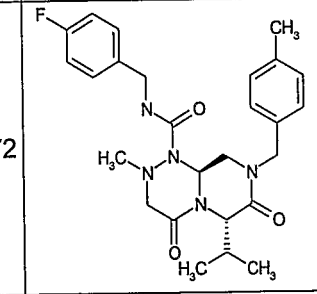
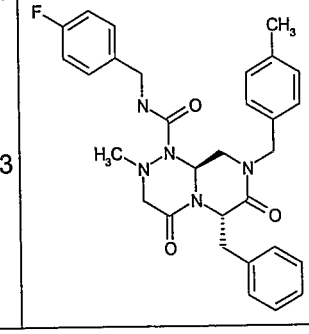
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2145		581	582
2146		566	567
2147		516	517
2148		502	503
2149		550	551

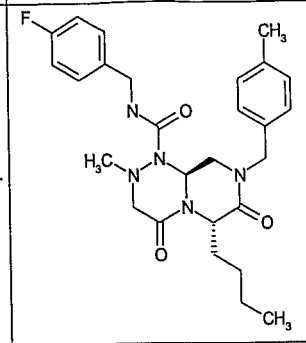
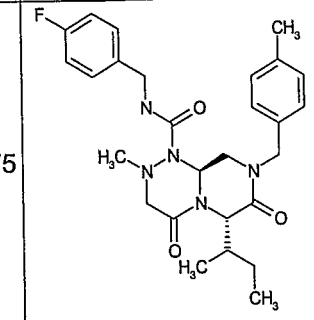
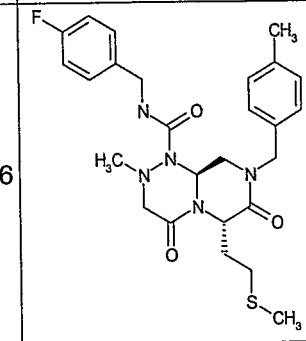
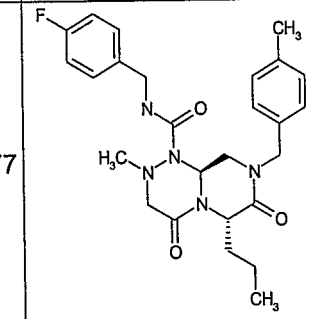
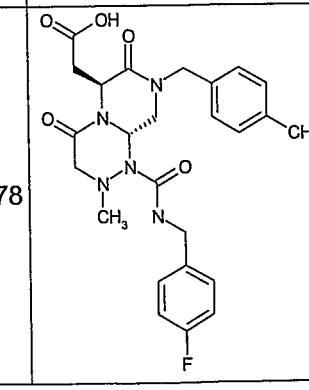
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2150		516	517
2151		516	517
2152		534	535
2153		502	503
2154		518	519

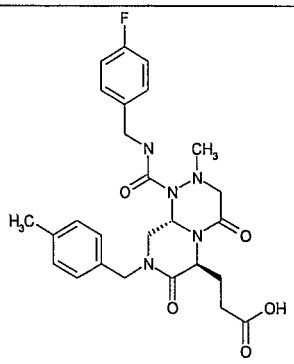
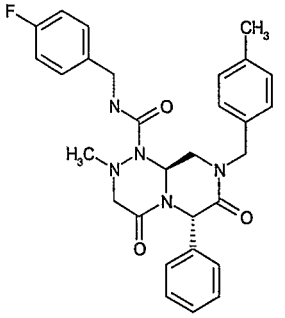
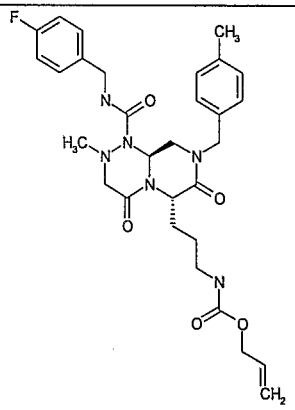
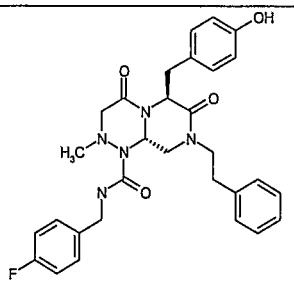
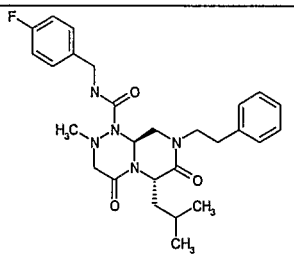
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2155		532	533
2156		536	537
2157		601	602
2158		600	601

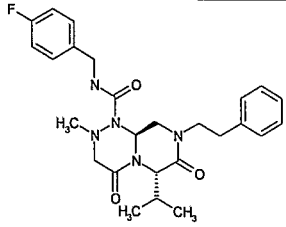
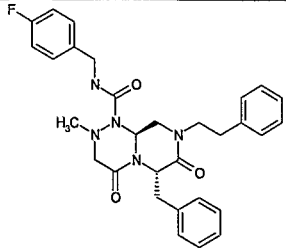
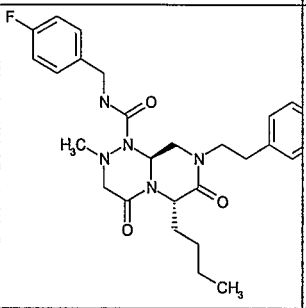
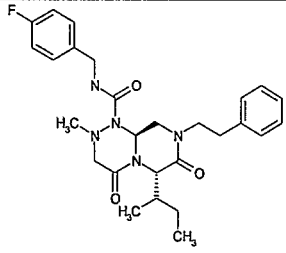
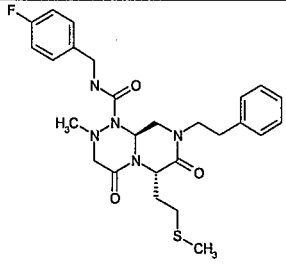
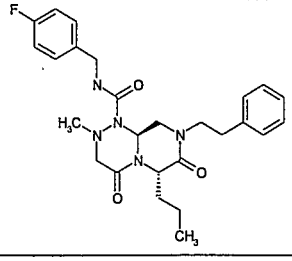
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2159		550	551
2160		536	537
2161		584	585
2162		550	551
2163		550	551

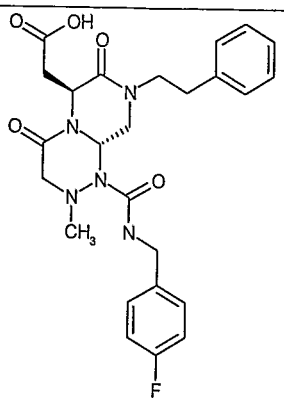
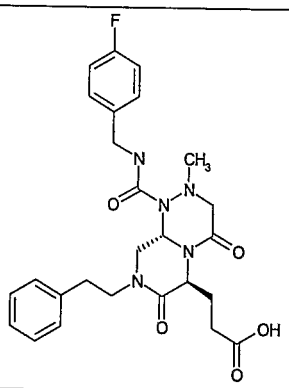
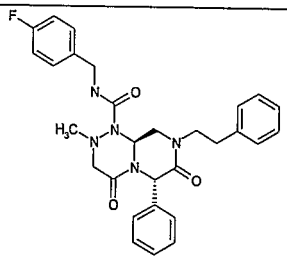
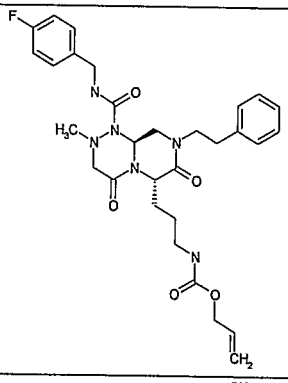
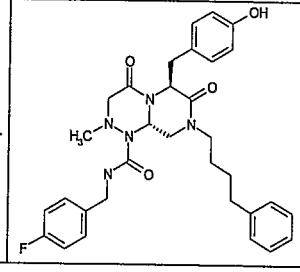
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2164		569	570
2165		536	537
2166		552	553
2167		566	567
2168		570	571

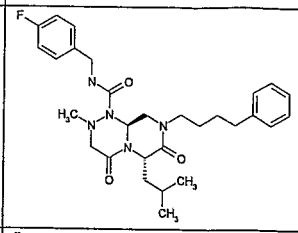
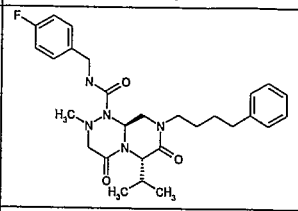
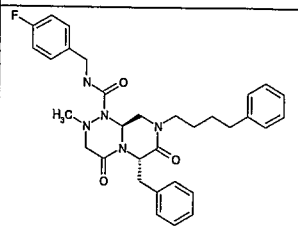
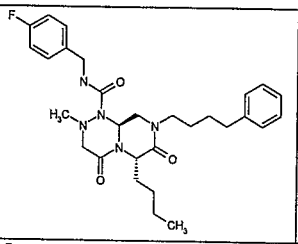
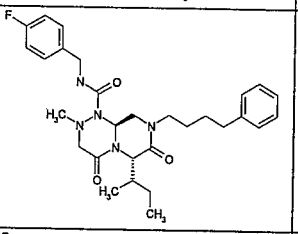
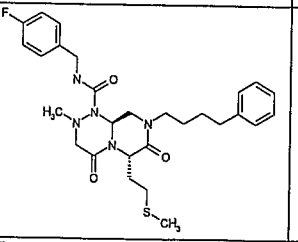
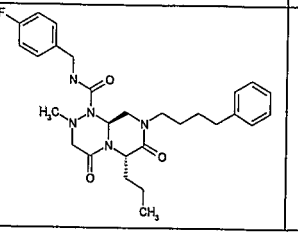
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2169		636	637
2170		546	547
2171		496	497
2172		482	483
2173		530	531

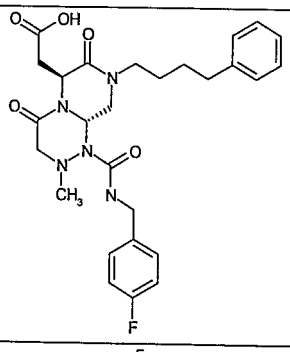
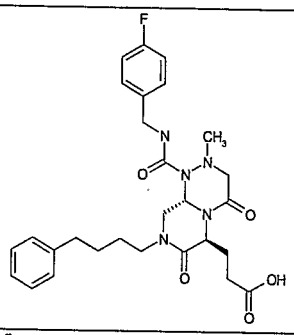
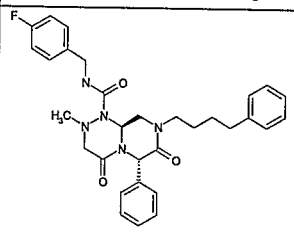
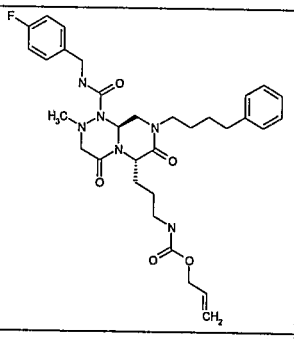
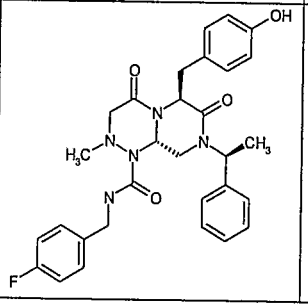
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2174		496	497
2175		496	497
2176		514	515
2177		482	483
2178		498	499

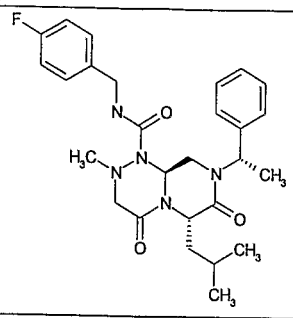
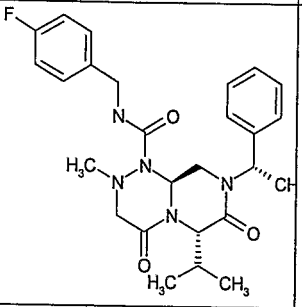
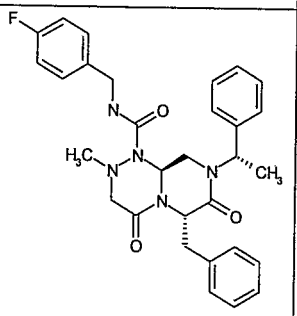
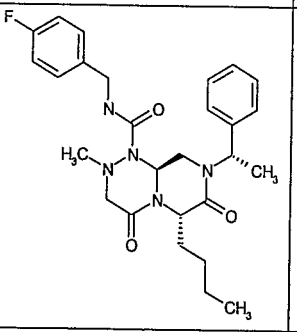
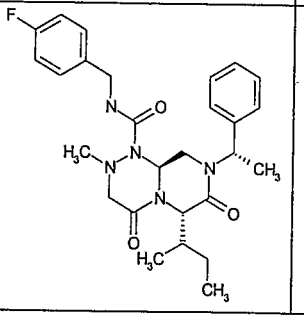
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2179		512	513
2180		516	517
2181		581	582
2182		546	547
2183		496	497

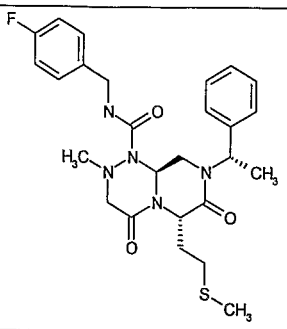
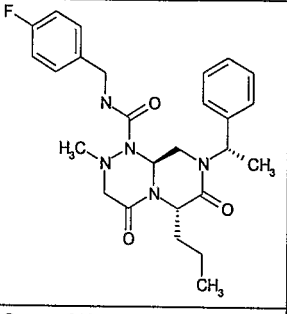
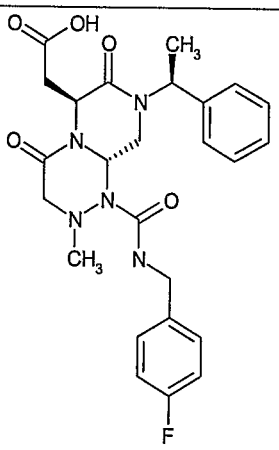
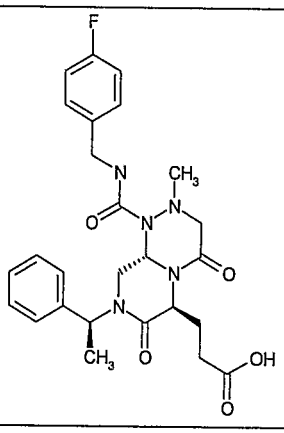
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2185		530	531
2186		496	497
2187		496	497
2188		514	515
2189		482	483

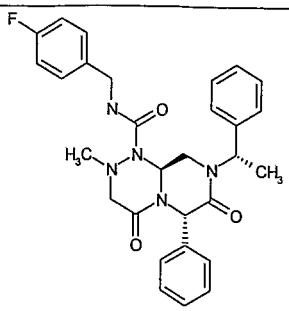
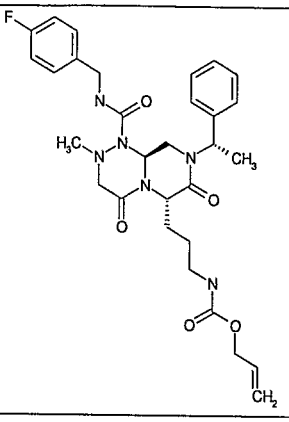
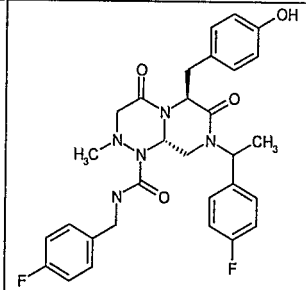
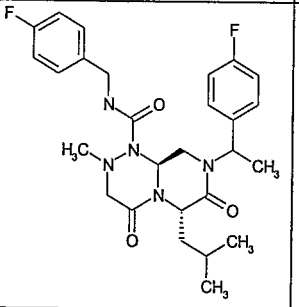
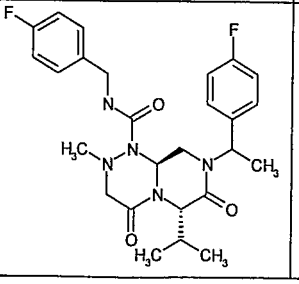
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2190		498	499
2191		512	513
2192		516	517
2193		581	582
2194		574	575

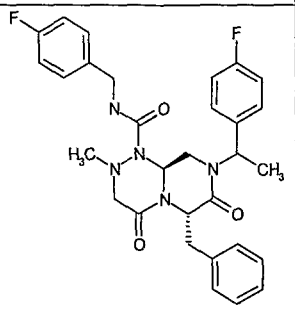
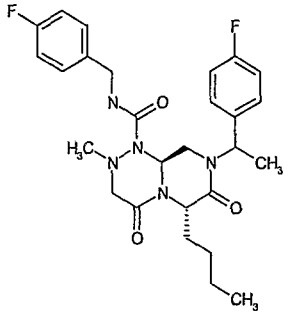
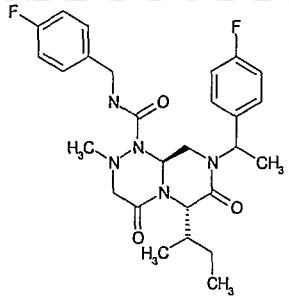
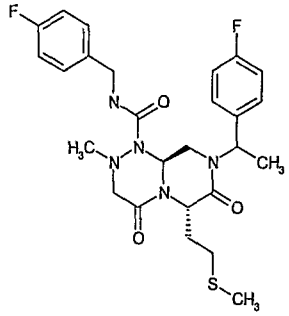
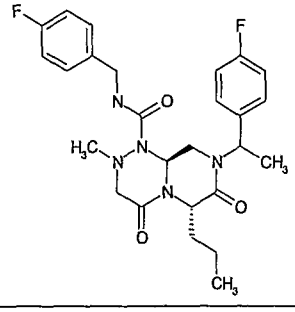
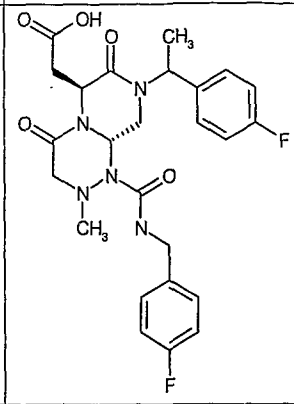
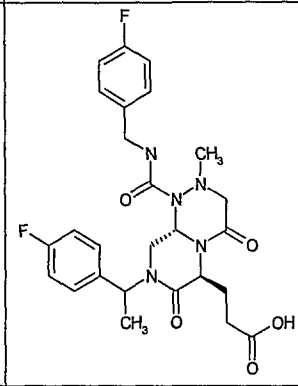
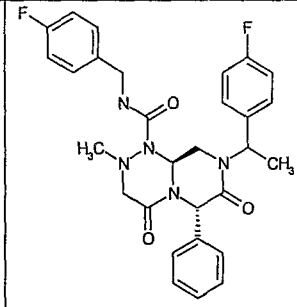
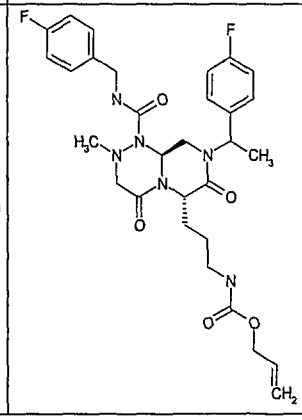
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2195		524	525
2196		510	511
2197		558	559
2198		524	525
2199		524	525
2200		542	543
2201		510	511

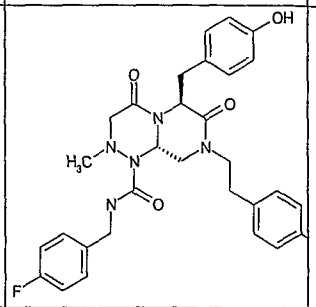
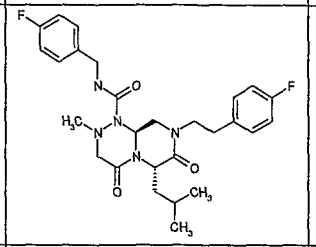
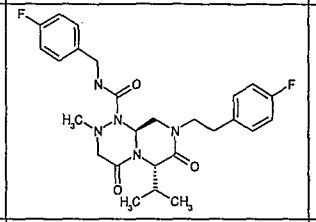
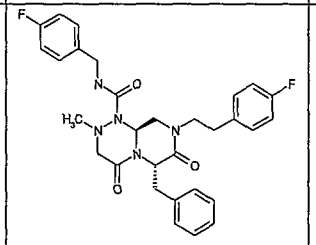
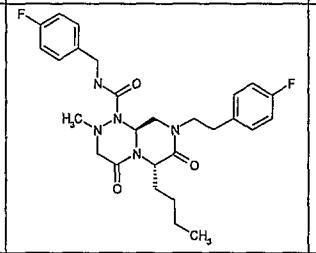
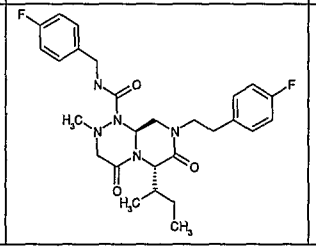
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2202		526	527
2203		540	541
2204		544	545
2205		609	610
2206		546	547

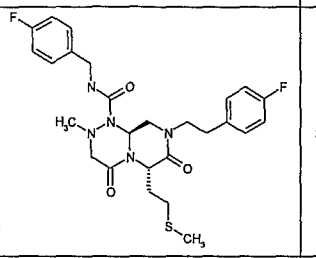
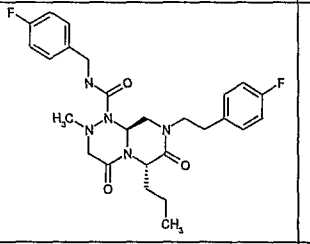
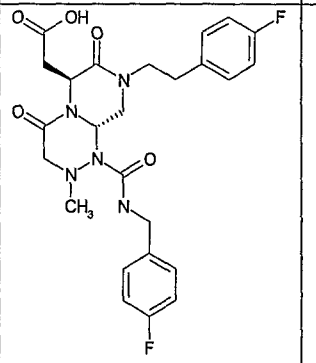
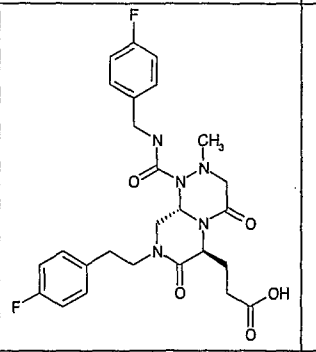
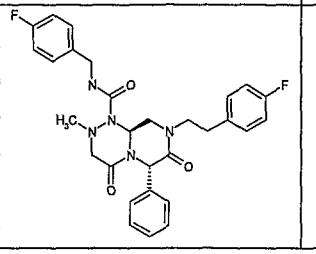
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2207		496	497
2208		482	483
2209		530	531
2210		496	497
2211		496	497

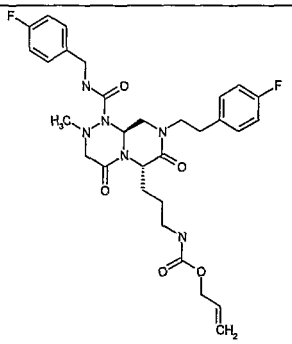
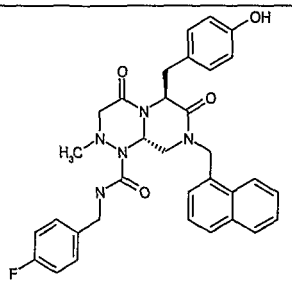
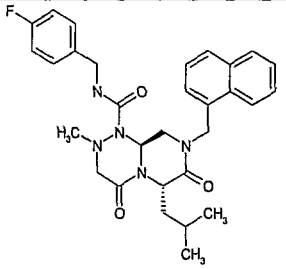
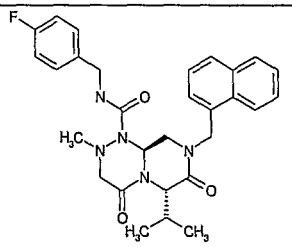
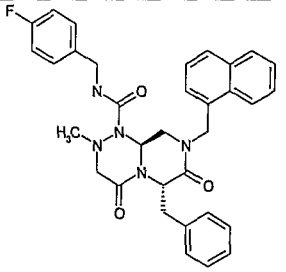
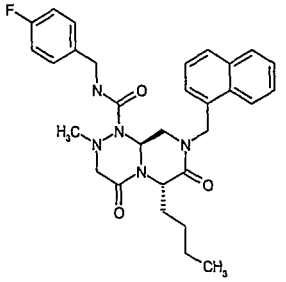
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2212		514	515
2213		482	483
2214		498	499
2215		512	513

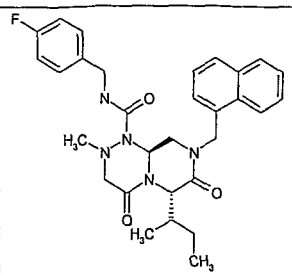
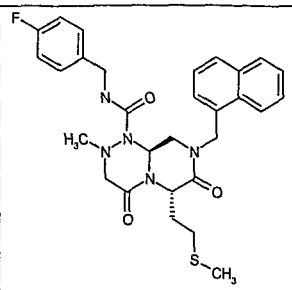
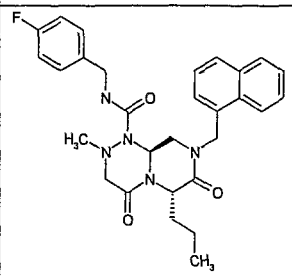
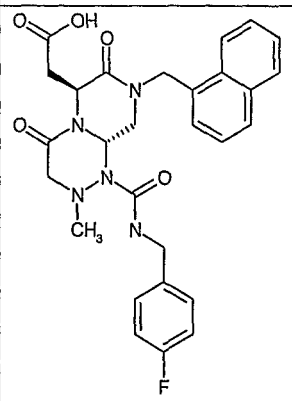
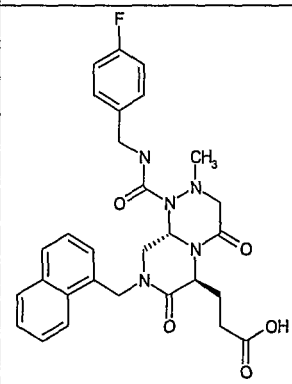
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2216		516	517
2217		581	582
2218		564	565
2219		514	515
2220		500	501

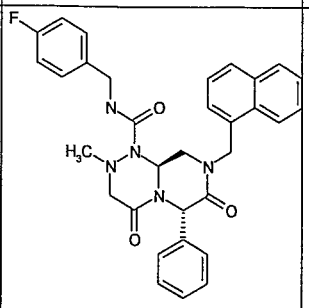
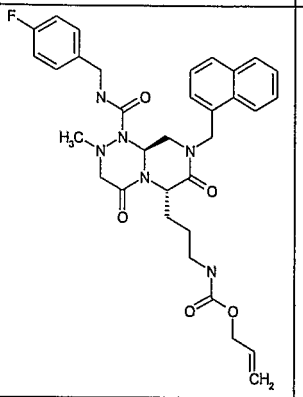
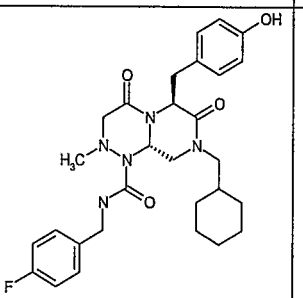
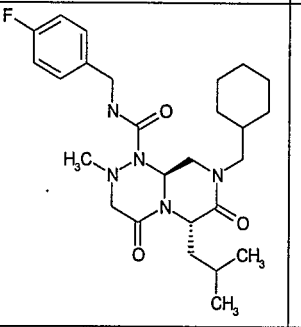
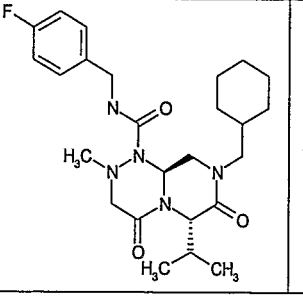
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2221		548	549
2222		514	515
2223		514	515
2224		532	533
2225		500	501
2226		516	517
2227		530	531
2228		534	535
2229		599	600

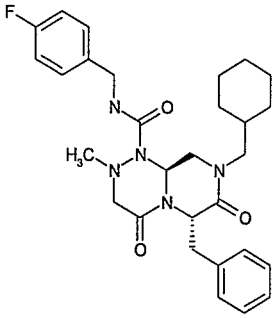
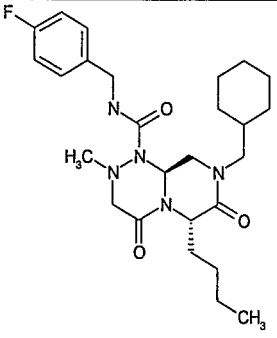
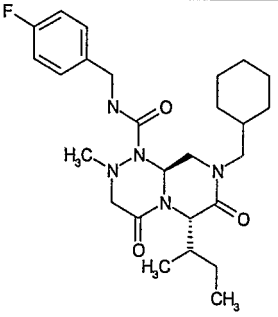
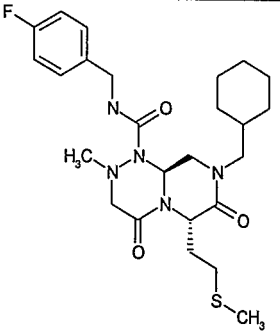
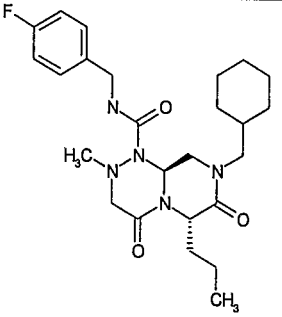
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2230		564	565
2231		514	515
2232		500	501
2233		548	549
2234		514	515
2235		514	515

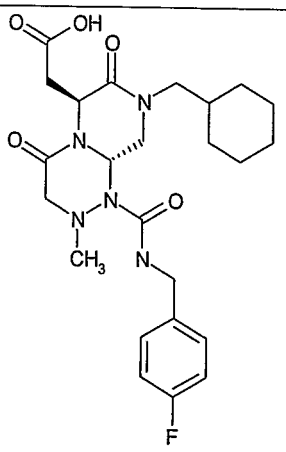
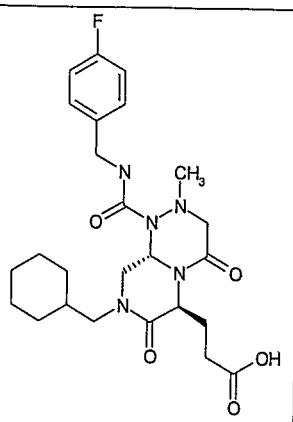
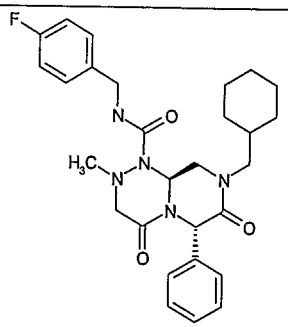
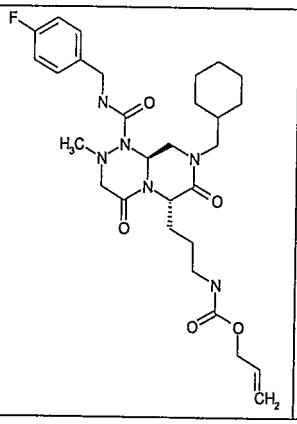
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2236		532	533
2237		500	501
2238		516	517
2239		530	531
2240		534	535

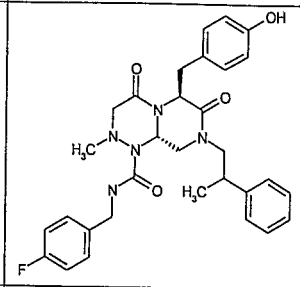
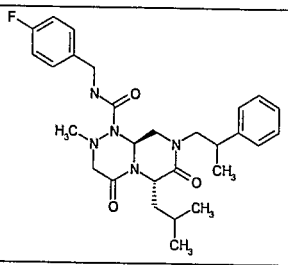
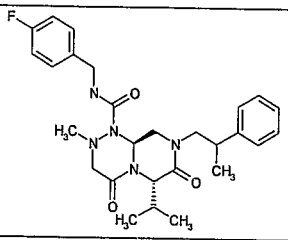
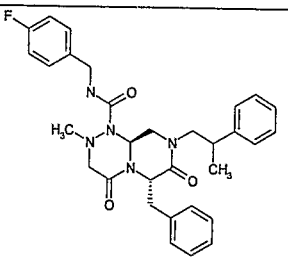
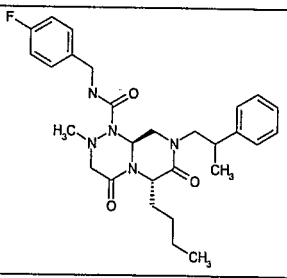
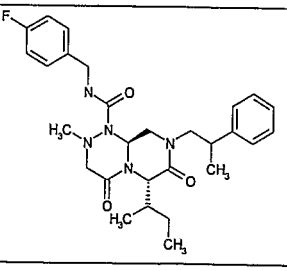
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2241		599	600
2242		582	583
2243		532	533
2244		518	519
2245		566	567
2246		532	533

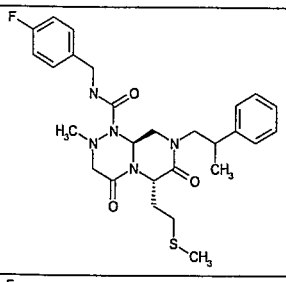
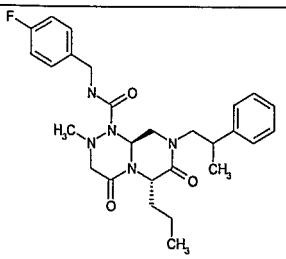
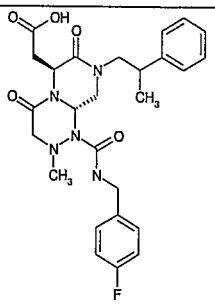
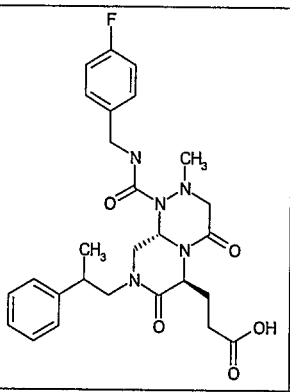
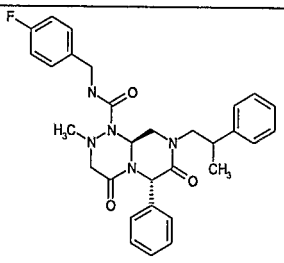
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2247		532	533
2248		550	551
2249		518	519
2250		534	535
2251		548	549

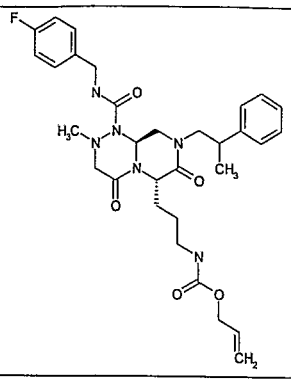
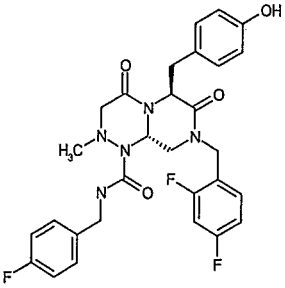
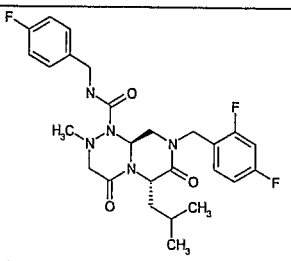
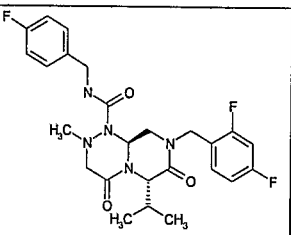
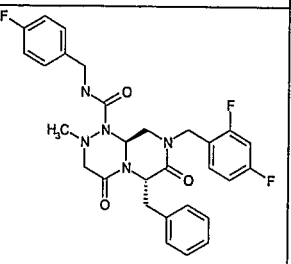
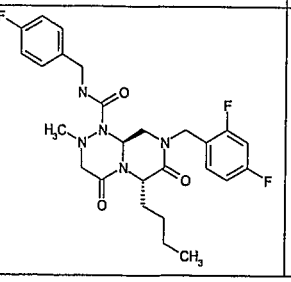
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2252		552	553
2253		617	618
2254		538	539
2255		488	489
2256		474	475

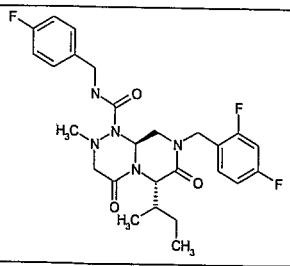
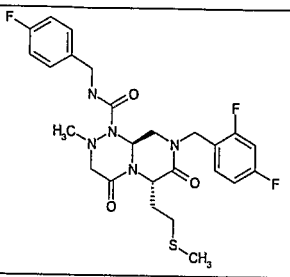
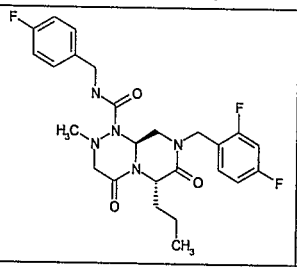
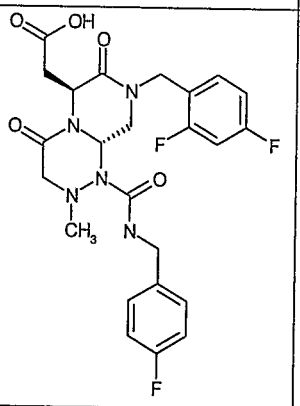
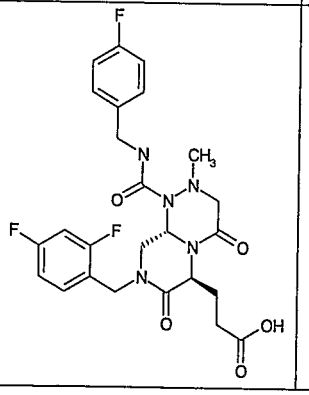
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2257		522	523
2258		488	489
2259		488	489
2260		506	507
2261		474	475

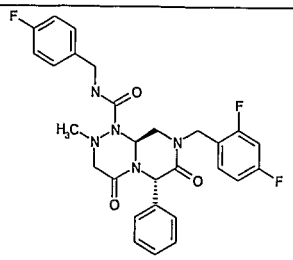
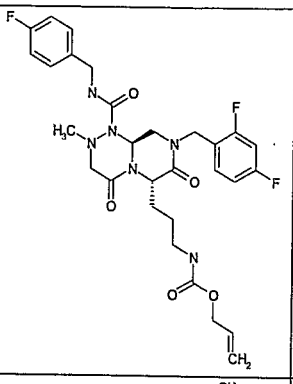
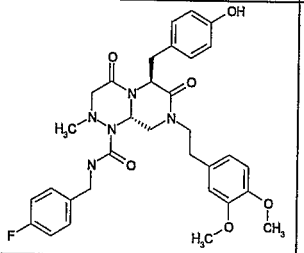
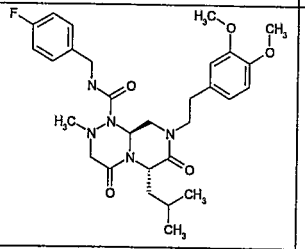
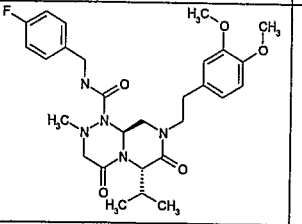
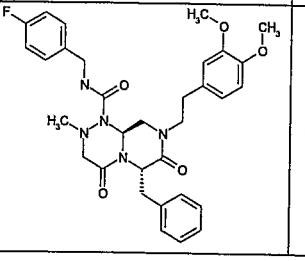
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2262		490	491
2263		504	505
2264		508	509
2265		573	574

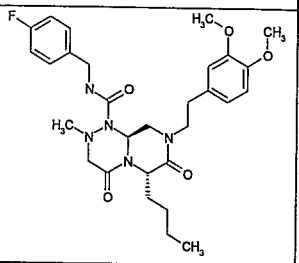
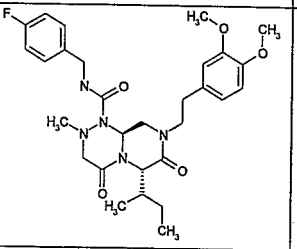
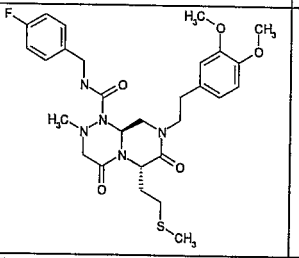
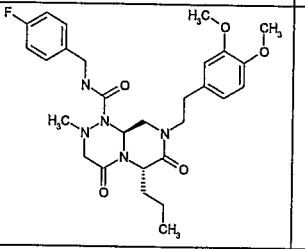
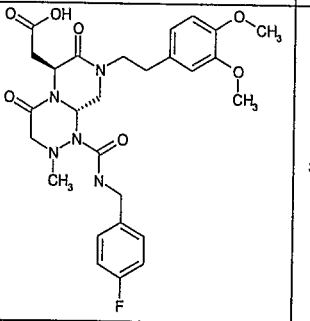
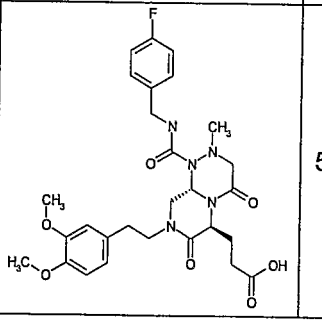
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2266		560	561
2267		510	511
2268		496	497
2269		544	545
2270		510	511
2271		510	511

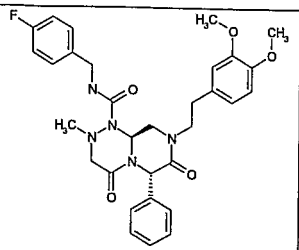
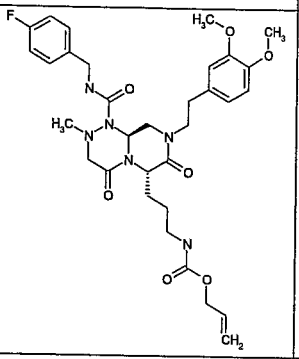
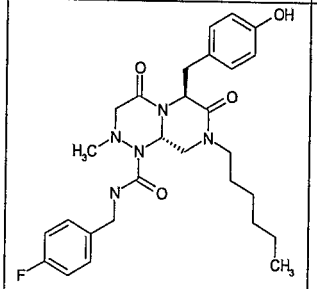
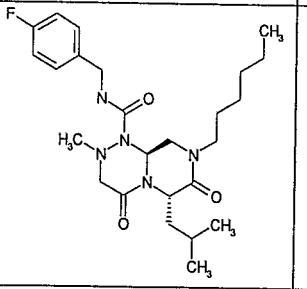
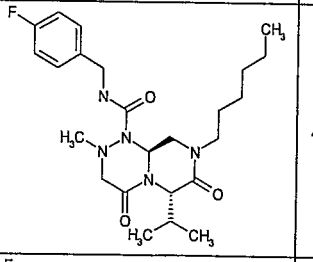
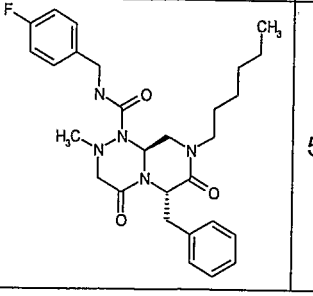
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2272		528	529
2273		496	497
2274		512	513
2275		526	527
2276		530	531

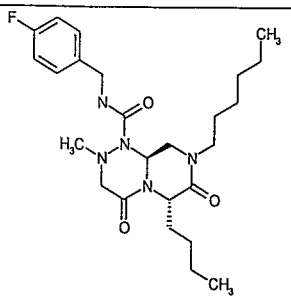
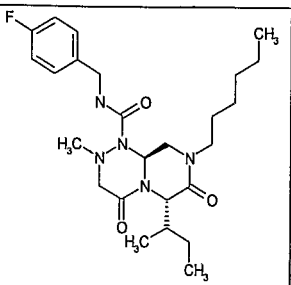
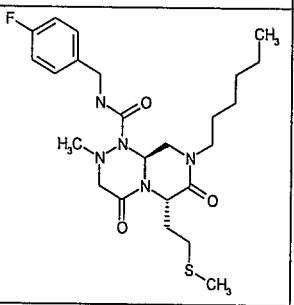
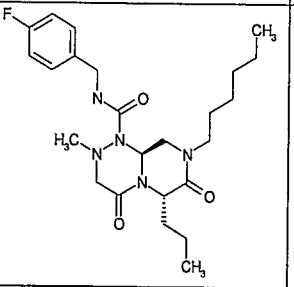
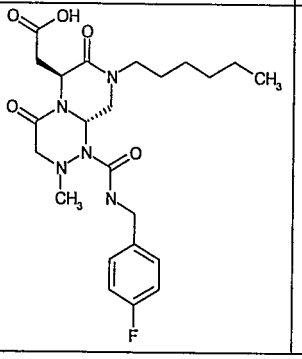
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2277		595	596
2278		568	569
2279		518	519
2280		504	505
2281		552	553
2282		518	519

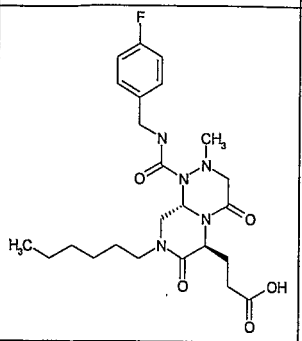
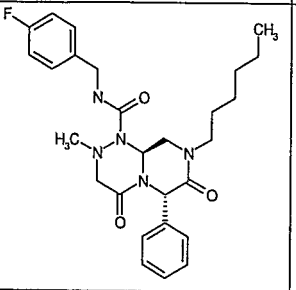
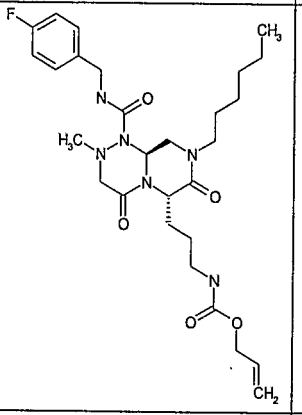
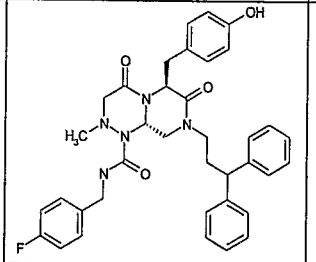
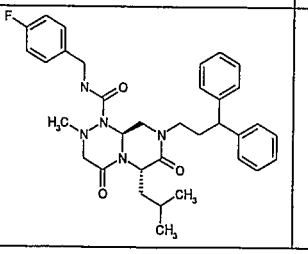
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2283		518	519
2284		536	537
2285		504	505
2286		519	520
2287		534	535

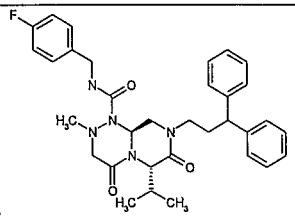
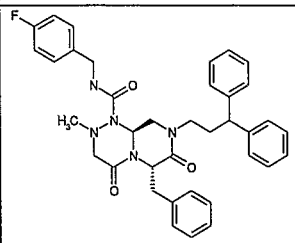
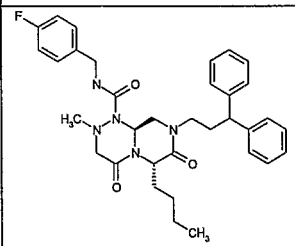
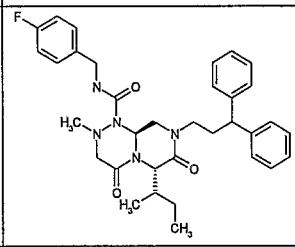
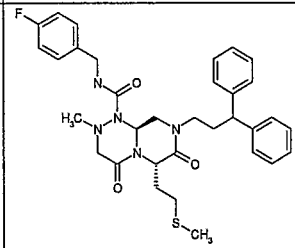
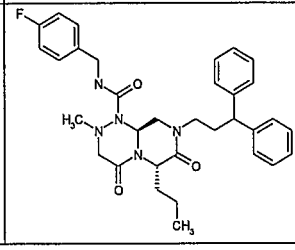
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2288		538	539
2289		603	604
2290		606	607
2291		556	557
2292		542	543
2293		590	591

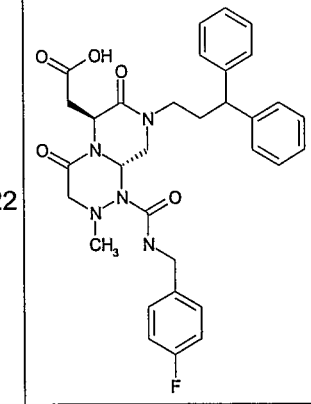
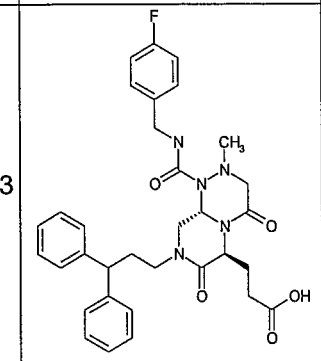
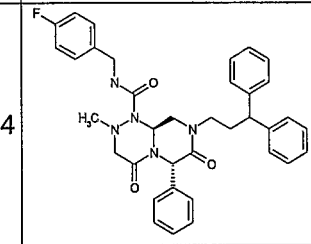
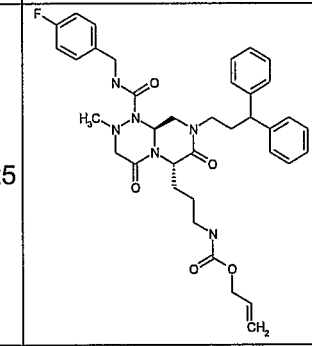
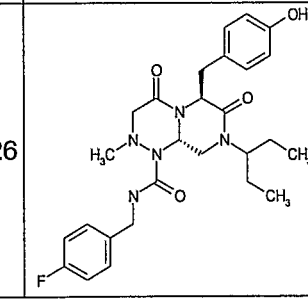
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2294		556	557
2295		556	557
2296		574	575
2297		542	543
2298		558	559
2299		572	573

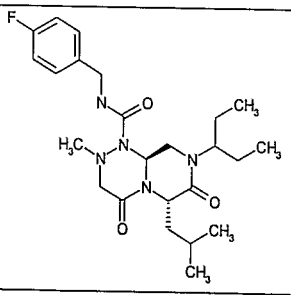
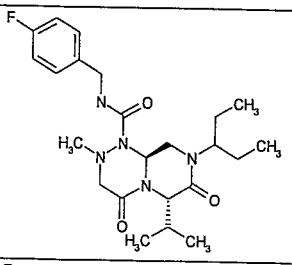
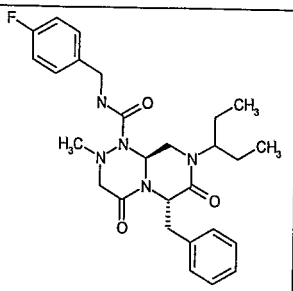
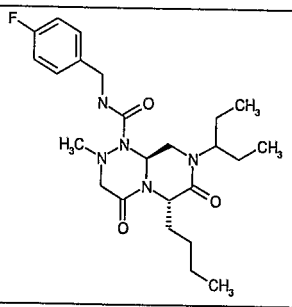
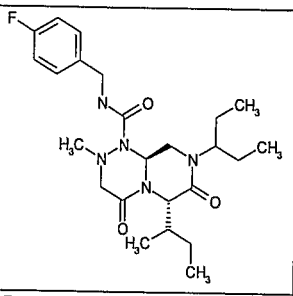
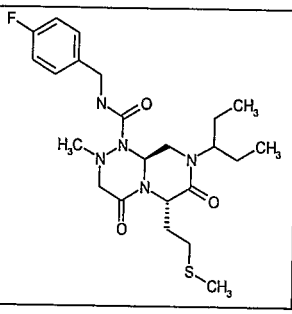
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2300		576	577
2301		641	642
2302		526	527
2303		476	477
2304		462	463
2305		510	511

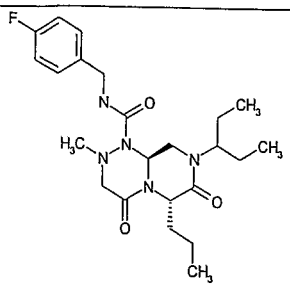
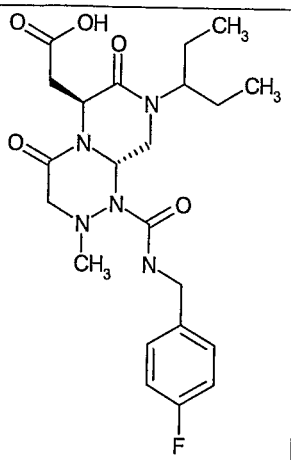
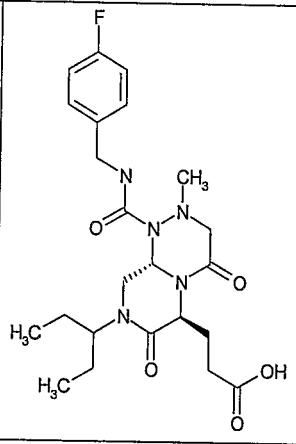
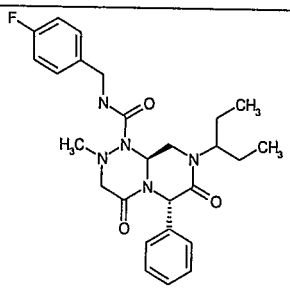
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2306		476	477
2307		476	477
2308		494	495
2309		462	463
2310		478	479

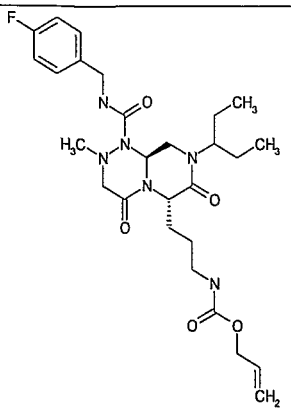
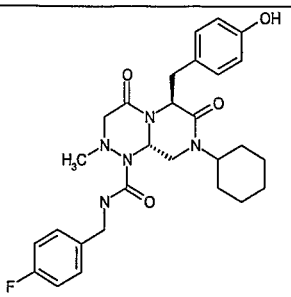
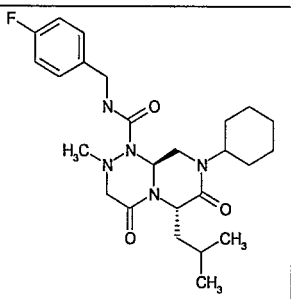
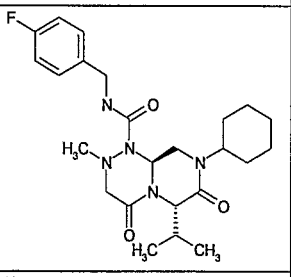
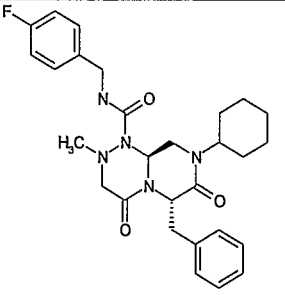
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2311		492	493
2312		496	497
2313		561	562
2314		636	637
2315		586	587

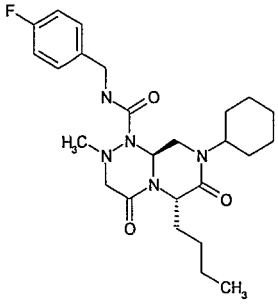
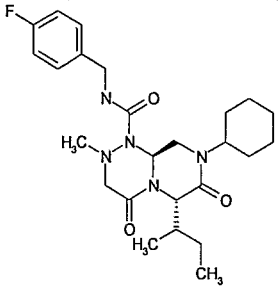
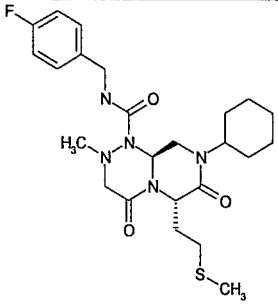
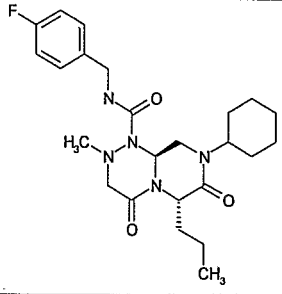
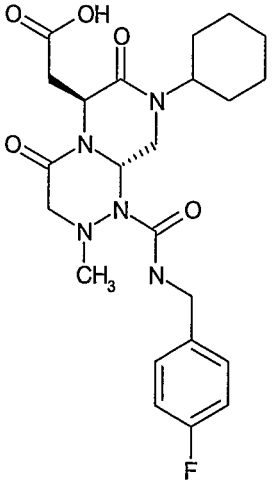
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2316		572	573
2317		620	621
2318		586	587
2319		586	587
2320		604	605
2321		572	573

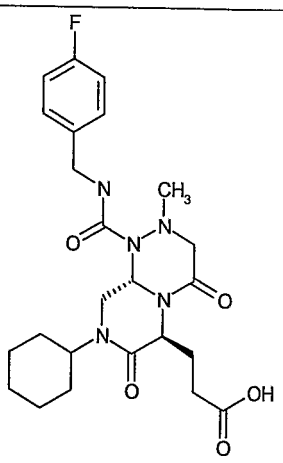
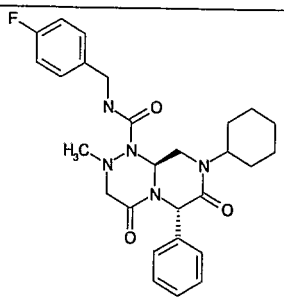
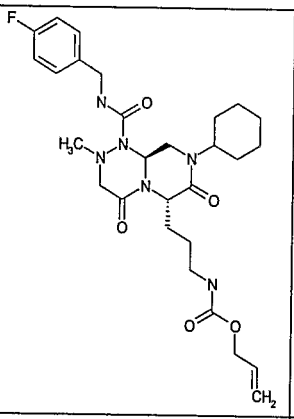
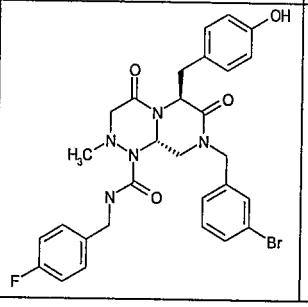
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2322		588	589
2323		602	603
2324		606	607
2325		671	672
2326		512	513

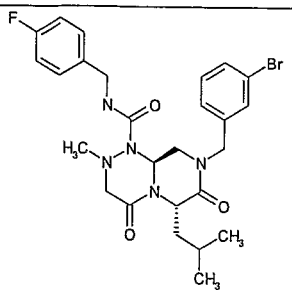
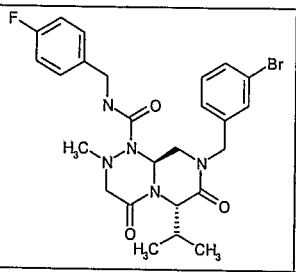
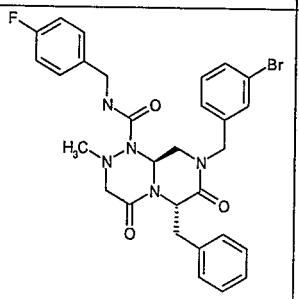
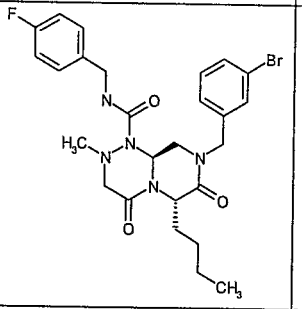
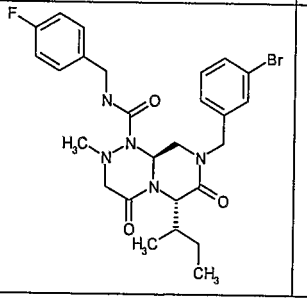
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2327		462	463
2328		448	449
2329		496	497
2330		462	463
2331		462	463
2332		480	481

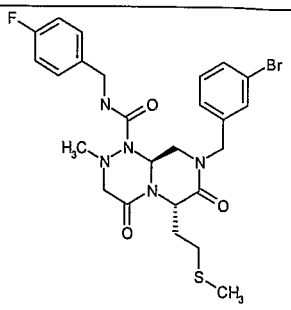
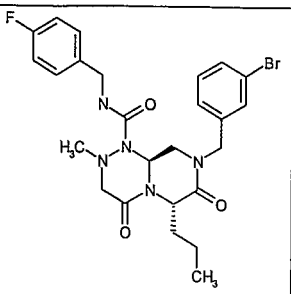
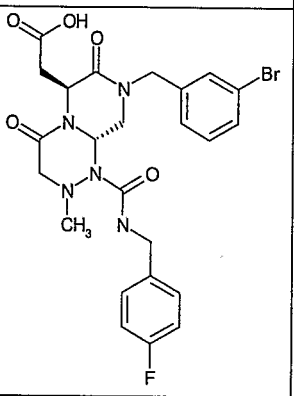
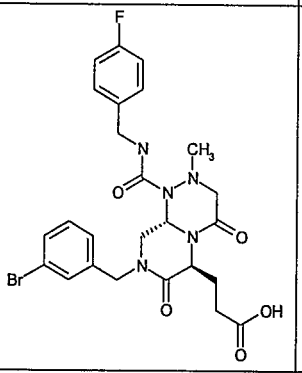
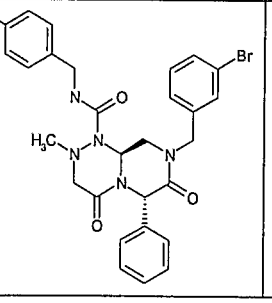
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2333		448	449
2334		464	465
2335		478	479
2336		482	483

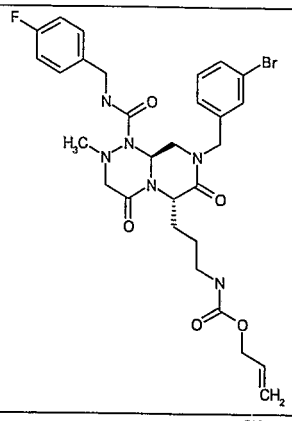
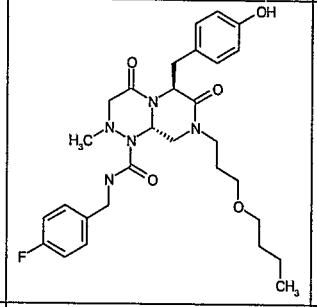
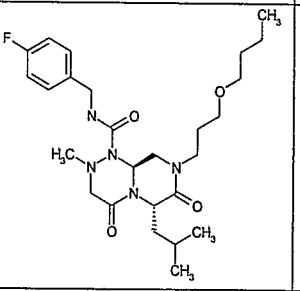
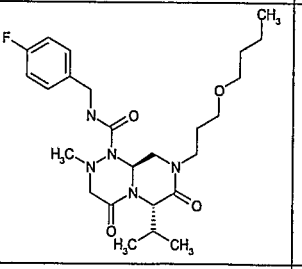
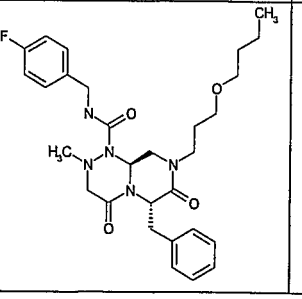
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2337		547	548
2338		524	525
2339		474	475
2340		460	461
2341		508	509

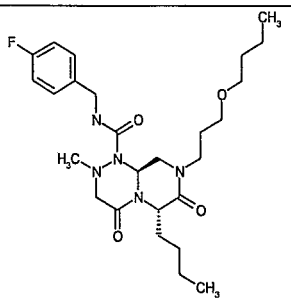
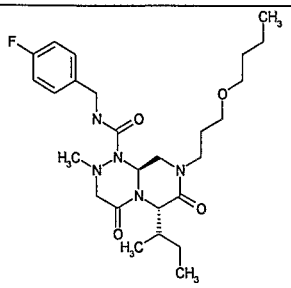
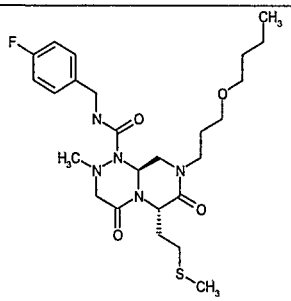
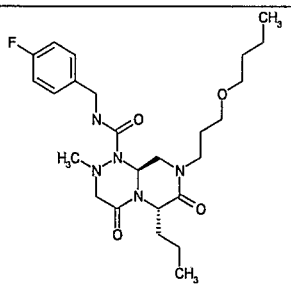
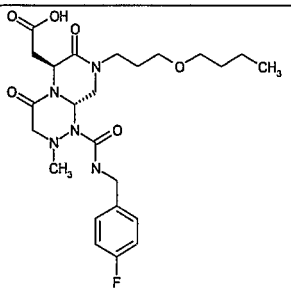
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2342		474	475
2343		474	475
2344		492	493
2345		460	461
2346		476	477

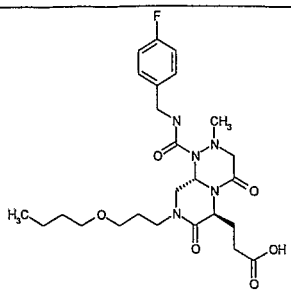
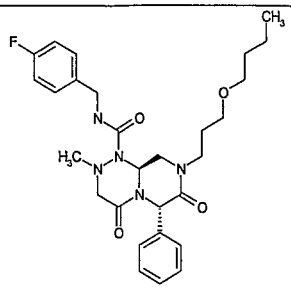
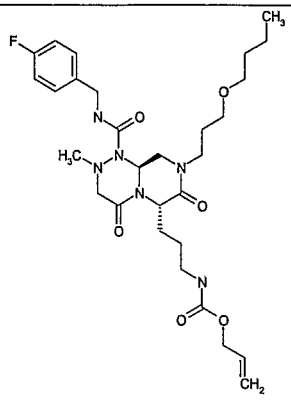
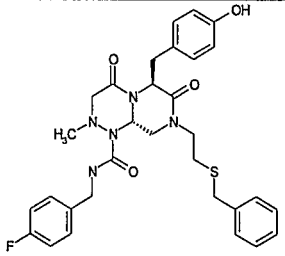
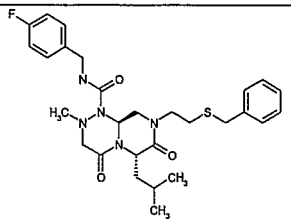
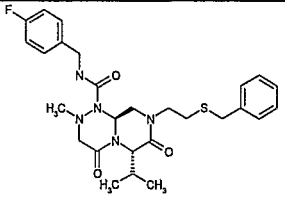
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2347		490	491
2348		494	495
2349		559	560
2350		610	611

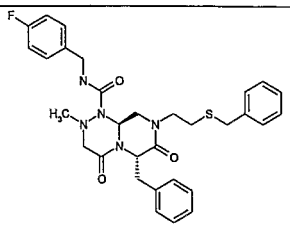
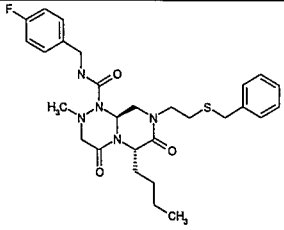
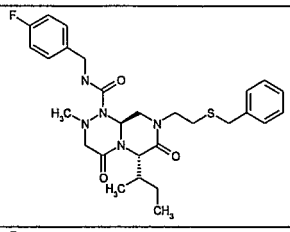
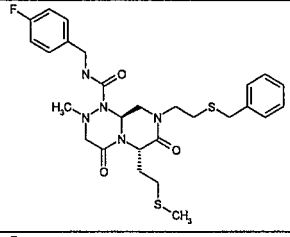
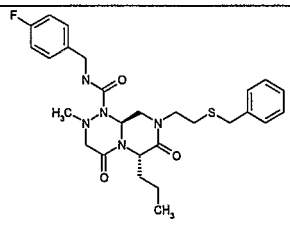
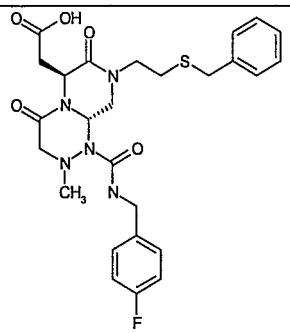
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2351		560	561
2352		546	547
2353		594	595
2354		560	561
2355		560	561

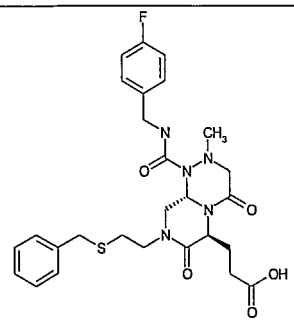
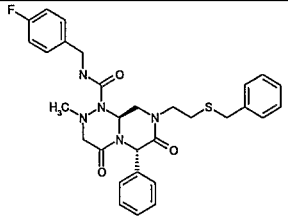
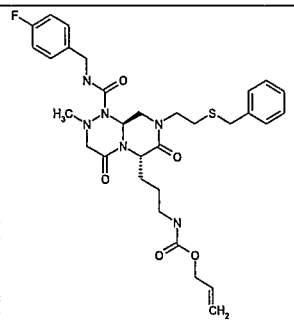
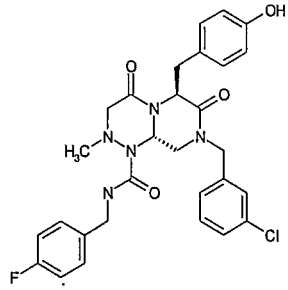
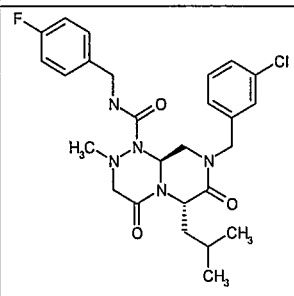
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2356		579	580
2357		546	547
2358		562	563
2359		576	577
2360		580	581

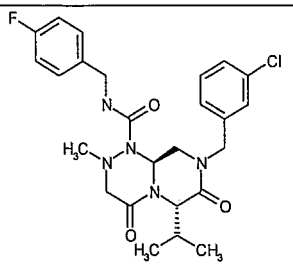
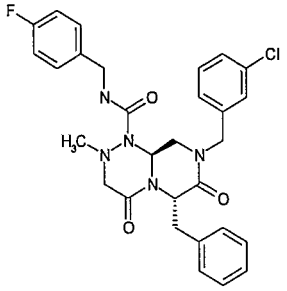
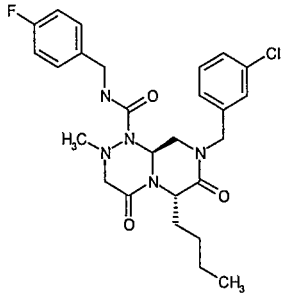
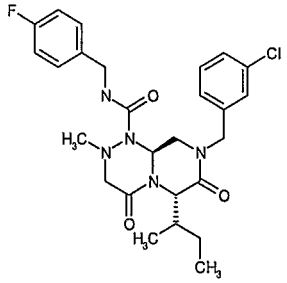
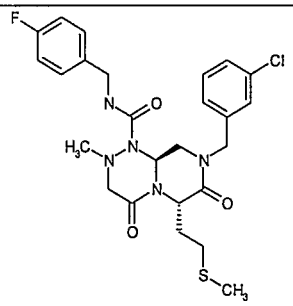
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2361		646	647
2362		556	557
2363		506	507
2364		492	493
2365		540	541

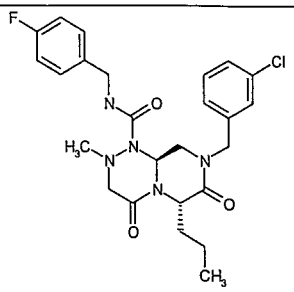
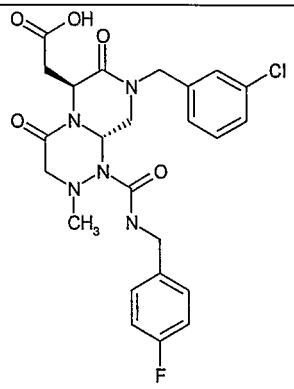
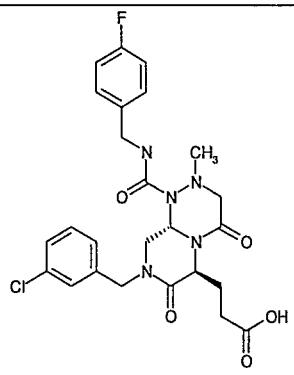
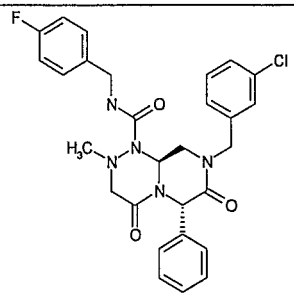
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2366		506	507
2367		506	507
2368		524	525
2369		492	493
2370		508	509

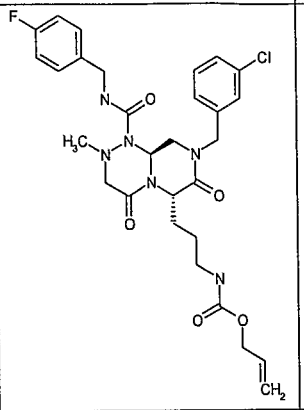
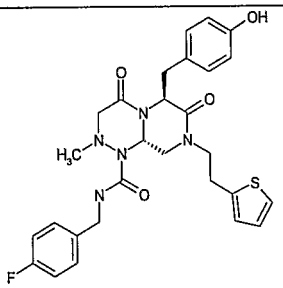
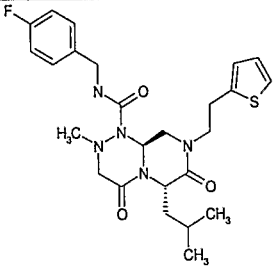
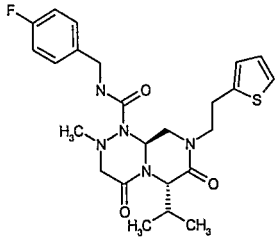
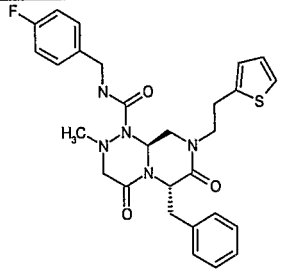
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2371		522	523
2372		526	527
2373		591	592
2374		592	593
2375		542	543
2376		528	529

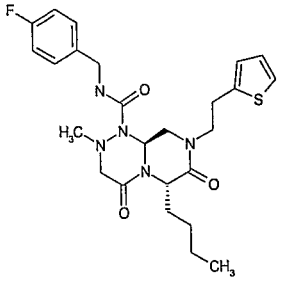
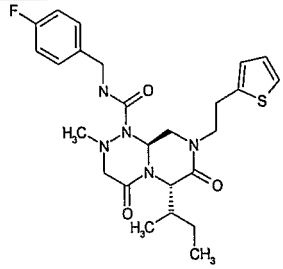
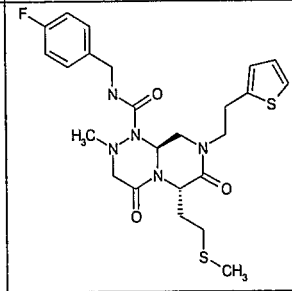
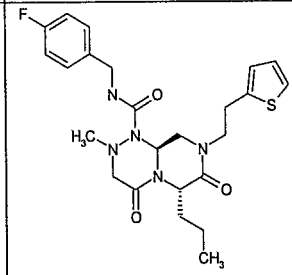
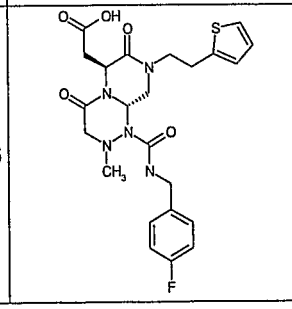
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2377		576	577
2378		542	543
2379		542	543
2380		560	561
2381		528	529
2382		544	545

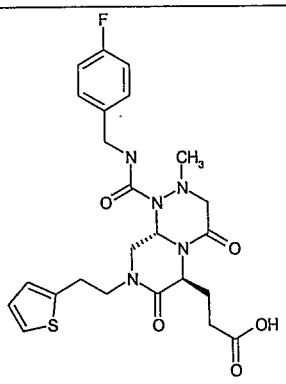
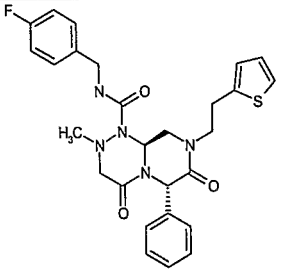
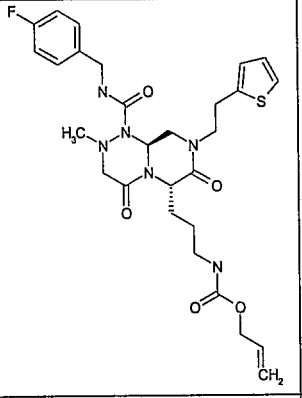
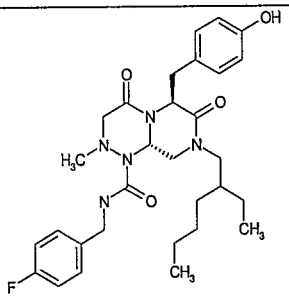
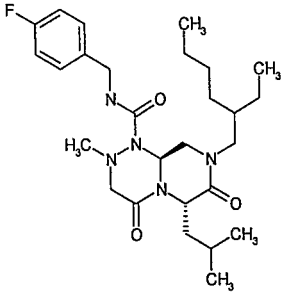
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2383		558	559
2384		562	563
2385		627	628
2386		566	567
2387		516	517

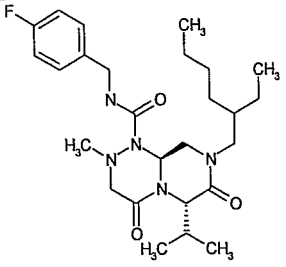
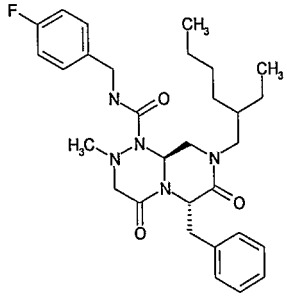
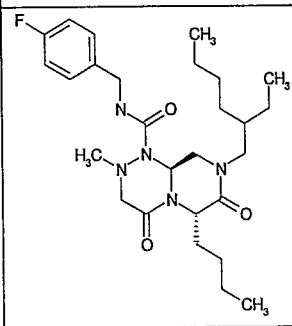
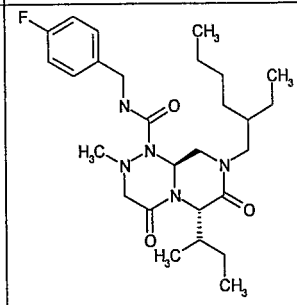
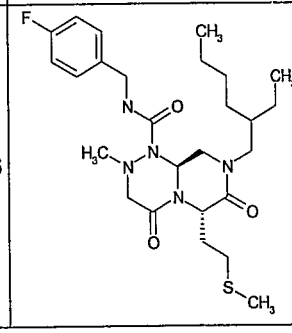
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2388		502	503
2389		550	551
2390		516	517
2391		516	517
2392		534	535

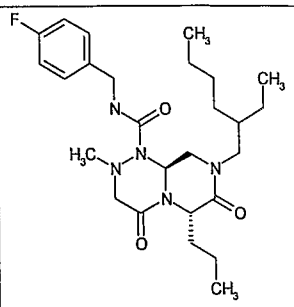
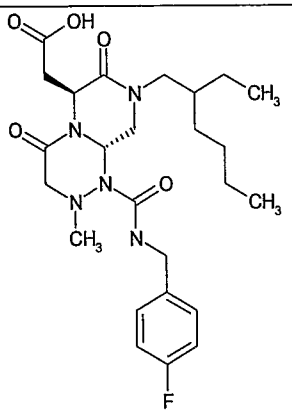
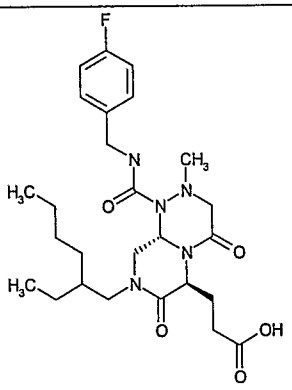
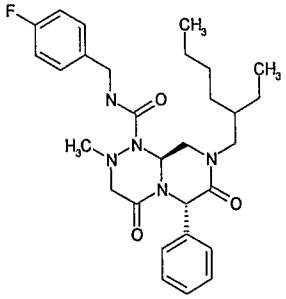
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2394		518	519
2395		532	533
2396		536	537

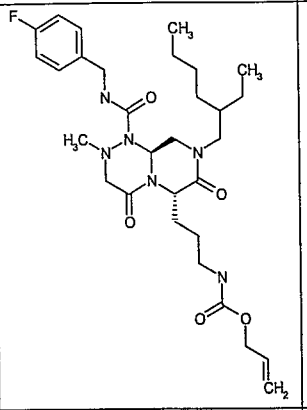
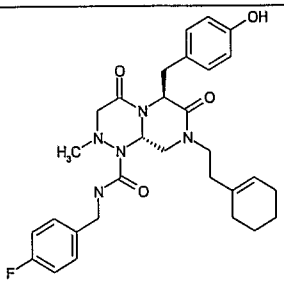
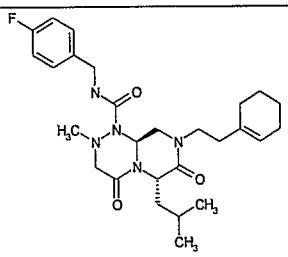
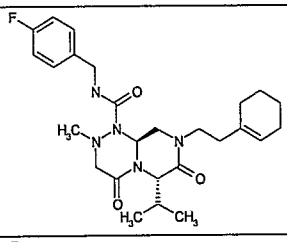
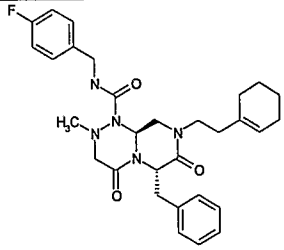
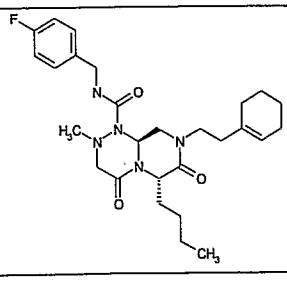
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2397		601	602
2398		552	553
2399		502	503
2400		488	489
2401		536	537

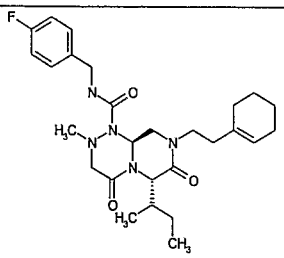
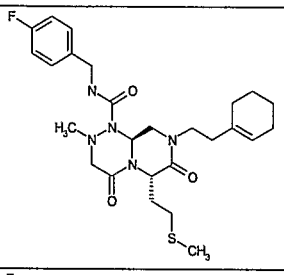
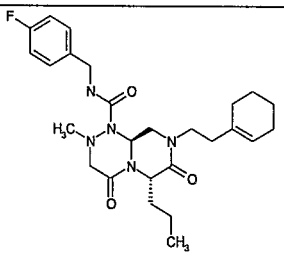
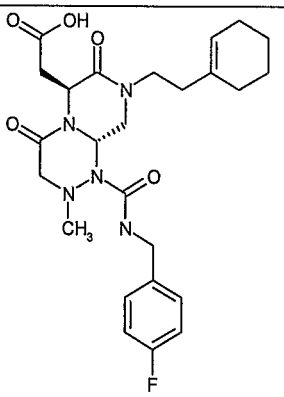
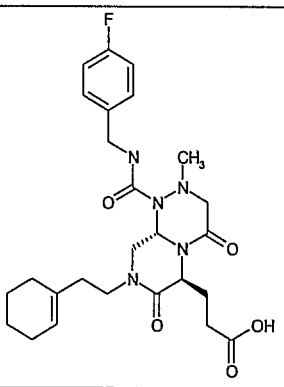
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2402		502	503
2403		502	503
2404		520	521
2405		488	489
2406		504	505

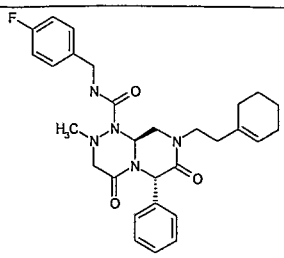
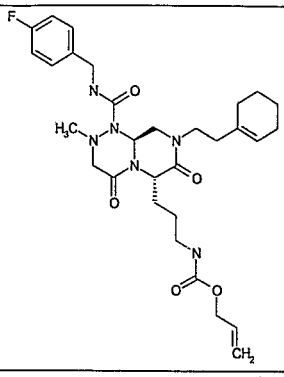
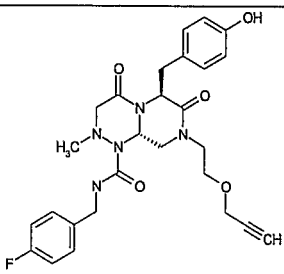
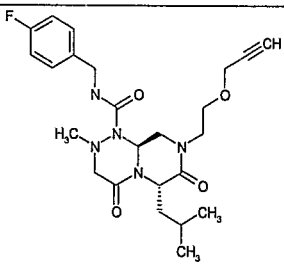
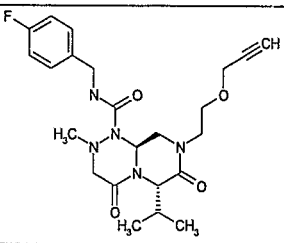
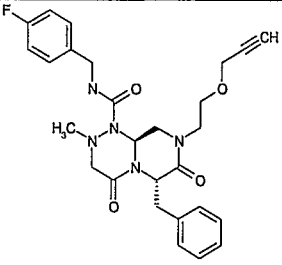
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2408		522	523
2409		587	588
2410		554	555
2411		504	505

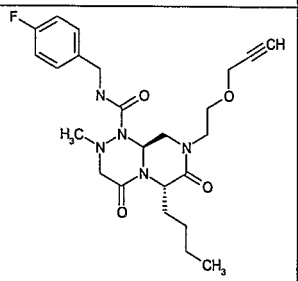
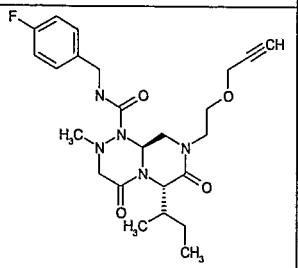
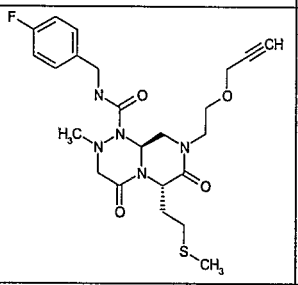
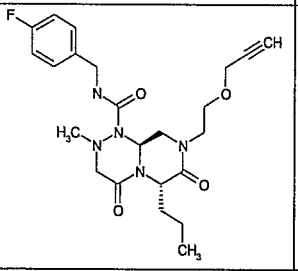
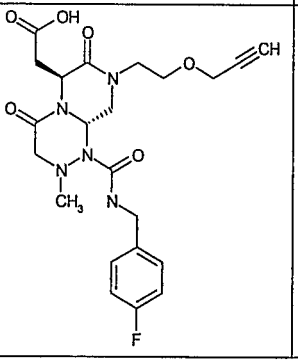
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2412		490	491
2413		538	539
2414		504	505
2415		504	505
2416		522	523

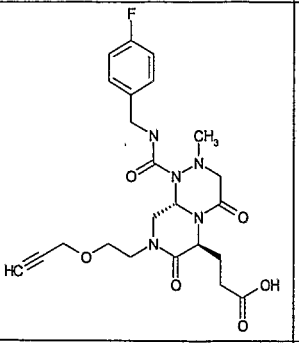
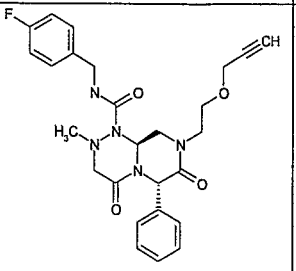
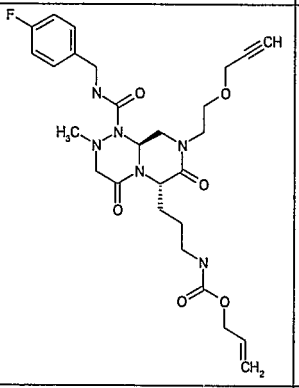
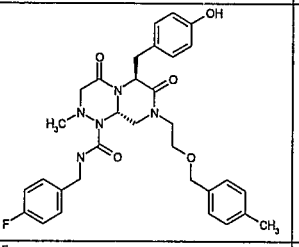
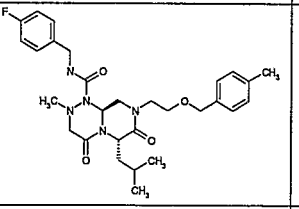
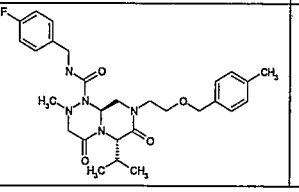
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2417		490	491
2418		506	507
2419		520	521
2420		524	525

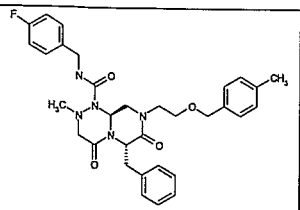
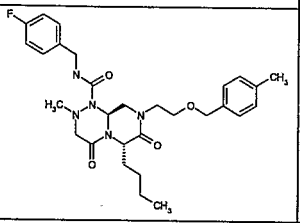
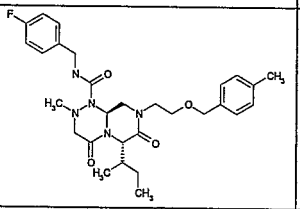
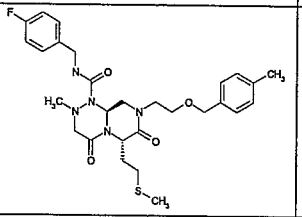
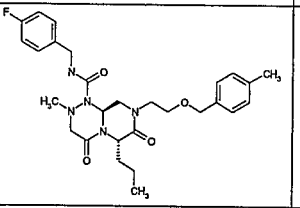
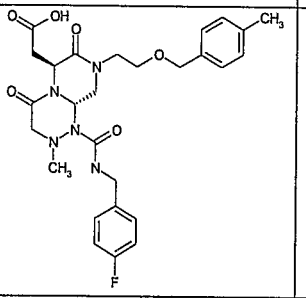
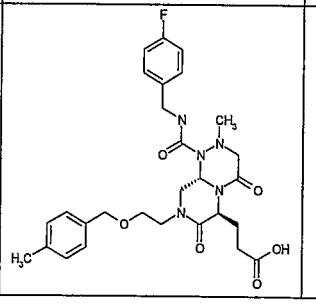
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2421		589	590
2422		550	551
2423		500	501
2424		486	487
2425		534	535
2426		500	501

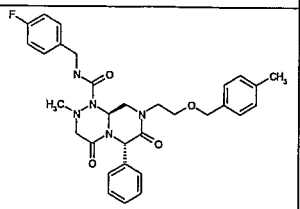
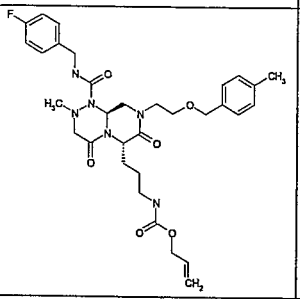
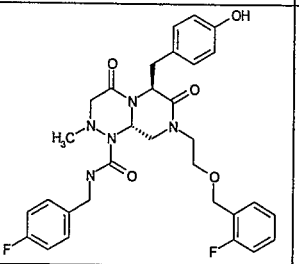
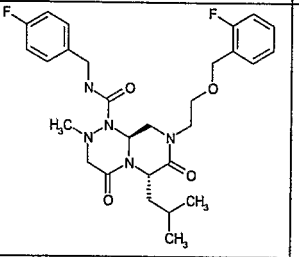
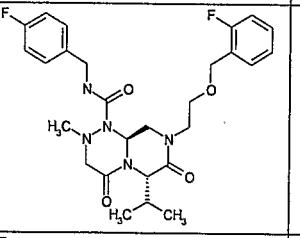
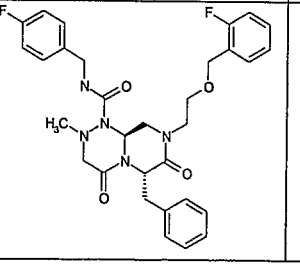
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2427		500	501
2428		518	519
2429		486	487
2430		502	503
2431		516	517

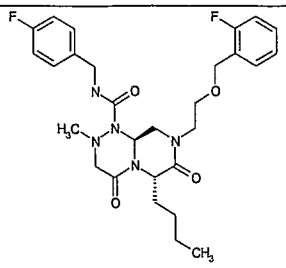
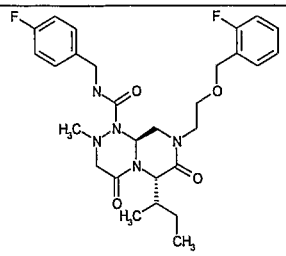
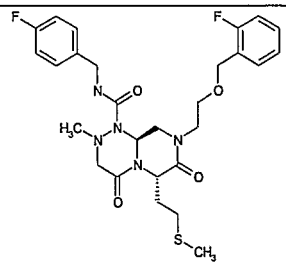
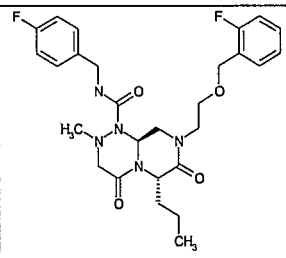
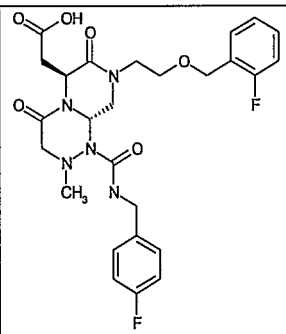
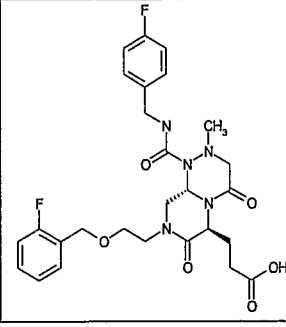
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2432		520	521
2433		585	586
2434		524	525
2435		474	475
2436		460	461
2437		508	509

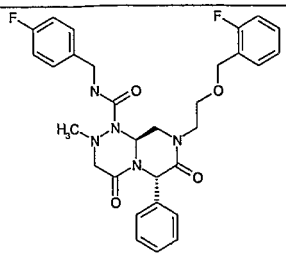
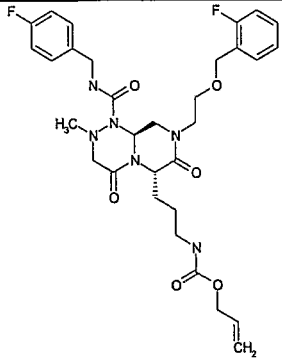
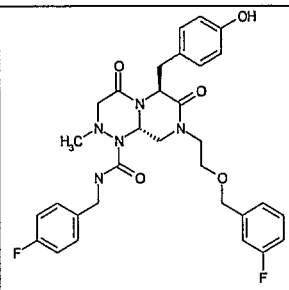
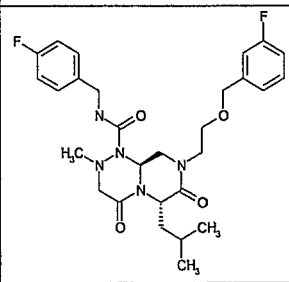
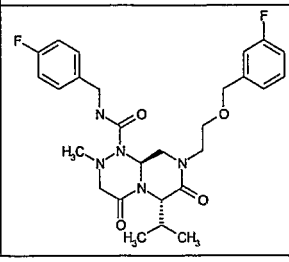
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2438		474	475
2439		474	475
2440		492	493
2441		460	461
2442		475	476

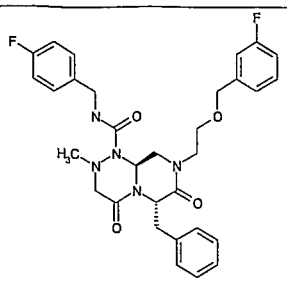
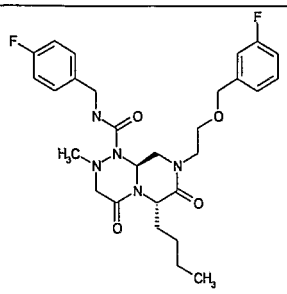
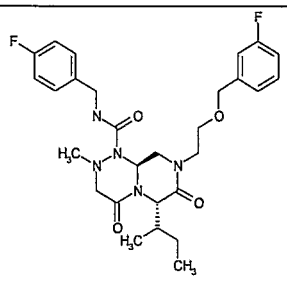
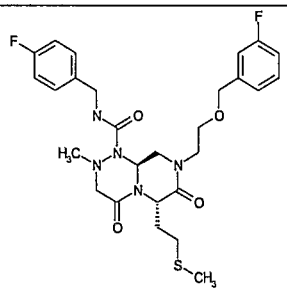
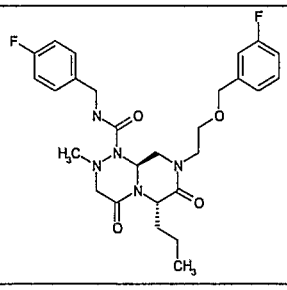
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2443		490	491
2444		494	495
2445		559	560
2446		590	591
2447		540	541
2448		526	527

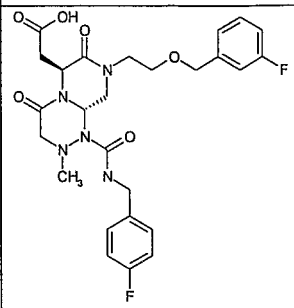
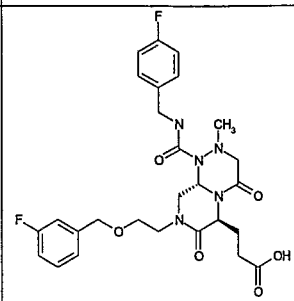
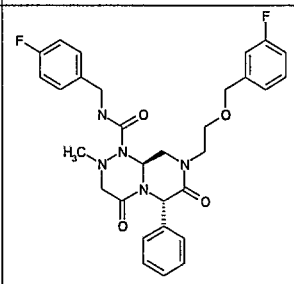
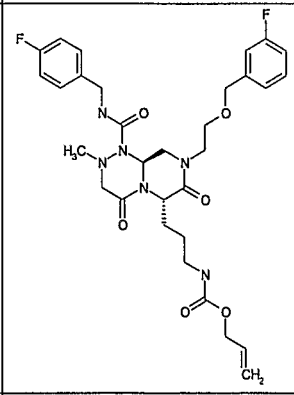
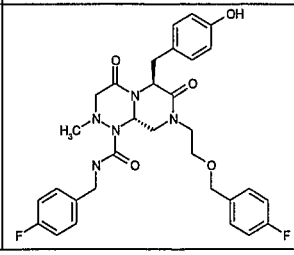
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2449		574	575
2450		540	541
2451		540	541
2452		558	559
2453		526	527
2454		542	543
2455		556	557

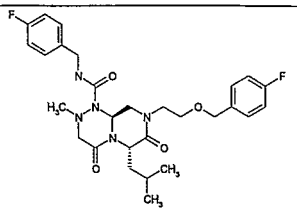
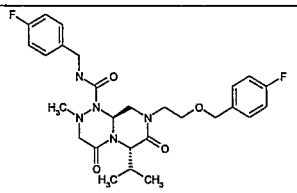
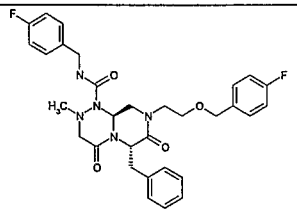
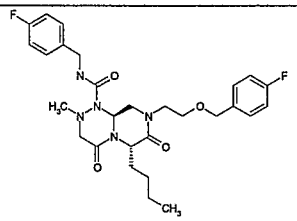
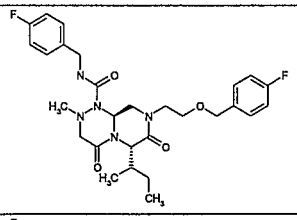
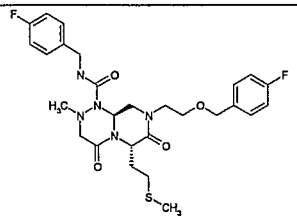
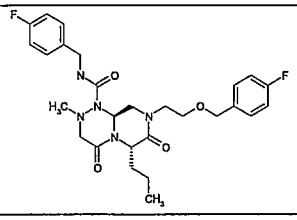
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2456		560	561
2457		625	626
2458		594	595
2459		544	545
2460		530	531
2461		578	579

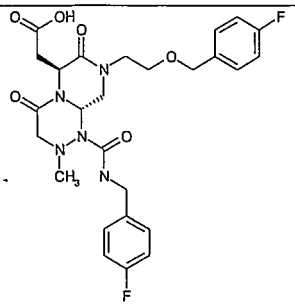
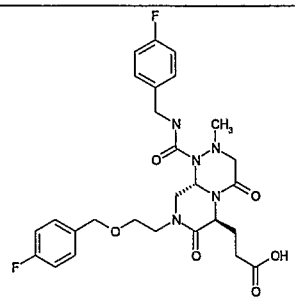
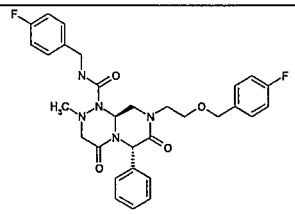
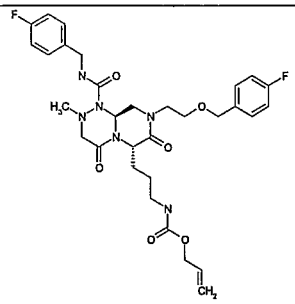
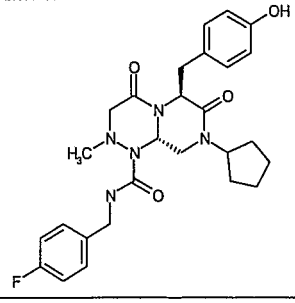
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2462		544	545
2463		544	545
2464		562	563
2465		530	531
2466		546	547
2467		560	561

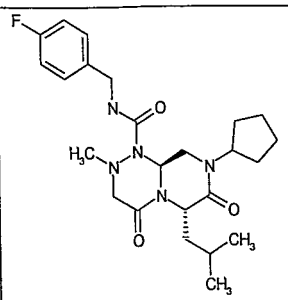
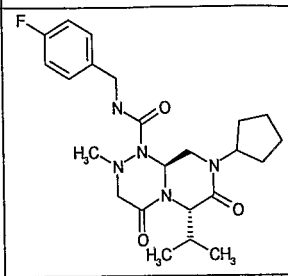
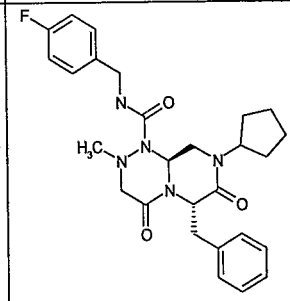
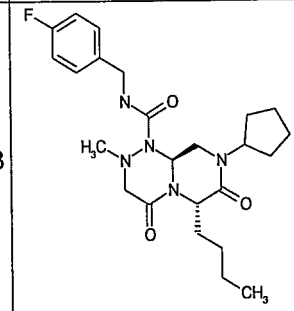
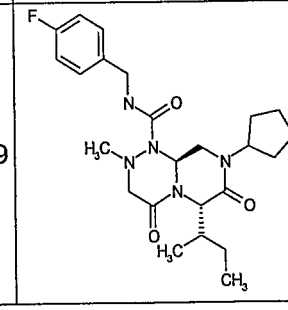
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2468		564	565
2469		629	630
2470		594	595
2471		544	545
2472		530	531

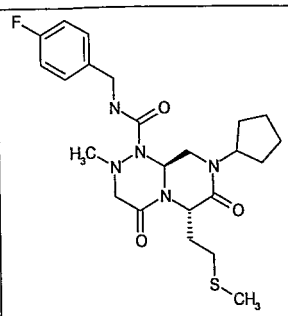
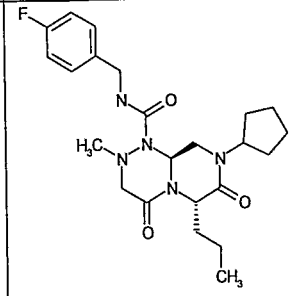
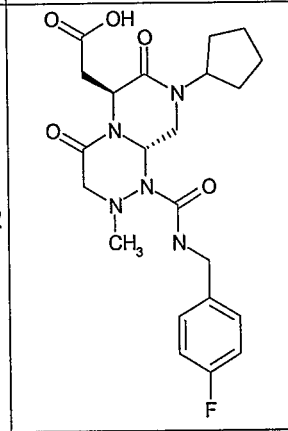
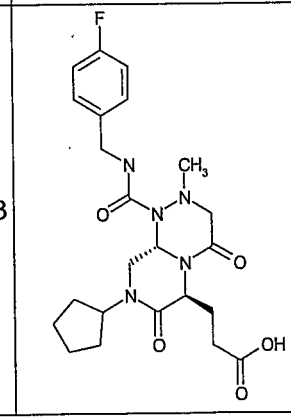
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2473		578	579
2474		544	545
2475		544	545
2476		562	563
2477		530	531

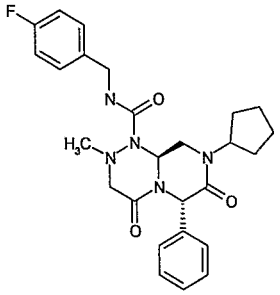
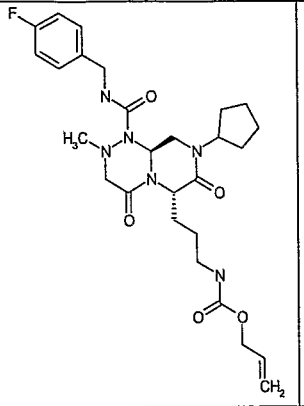
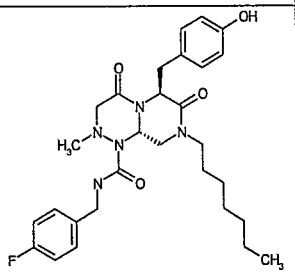
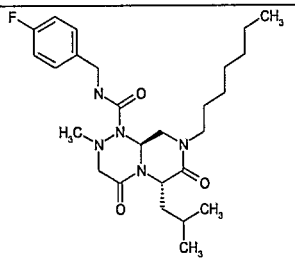
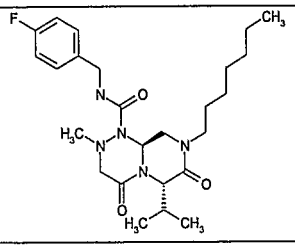
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2478		546	547
2479		560	561
2480		564	565
2481		629	630
2482		594	595

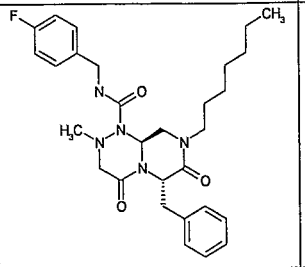
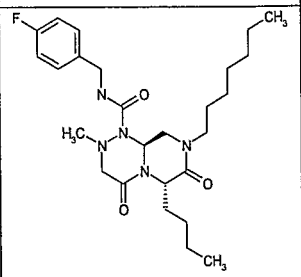
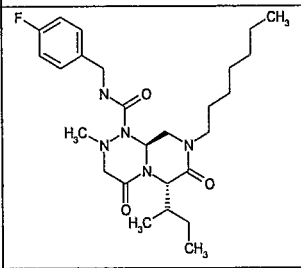
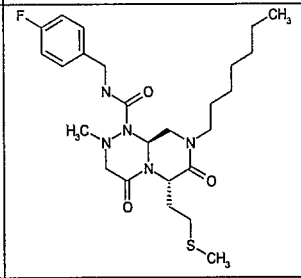
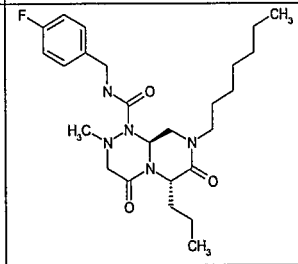
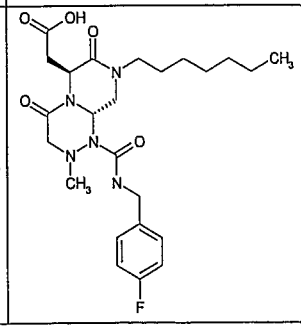
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2483		544	545
2484		530	531
2485		578	579
2486		544	545
2487		544	545
2488		562	563
2489		530	531

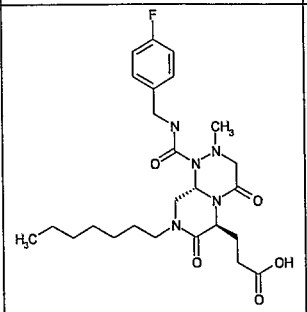
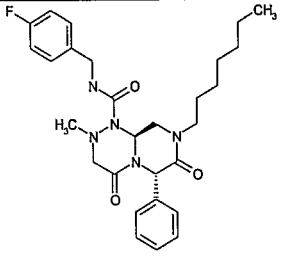
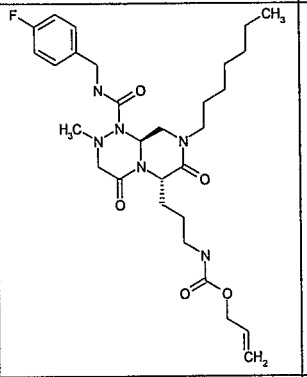
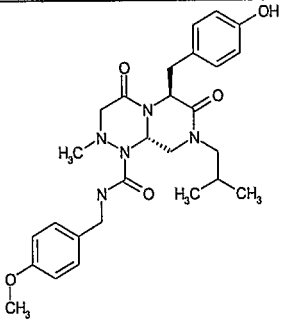
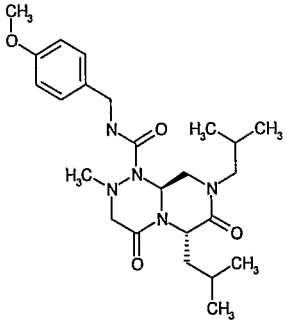
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2490		546	547
2491		560	561
2492		564	565
2493		629	630
2494		510	511

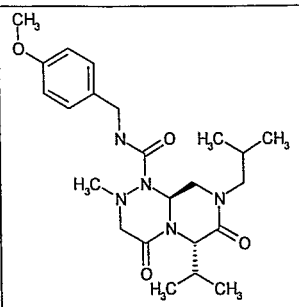
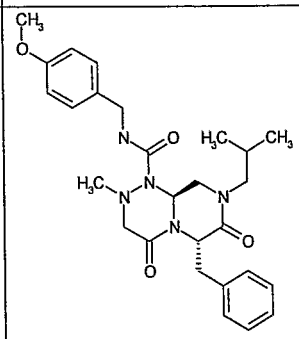
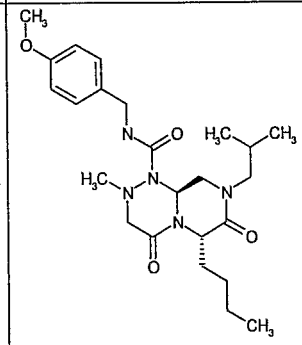
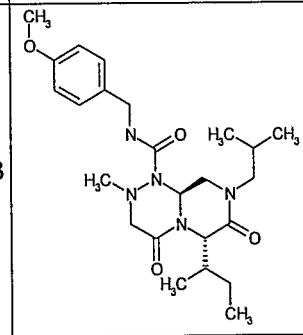
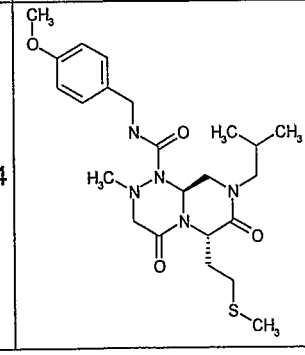
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2495		460	461
2496		446	447
2497		494	495
2498		460	461
2499		460	461

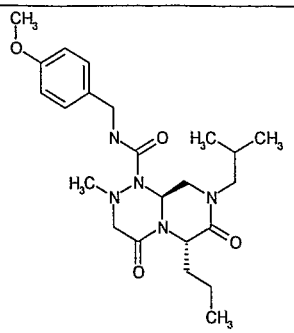
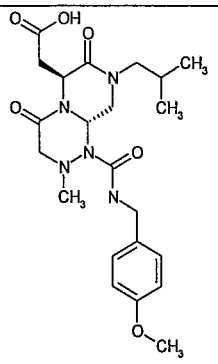
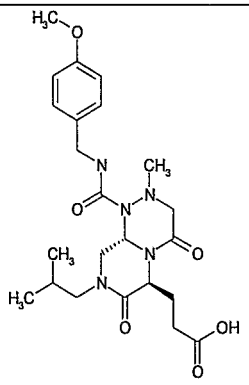
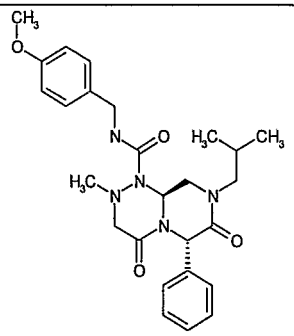
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2500		478	479
2501		446	447
2502		461	462
2503		476	477

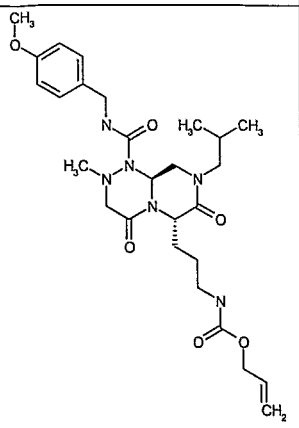
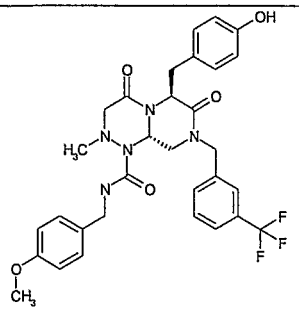
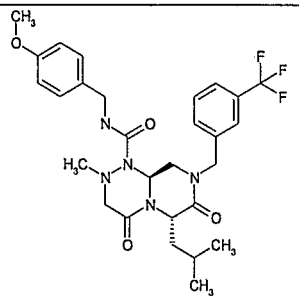
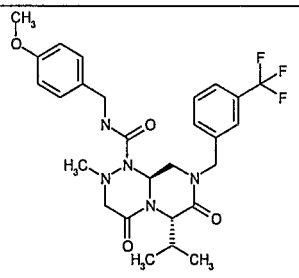
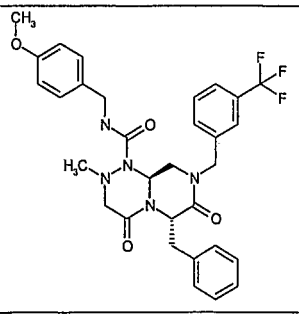
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2504		480	481
2505		545	546
2506		540	541
2507		490	491
2508		476	477

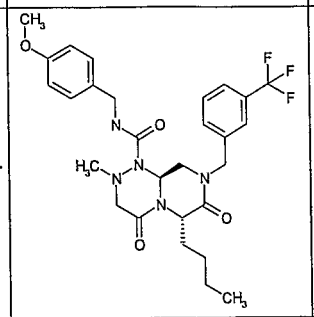
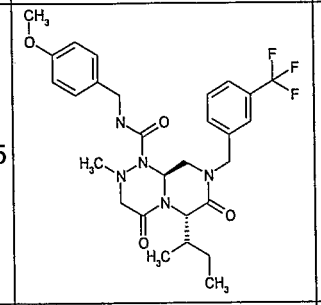
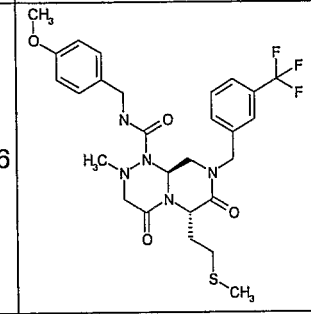
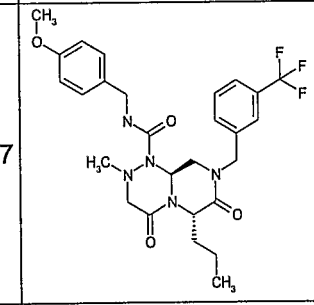
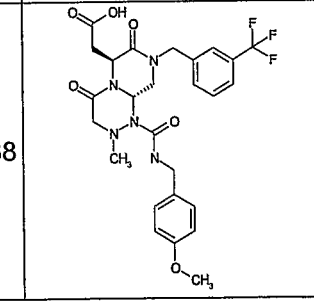
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2509		524	525
2510		490	491
2511		490	491
2512		508	509
2513		476	477
2514		492	493

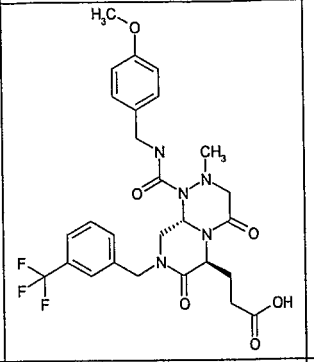
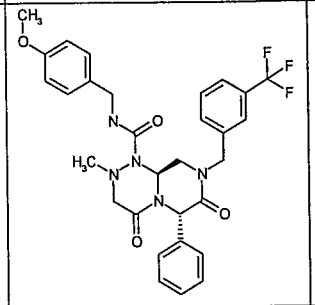
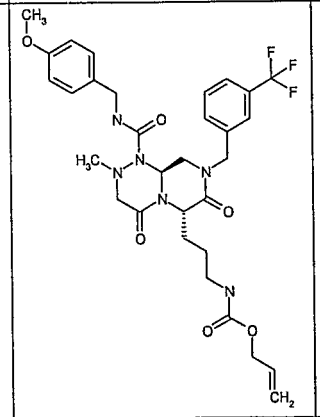
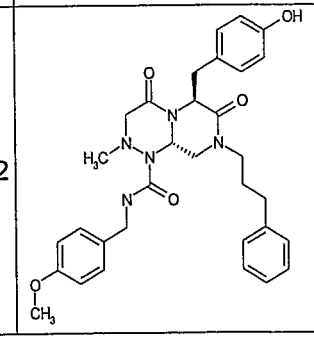
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2515		506	507
2516		510	511
2517		575	576
2518		510	511
2519		460	461

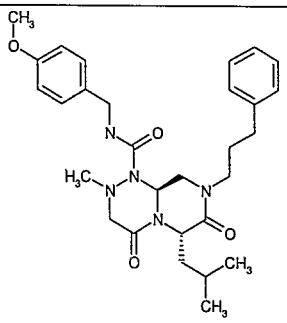
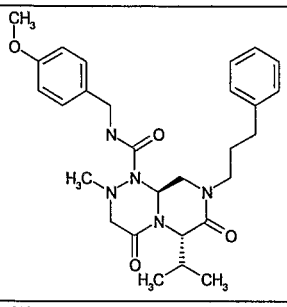
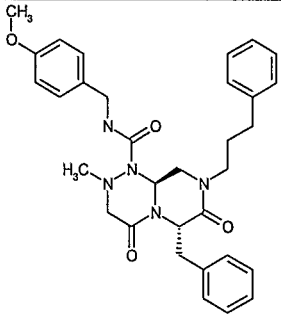
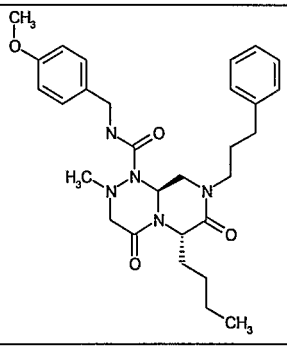
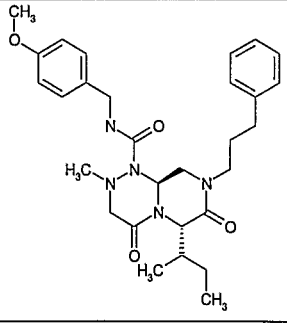
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2520		446	447
2521		494	495
2522		460	461
2523		460	461
2524		478	479

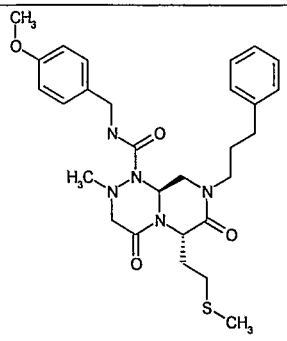
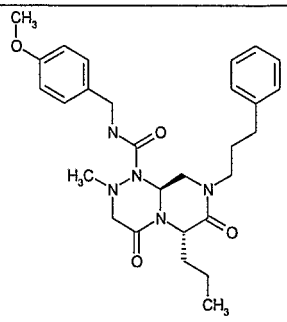
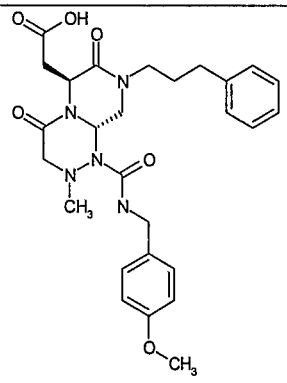
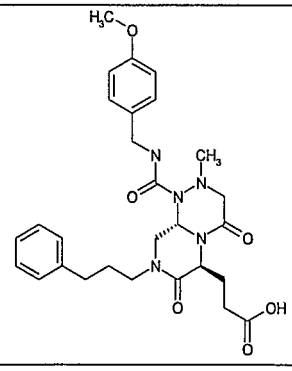
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2525		446	447
2526		462	463
2527		476	477
2528		480	481

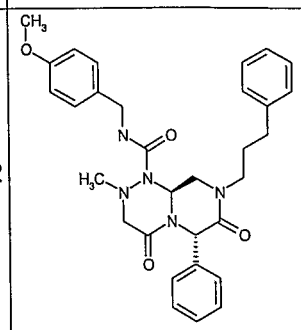
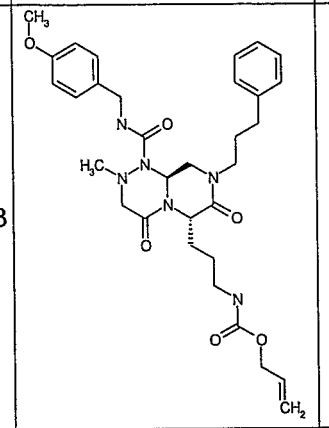
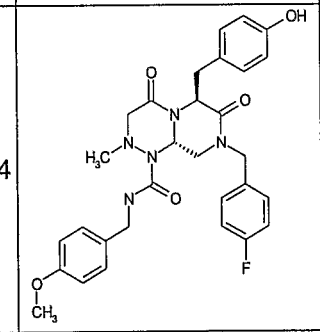
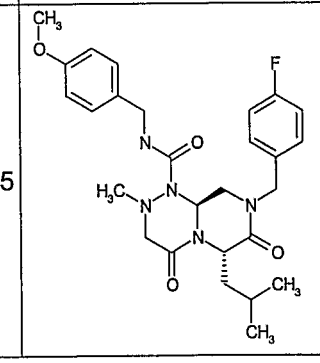
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2529		545	546
2530		612	613
2531		562	563
2532		548	549
2533		596	597

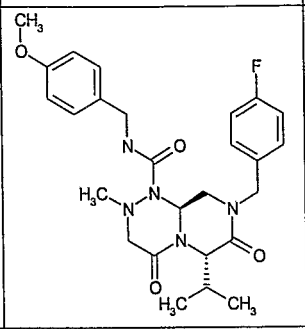
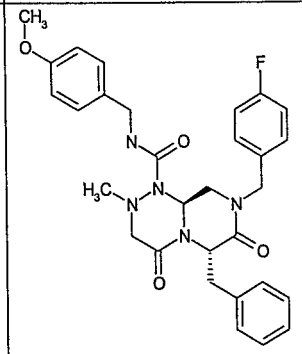
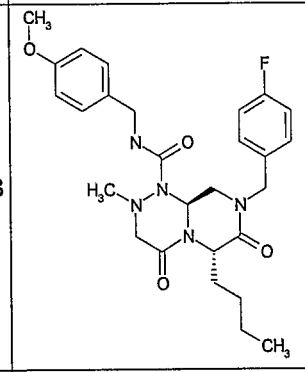
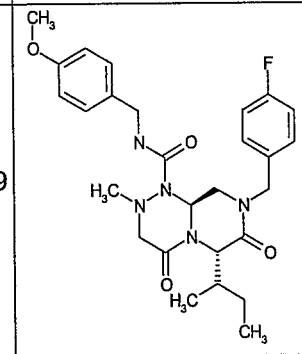
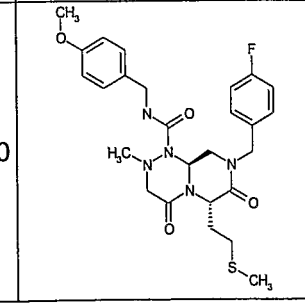
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2534		562	563
2535		562	563
2536		580	581
2537		548	549
2538		564	565

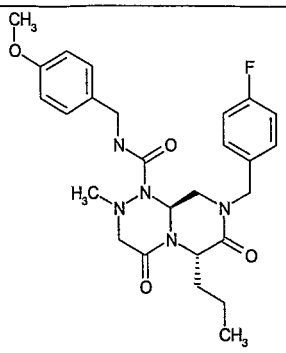
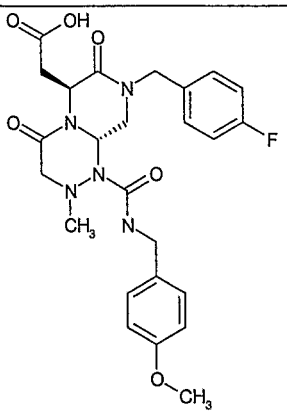
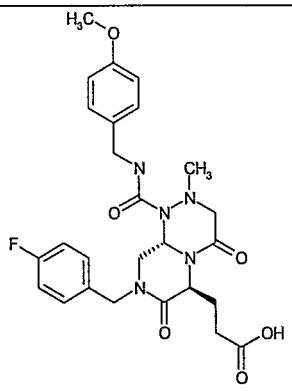
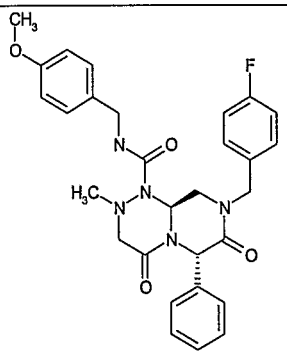
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2539		578	579
2540		582	583
2541		647	648
2542		572	573

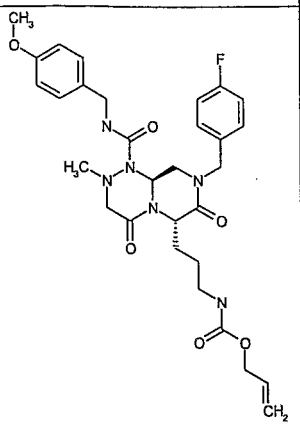
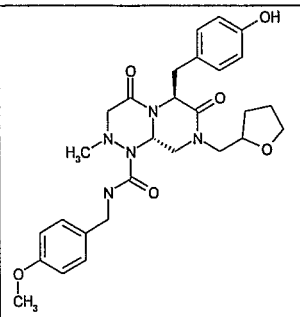
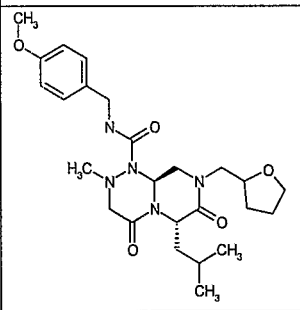
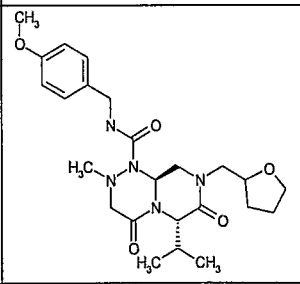
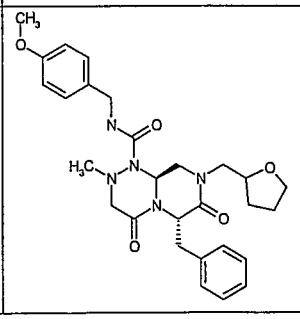
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2543		522	523
2544		508	509
2545		556	557
2546		522	523
2547		522	523

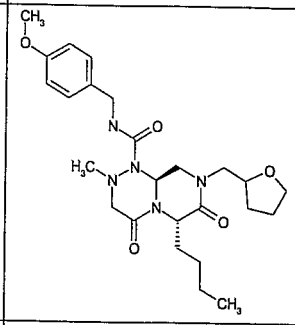
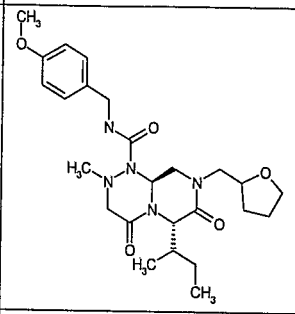
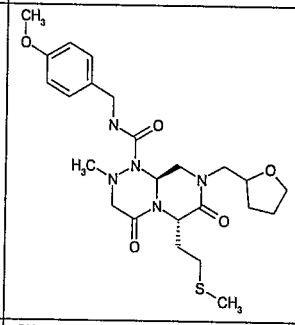
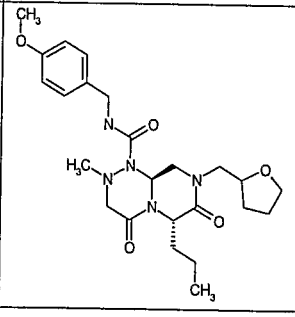
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2548		540	541
2549		508	509
2550		524	525
2551		538	539

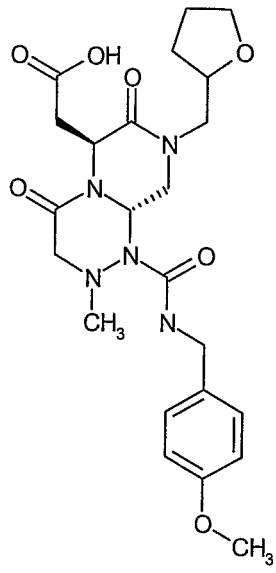
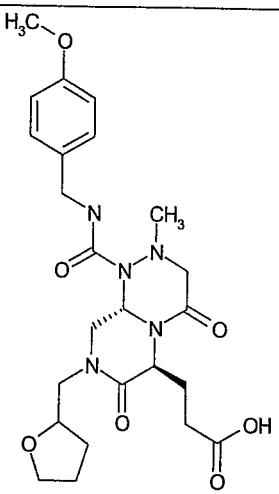
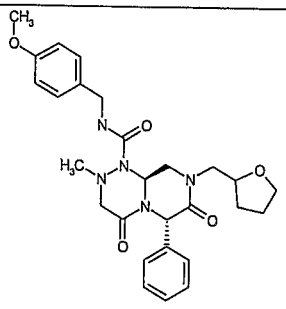
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2552		542	543
2553		607	608
2554		562	563
2555		512	513

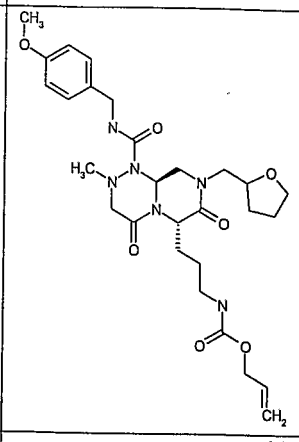
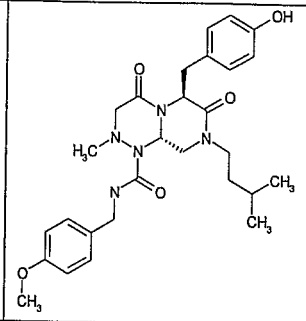
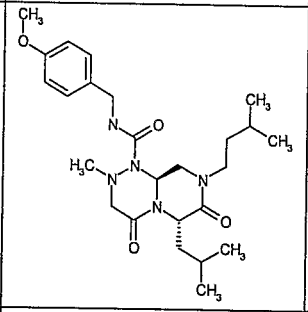
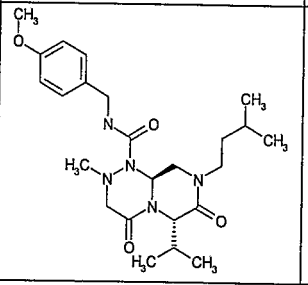
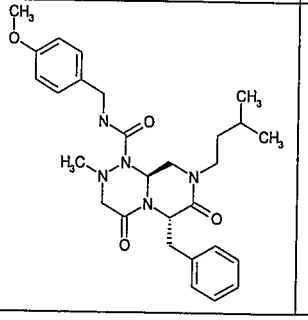
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2556		498	499
2557		546	547
2558		512	513
2559		512	513
2560		530	531

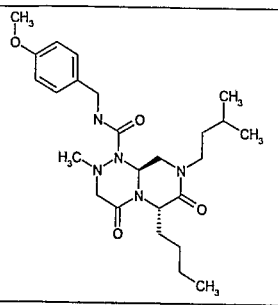
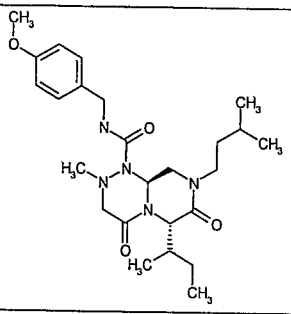
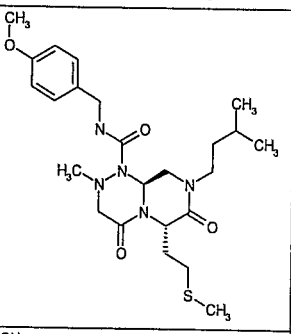
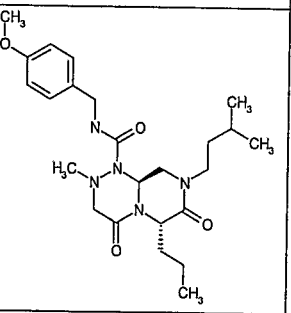
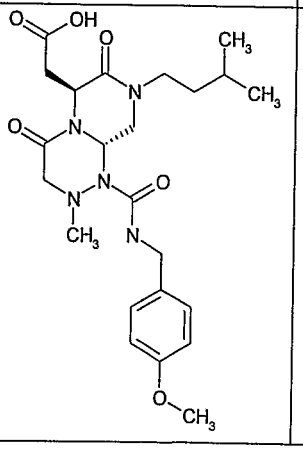
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2562		514	515
2563		528	529
2564		532	533

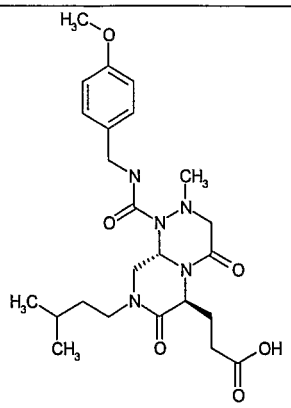
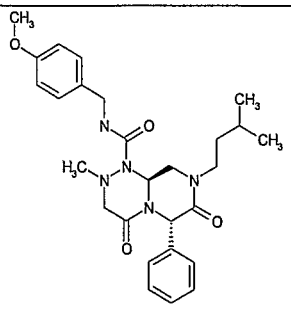
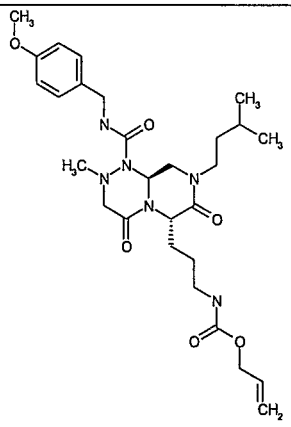
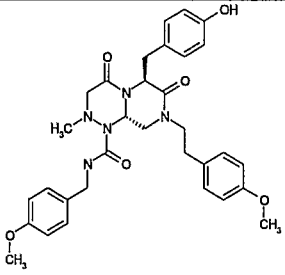
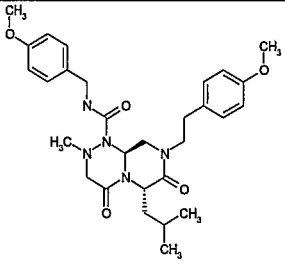
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2565		597	598
2566		538	539
2567		488	489
2568		474	475
2569		522	523

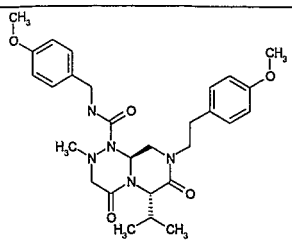
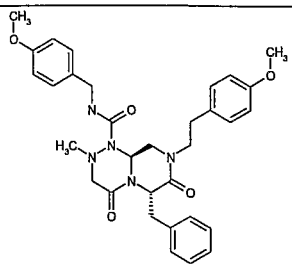
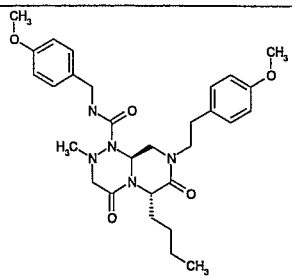
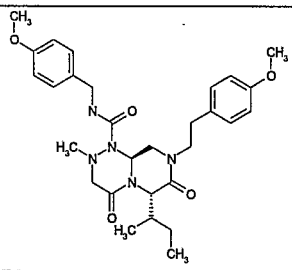
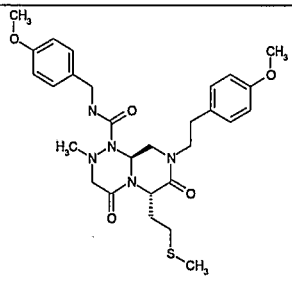
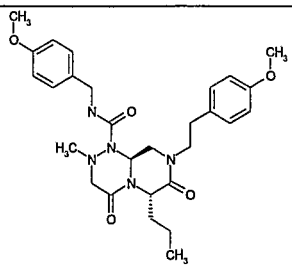
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2570		488	489
2571		488	489
2572		506	507
2573		474	475

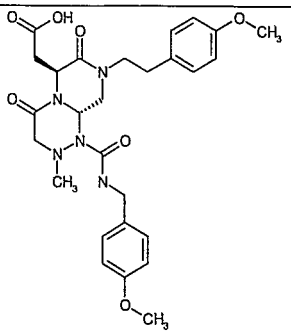
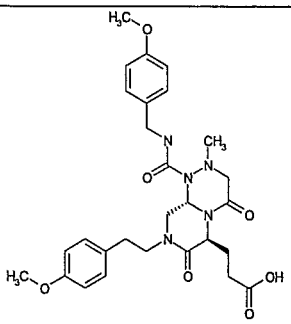
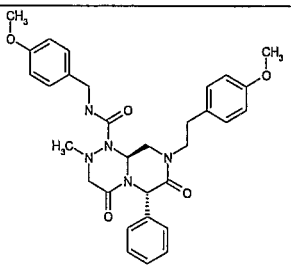
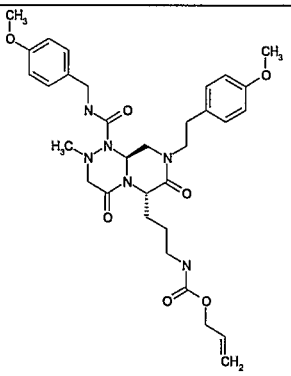
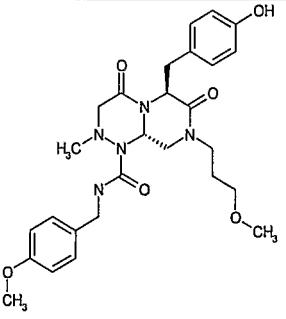
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2574		490	491
2575		504	505
2576		508	509

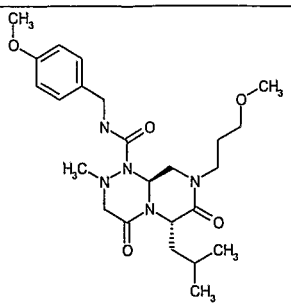
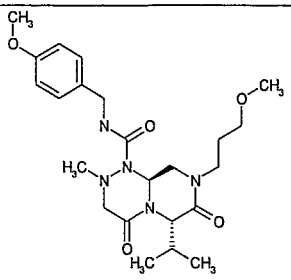
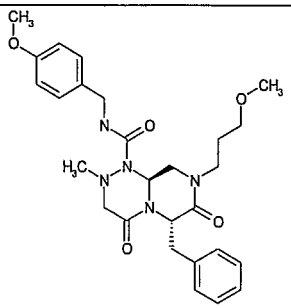
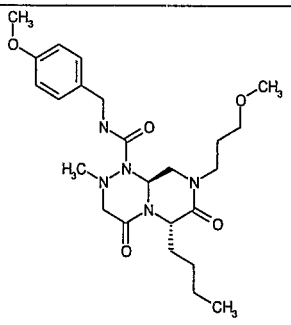
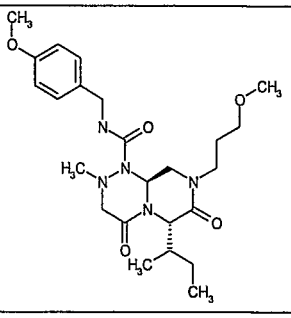
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2577		573	574
2578		524	525
2579		474	475
2580		460	461
2581		508	509

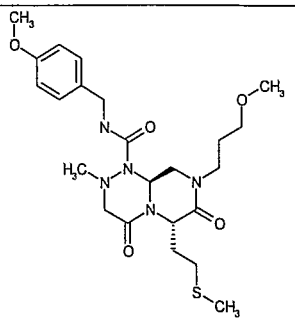
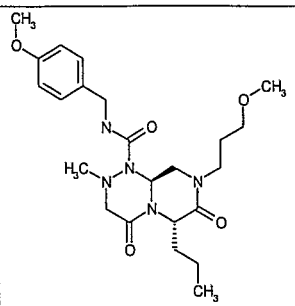
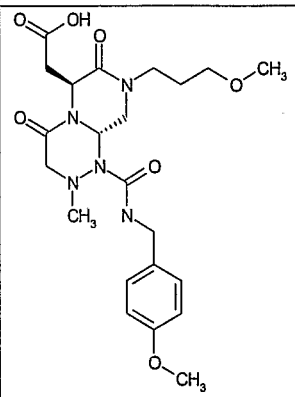
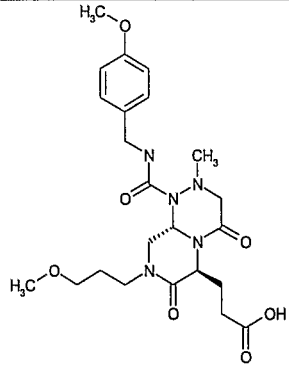
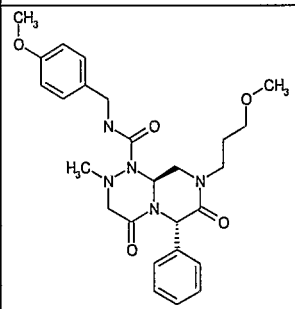
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2582		474	475
2583		474	475
2584		492	493
2585		460	461
2586		476	477

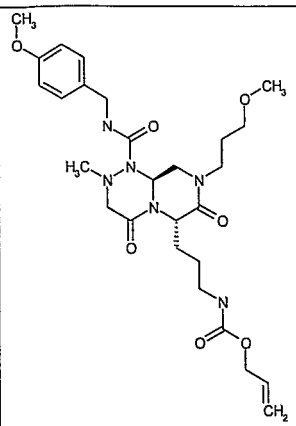
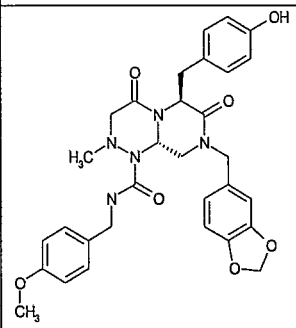
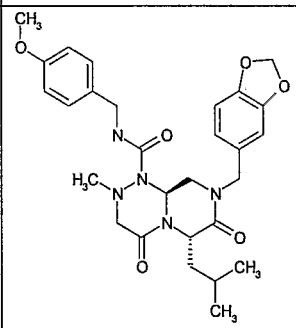
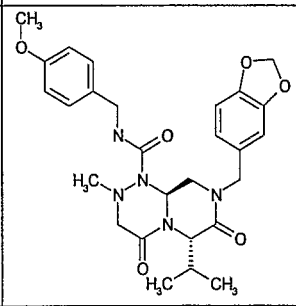
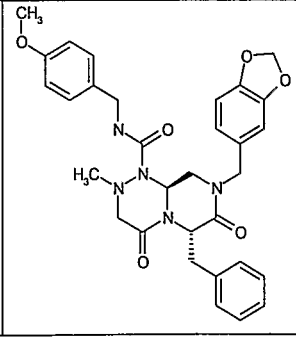
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2587		490	491
2588		494	495
2589		559	560
2590		588	589
2591		538	539

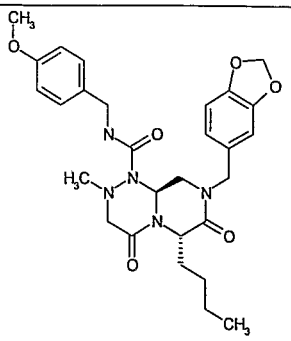
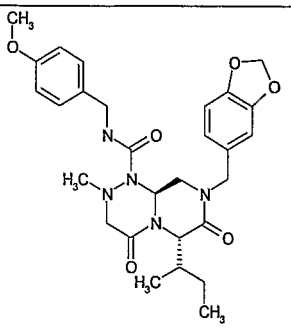
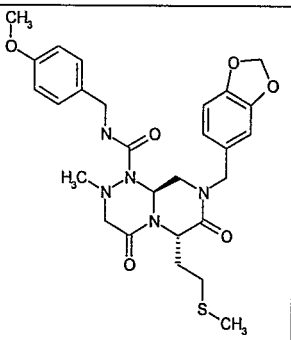
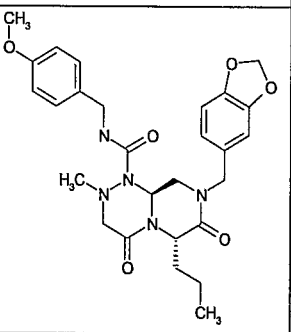
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2592		524	525
2593		572	573
2594		538	539
2595		538	539
2596		556	557
2597		524	525

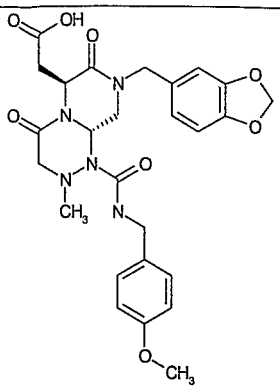
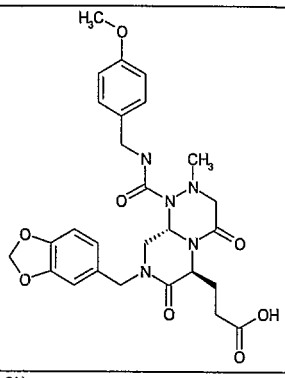
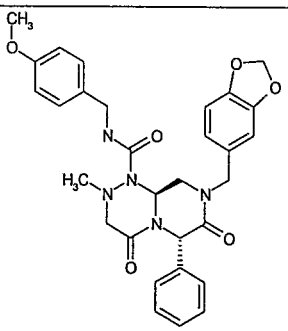
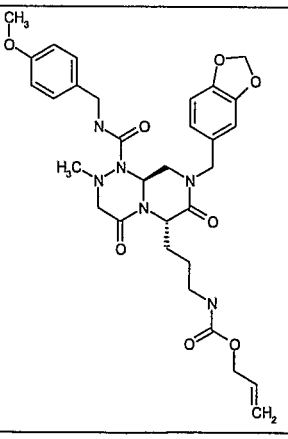
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2598		540	541
2599		554	555
2600		558	559
2601		623	624
2602		526	527

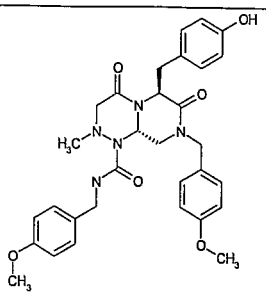
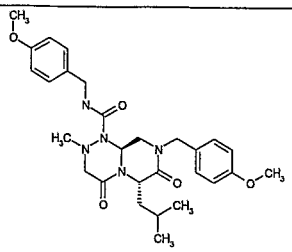
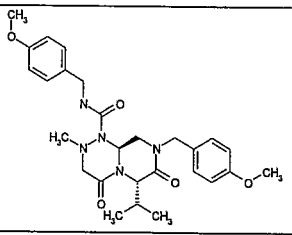
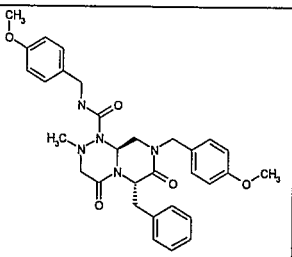
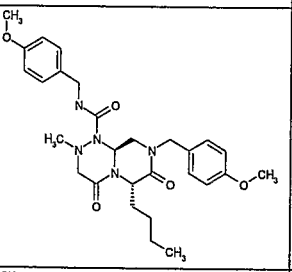
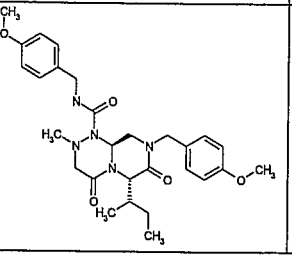
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2603		476	477
2604		462	463
2605		510	511
2606		476	477
2607		476	477

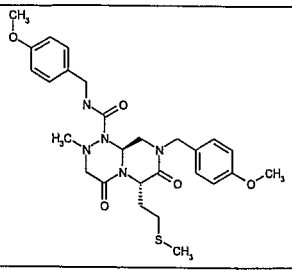
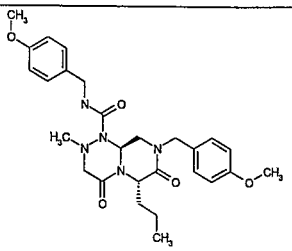
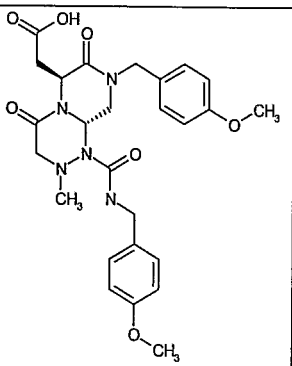
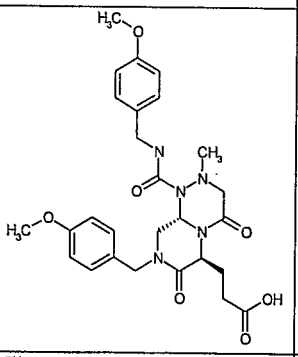
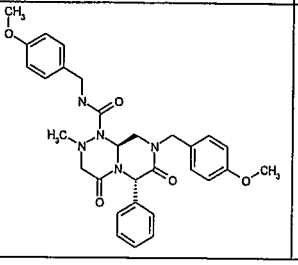
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2608		494	495
2609		462	463
2610		478	479
2611		492	493
2612		496	497

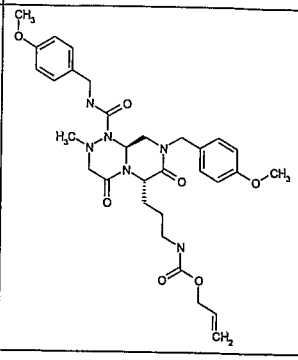
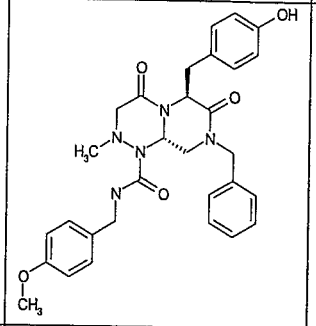
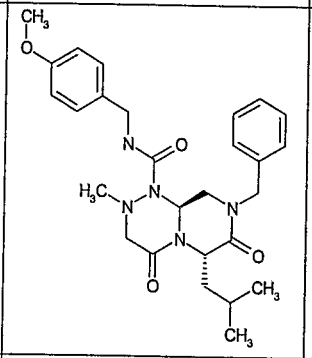
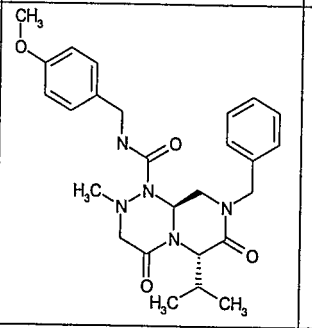
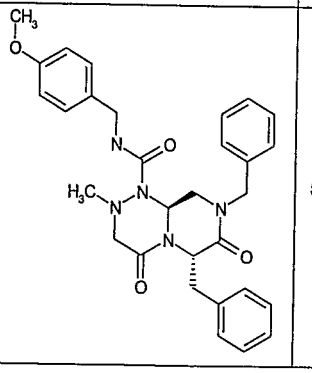
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2613		561	562
2614		588	589
2615		538	539
2616		524	525
2617		572	573

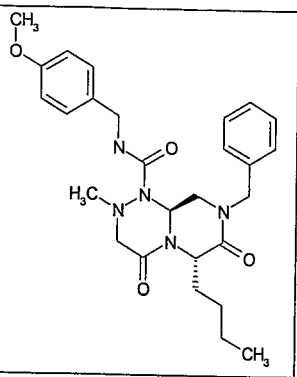
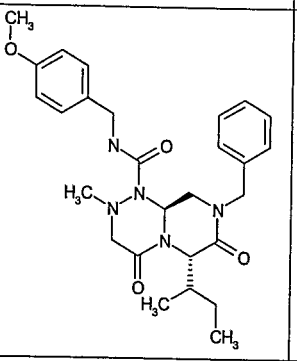
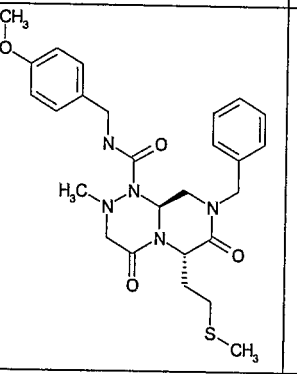
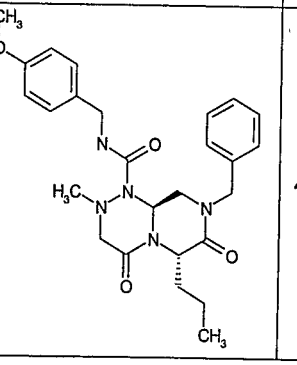
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2618		538	539
2619		538	539
2620		556	557
2621		524	525

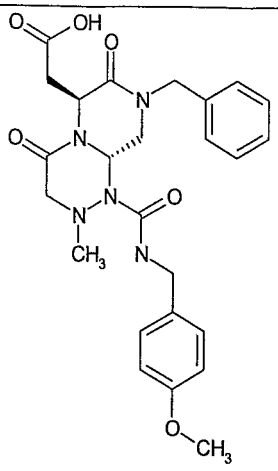
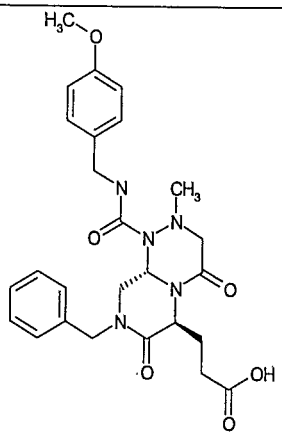
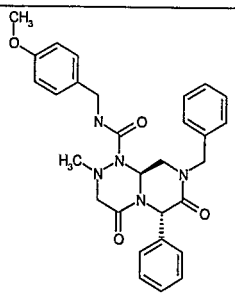
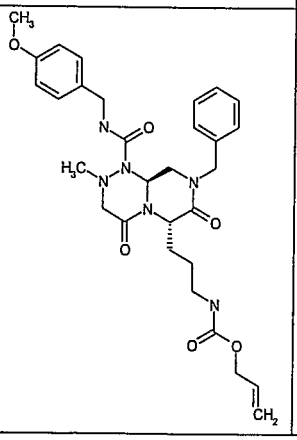
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2622		540	541
2623		554	555
2624		558	559
2625		623	624

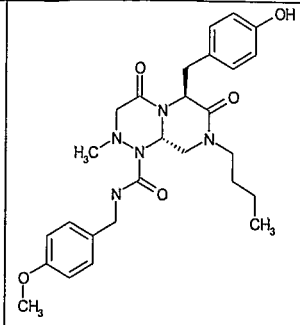
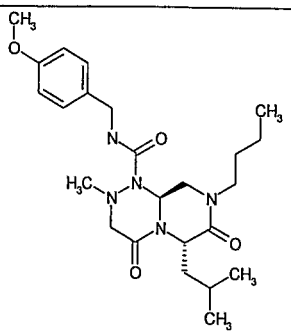
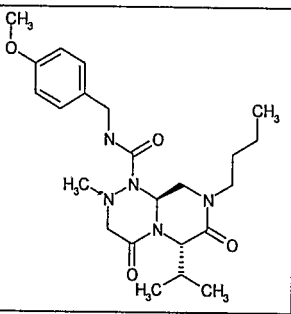
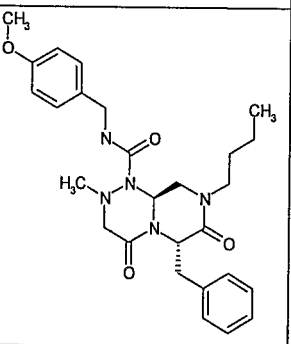
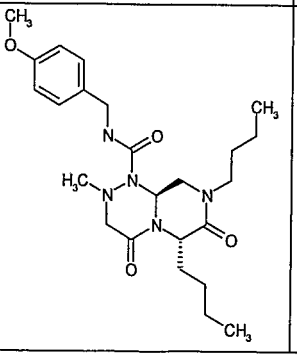
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2627		524	525
2628		510	511
2629		558	559
2630		524	525
2631		524	525

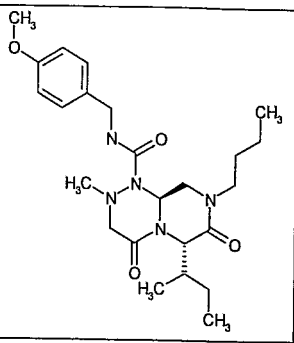
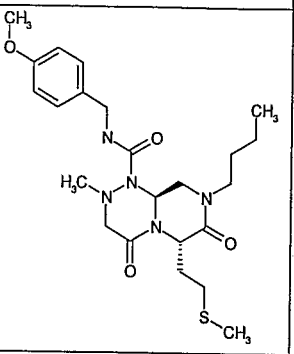
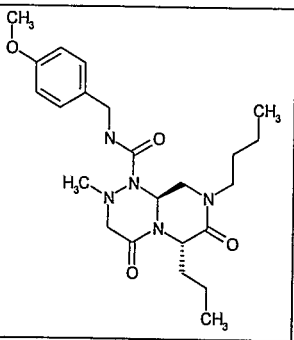
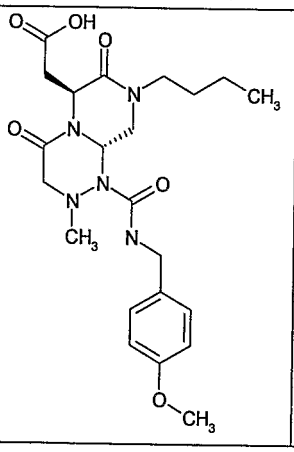
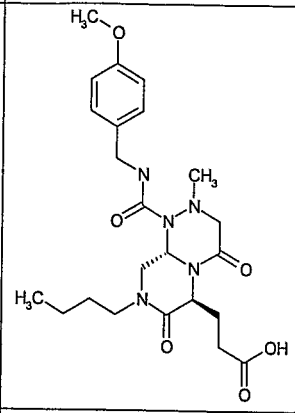
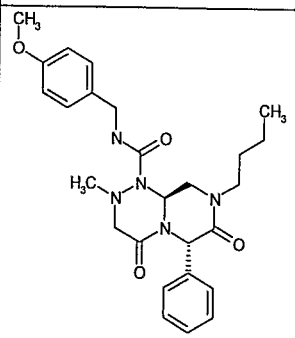
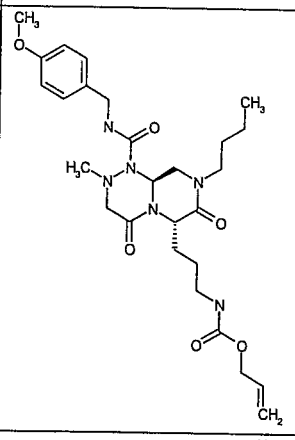
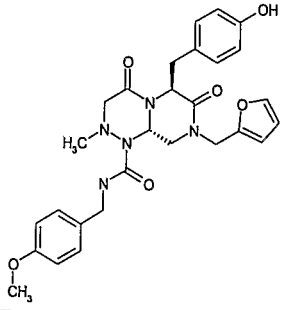
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2632		542	543
2633		510	511
2634		526	527
2635		540	541
2636		544	545

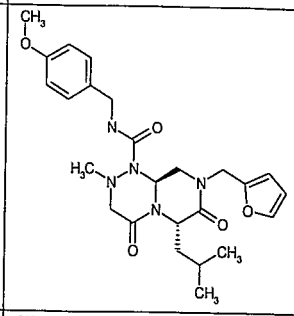
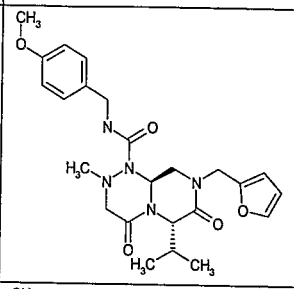
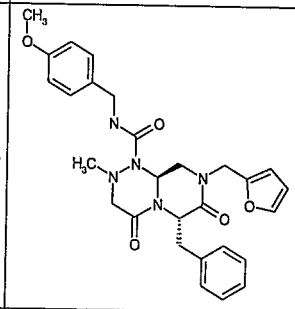
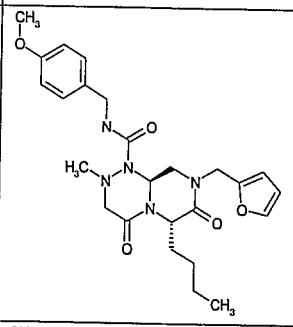
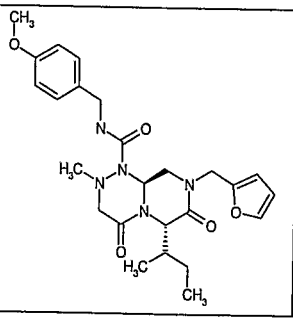
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2637		609	610
2638		544	545
2639		494	495
2640		480	481
2641		528	529

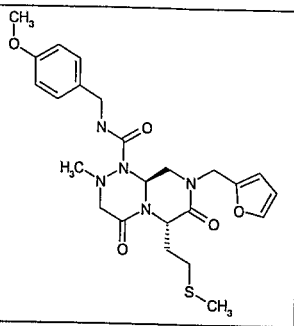
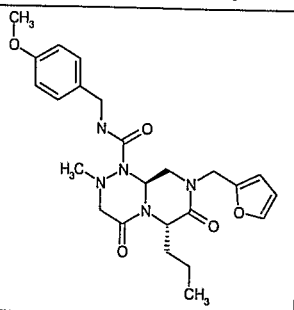
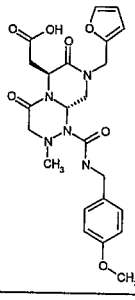
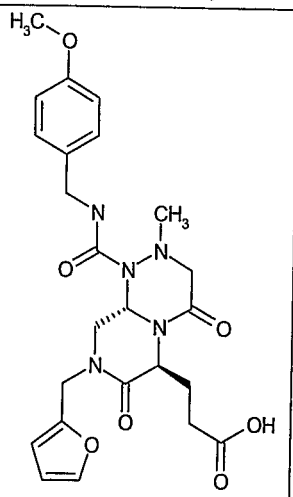
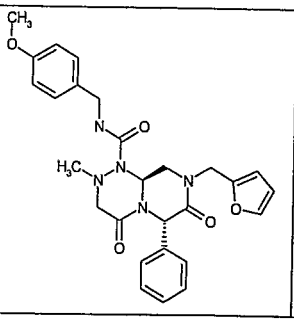
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2642		494	495
2643		494	495
2644		512	513
2645		480	481

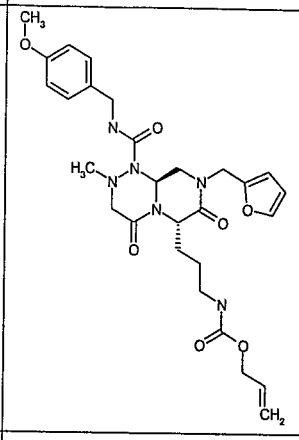
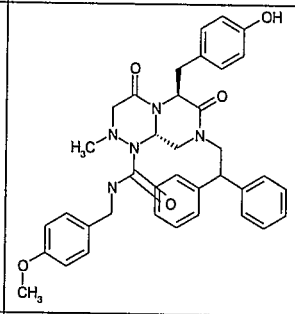
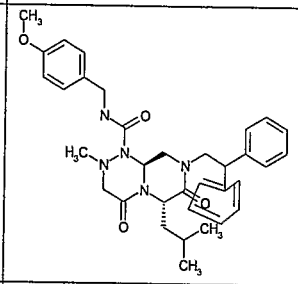
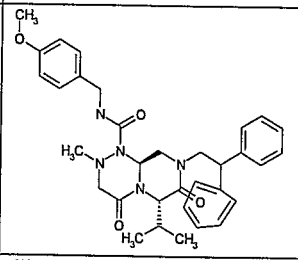
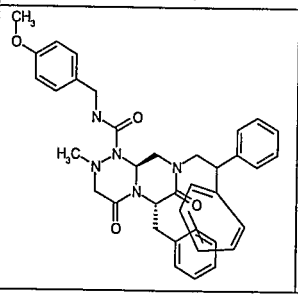
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2646		496	497
2647		510	511
2648		514	515
2649		579	580

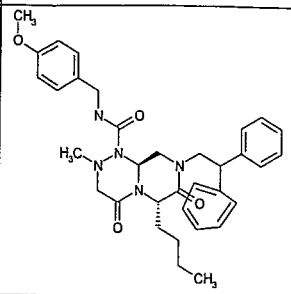
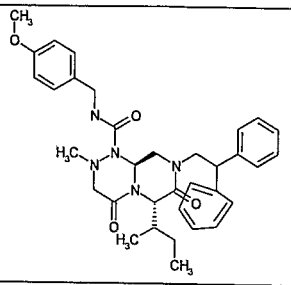
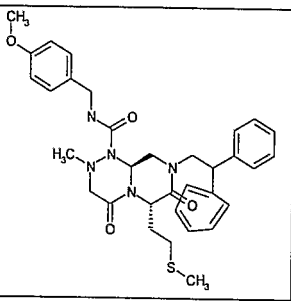
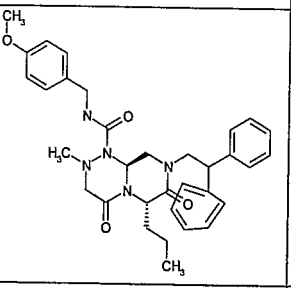
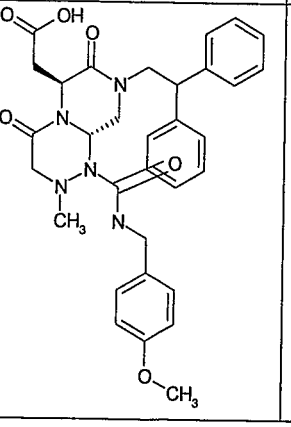
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2650		510	511
2651		460	461
2652		446	447
2653		494	495
2654		460	461

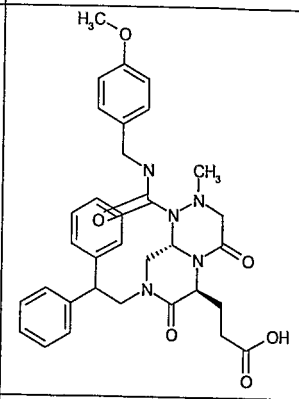
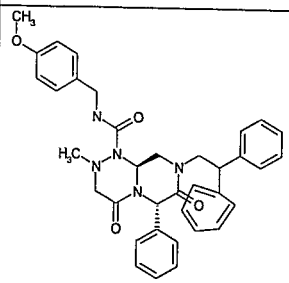
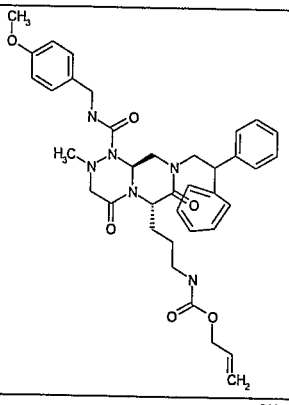
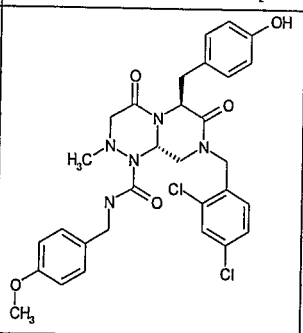
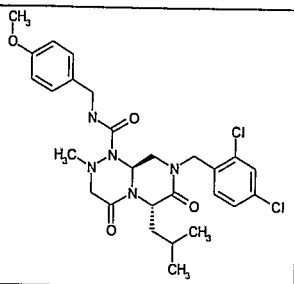
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2655		460	461
2656		478	479
2657		446	447
2658		462	463
2659		476	477
2660		480	481
2661		545	546
2662		534	535

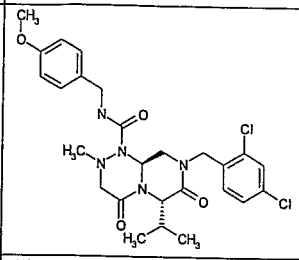
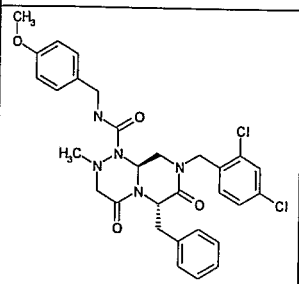
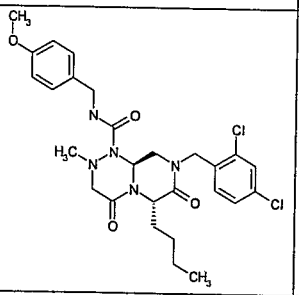
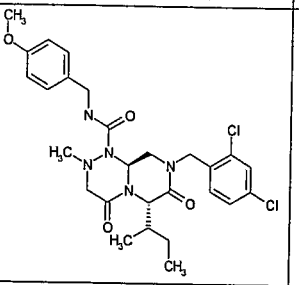
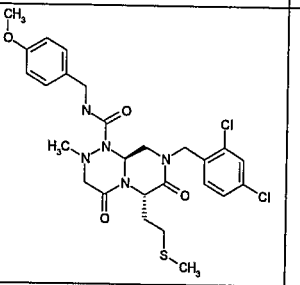
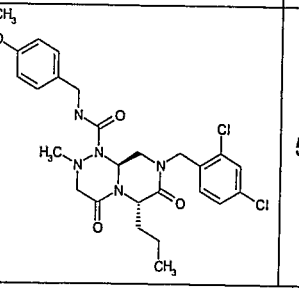
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2663		484	485
2664		470	471
2665		518	519
2666		484	485
2667		484	485

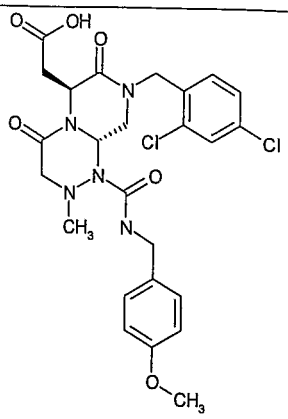
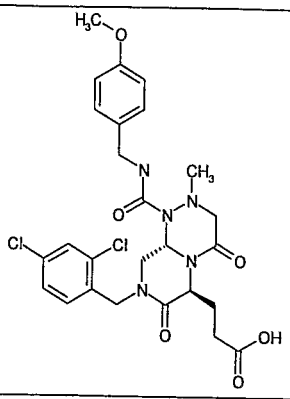
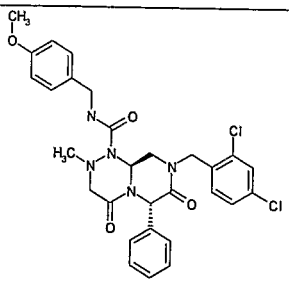
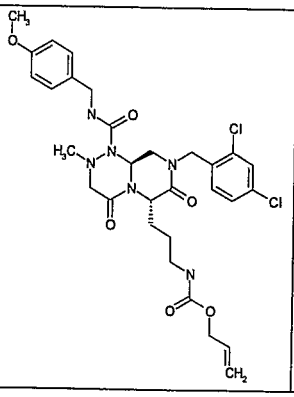
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2668		502	503
2669		470	471
2670		486	487
2671		500	501
2672		504	505

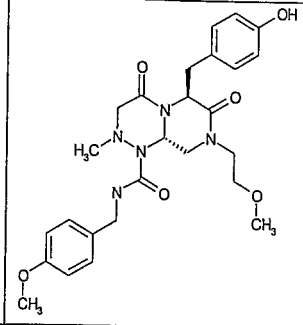
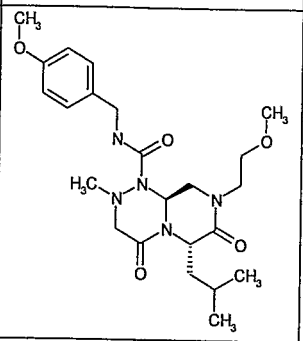
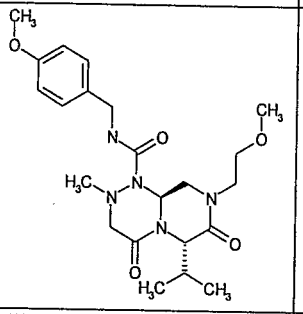
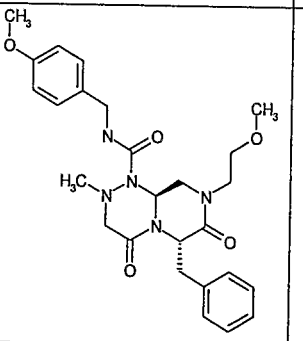
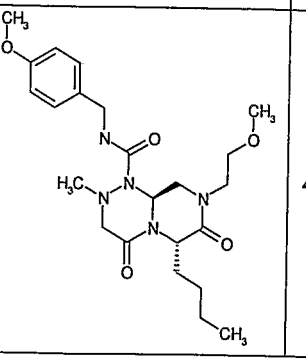
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2673		569	570
2674		634	635
2675		584	585
2676		570	571
2677		618	619

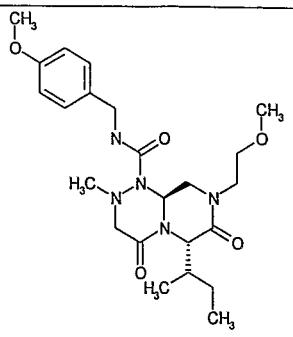
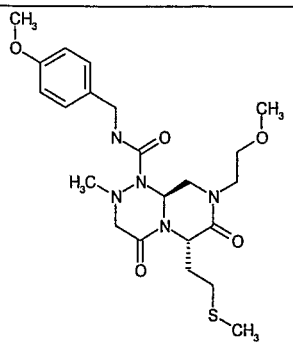
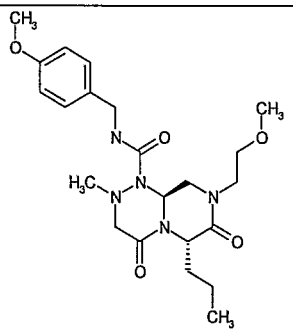
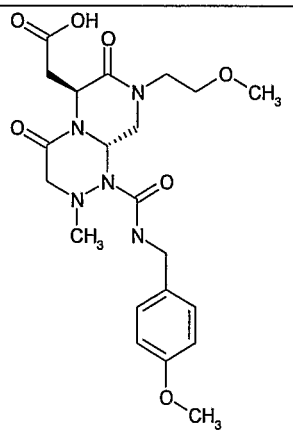
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2678		584	585
2679		584	585
2680		602	603
2681		570	571
2682		586	587

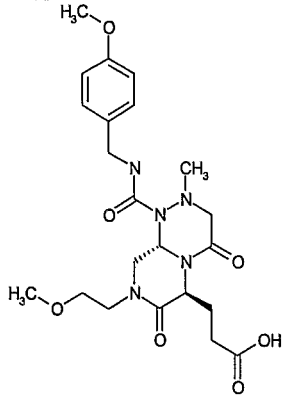
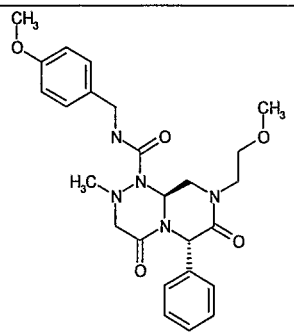
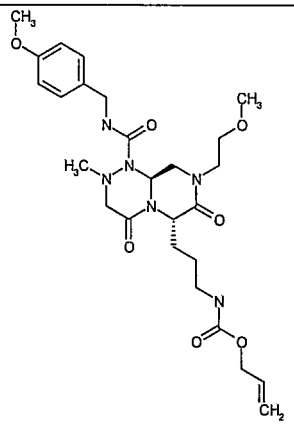
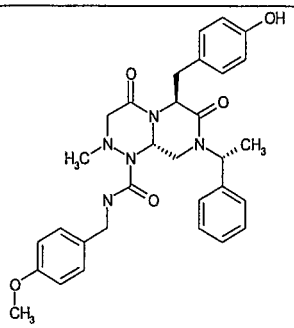
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2683		600	601
2684		604	605
2685		669	670
2686		613	614
2687		563	564

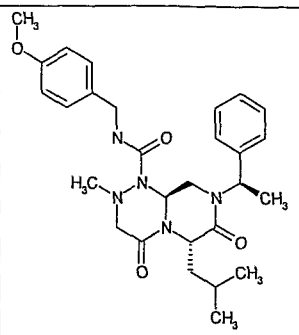
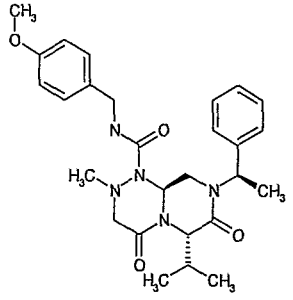
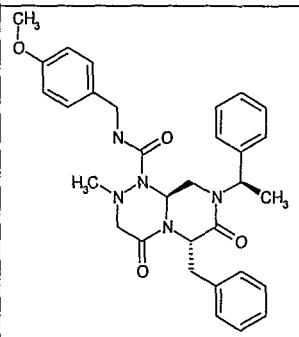
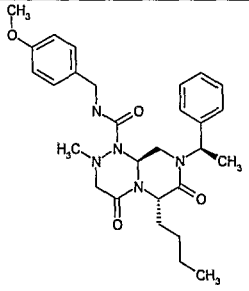
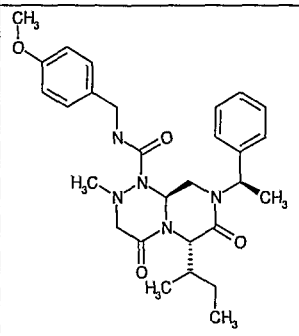
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2688		548	549
2689		597	598
2690		563	564
2691		563	564
2692		581	582
2693		548	549

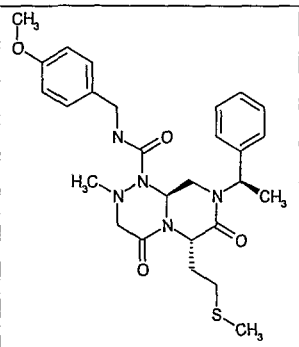
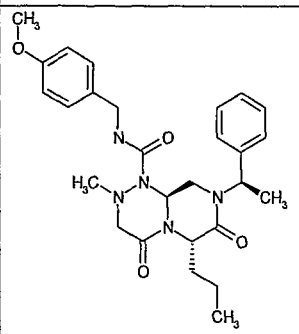
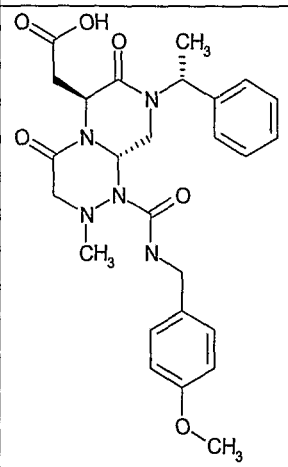
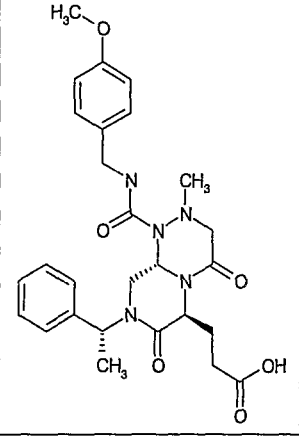
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2694		564	565
2695		578	579
2696		582	583
2697		648	649

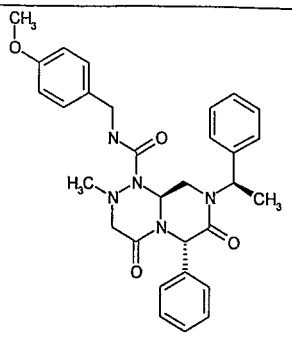
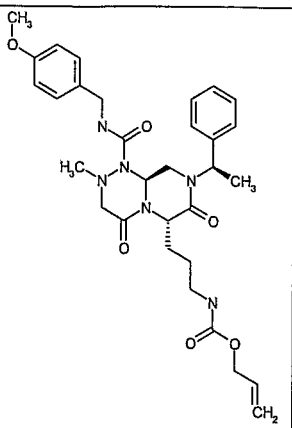
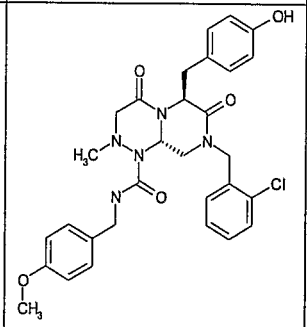
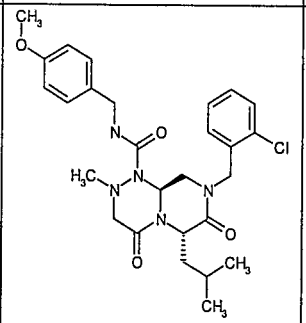
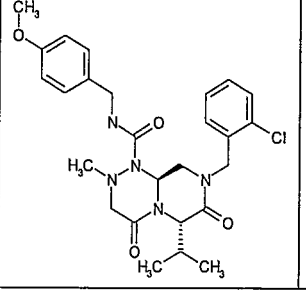
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2698		512	513
2699		462	463
2700		448	449
2701		496	497
2702		462	463

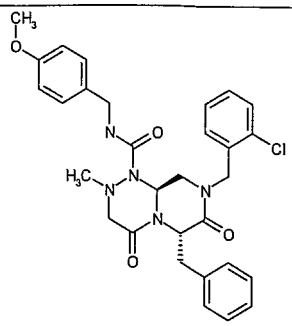
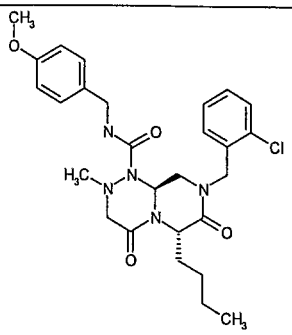
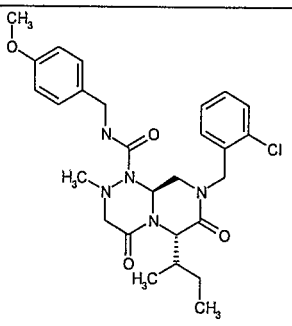
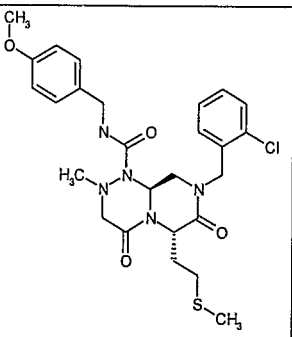
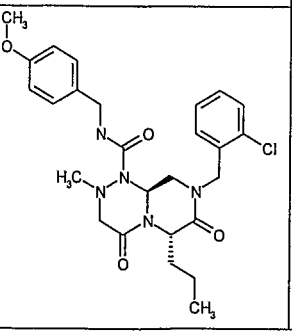
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2703		462	463
2704		480	481
2705		448	449
2706		463	464

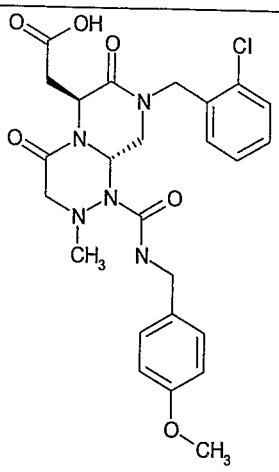
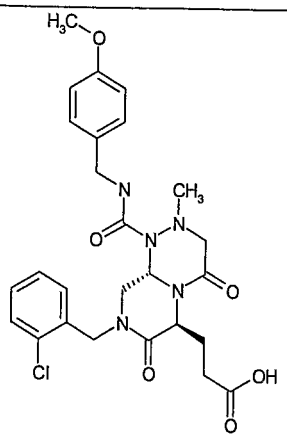
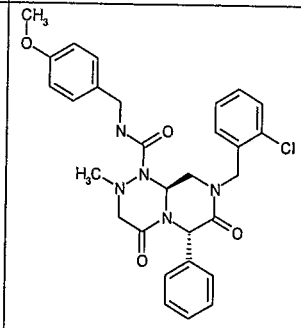
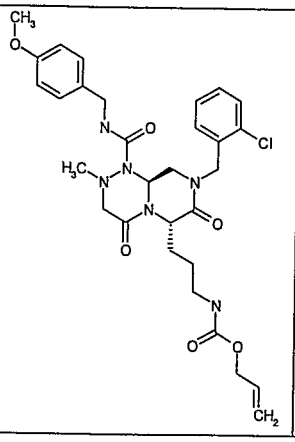
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2707		478	479
2708		482	483
2709		547	548
2710		558	559

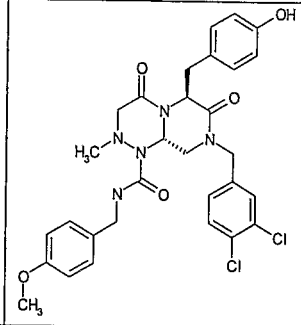
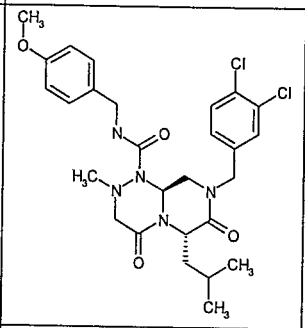
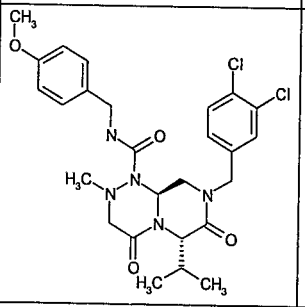
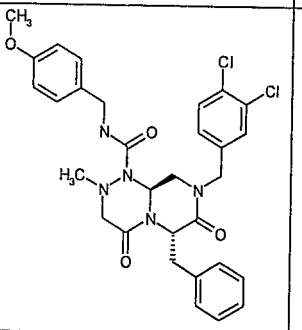
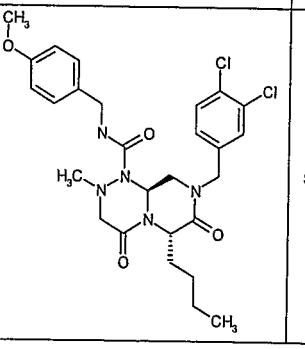
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2711		508	509
2712		494	495
2713		542	543
2714		508	509
2715		508	509

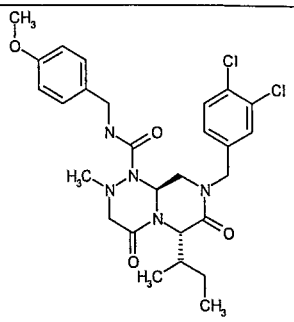
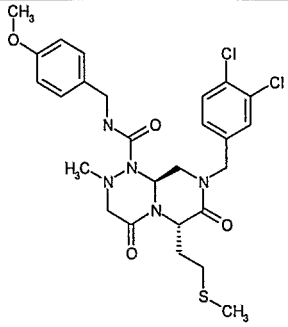
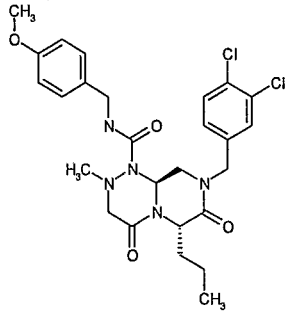
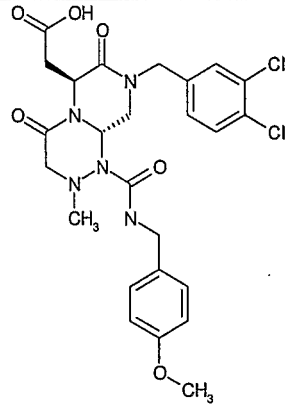
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2716		526	527
2717		494	495
2718		510	511
2719		524	525

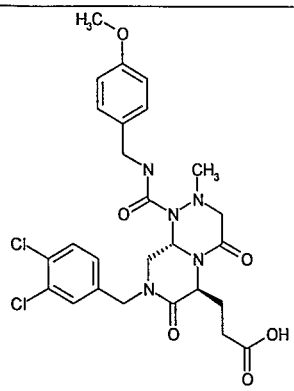
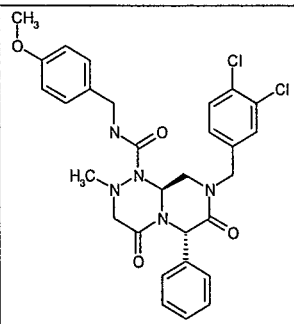
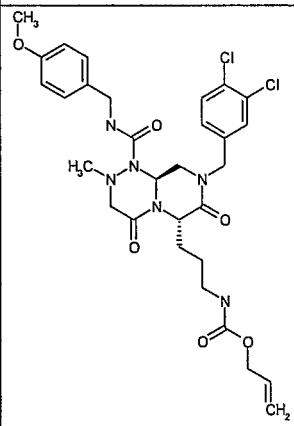
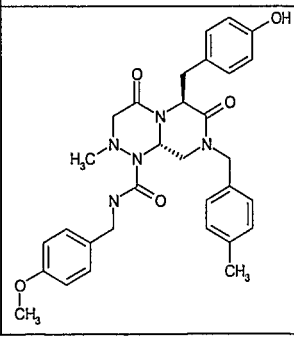
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2720		528	529
2721		593	594
2722		578	579
2723		528	529
2724		514	515

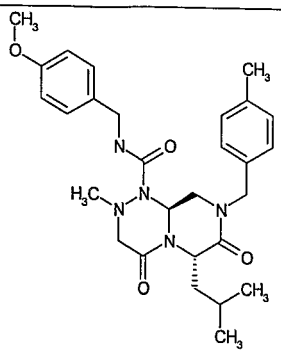
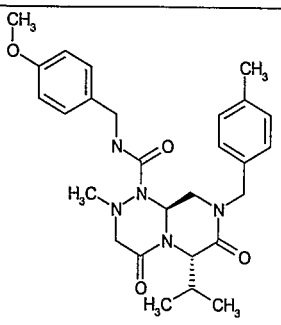
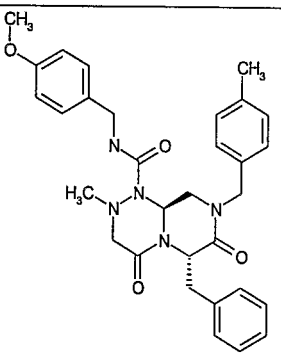
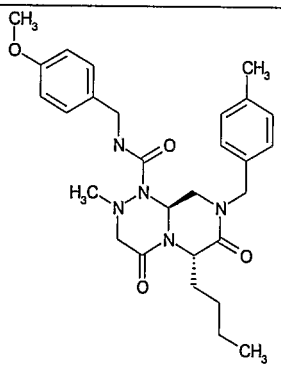
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2725		562	563
2726		528	529
2727		528	529
2728		546	547
2729		514	515

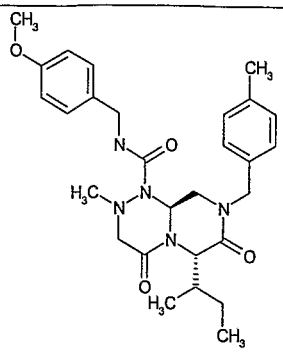
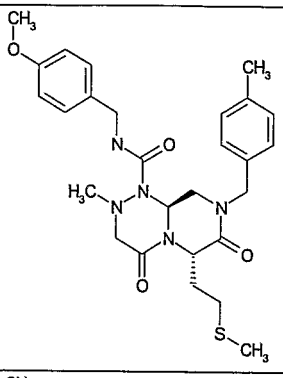
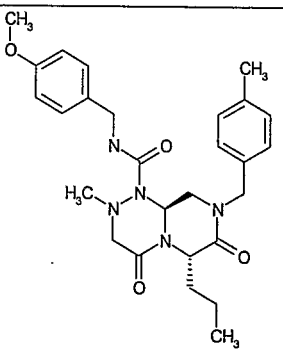
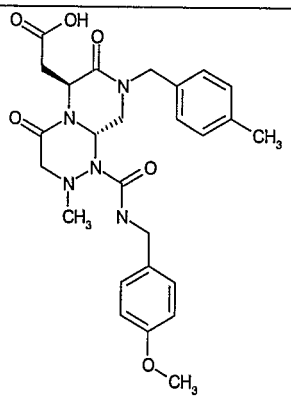
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2730		530	531
2731		544	545
2732		548	549
2733		613	614

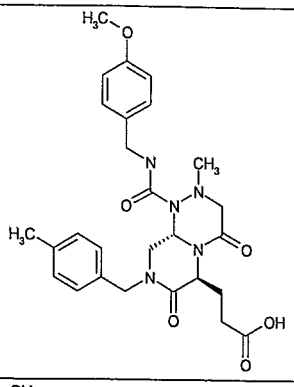
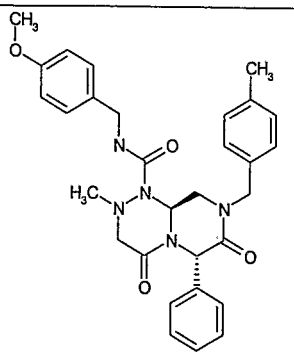
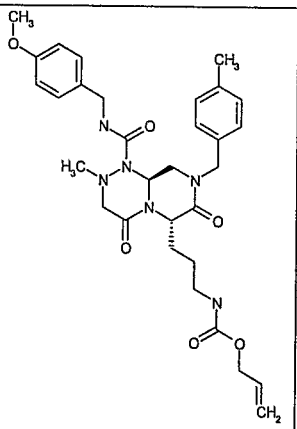
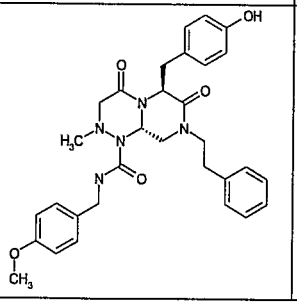
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2734		613	614
2735		563	564
2736		548	549
2737		597	598
2738		563	564

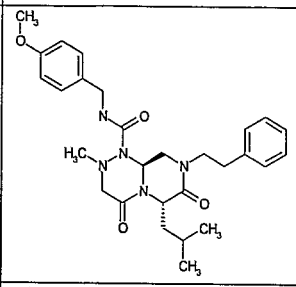
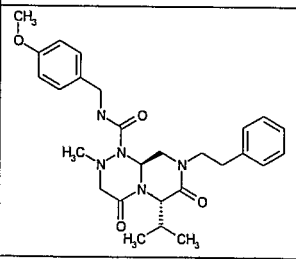
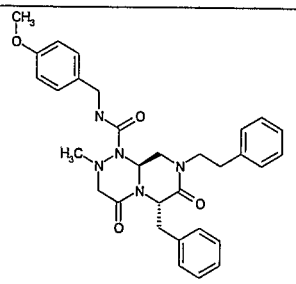
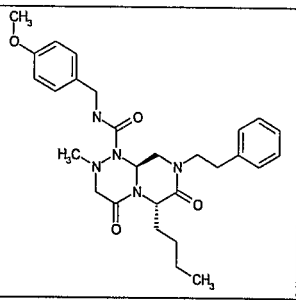
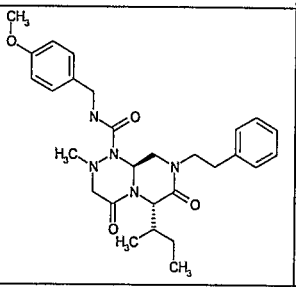
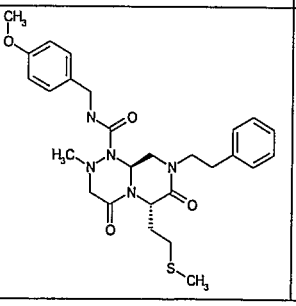
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2739		563	564
2740		581	582
2741		548	549
2742		564	565

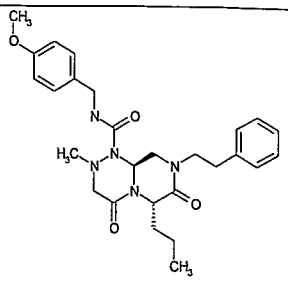
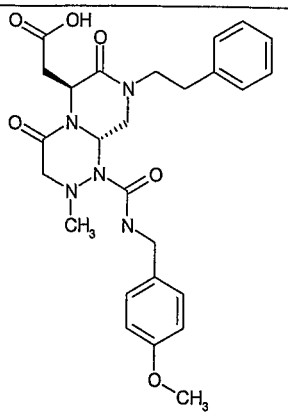
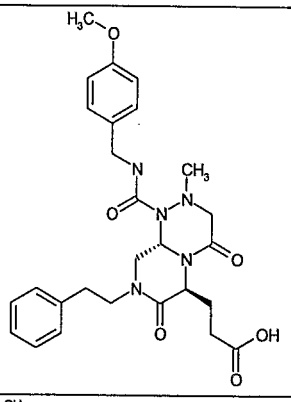
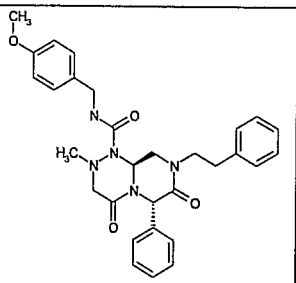
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2743		578	579
2744		582	583
2745		648	649
2746		558	559

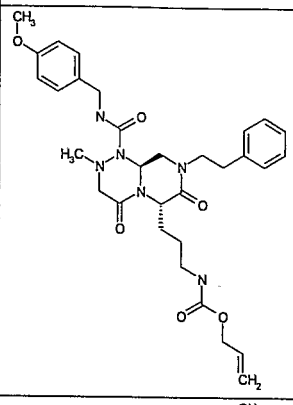
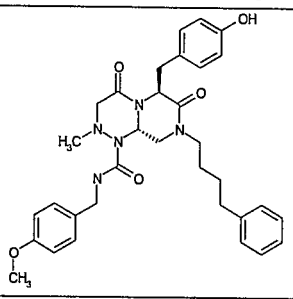
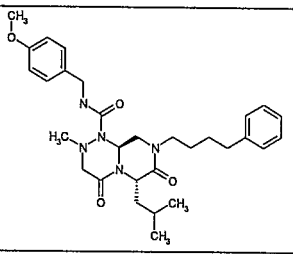
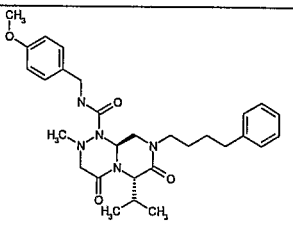
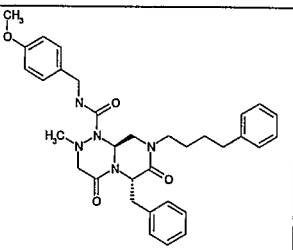
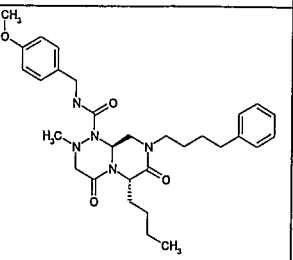
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2747		508	509
2748		494	495
2749		542	543
2750		508	509

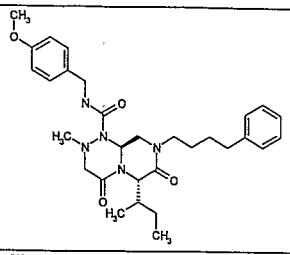
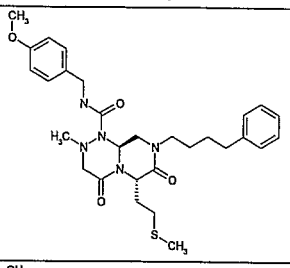
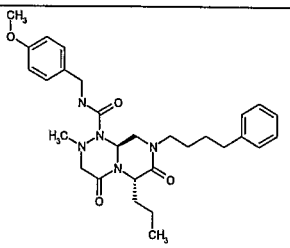
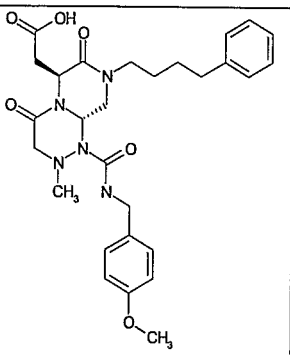
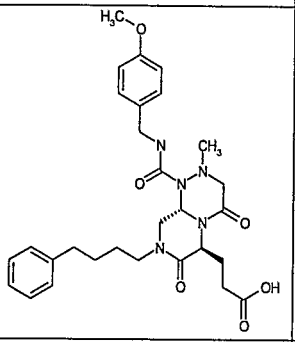
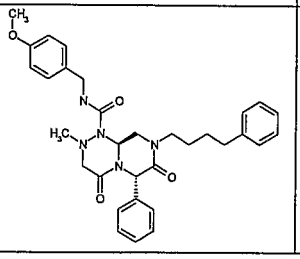
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2751		508	509
2752		526	527
2753		494	495
2754		510	511

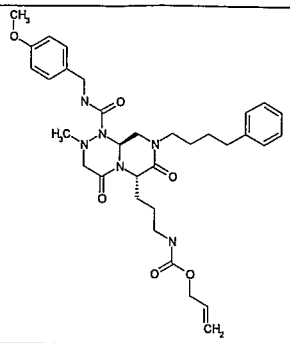
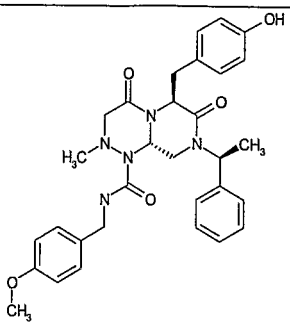
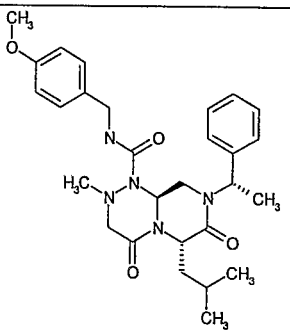
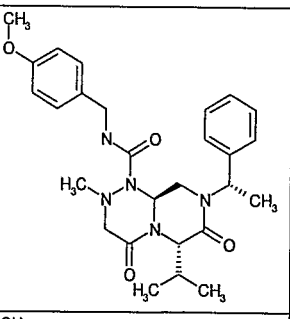
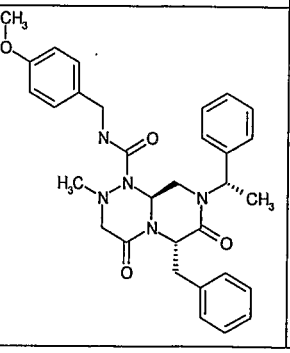
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2755		524	525
2756		528	529
2757		593	594
2758		558	559

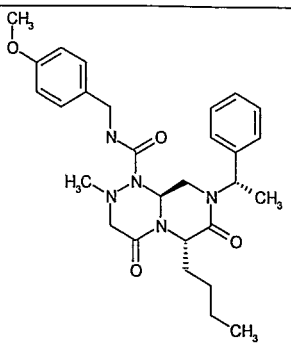
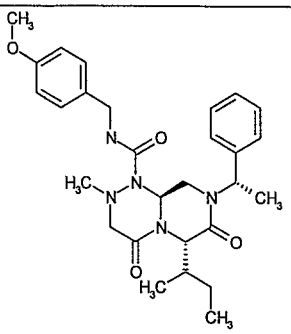
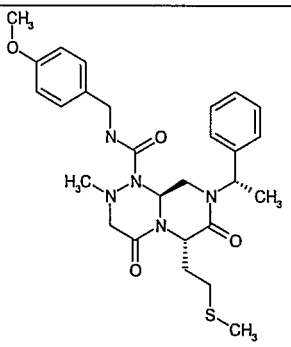
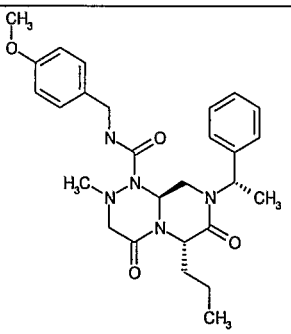
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2759		508	509
2760		494	495
2761		542	543
2762		508	509
2763		508	509
2764		526	527

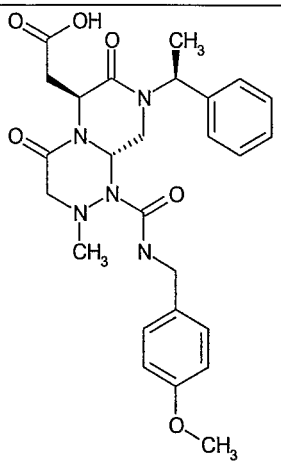
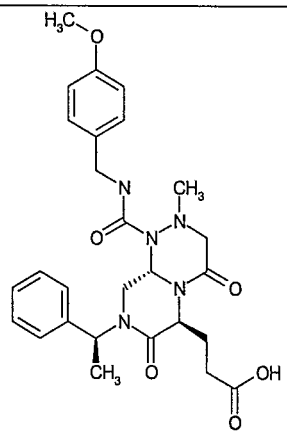
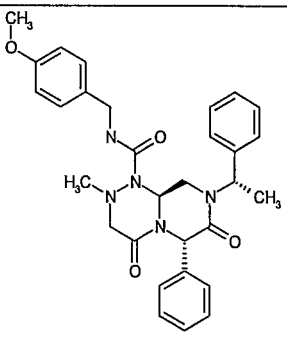
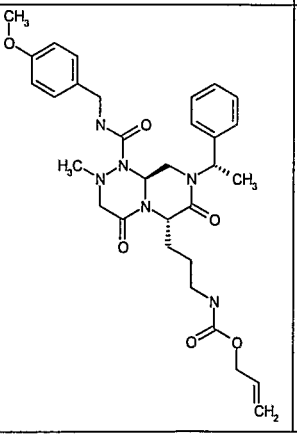
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2765		494	495
2766		510	511
2767		524	525
2768		528	529

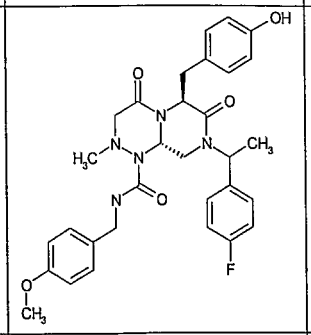
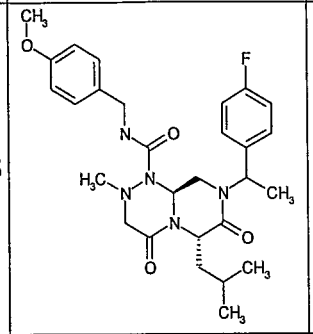
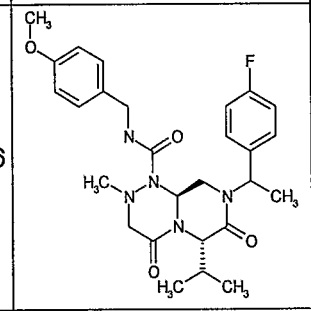
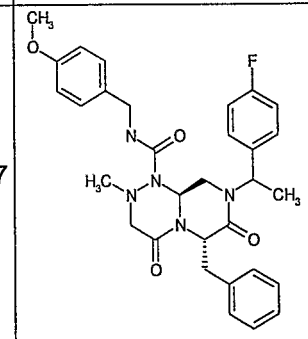
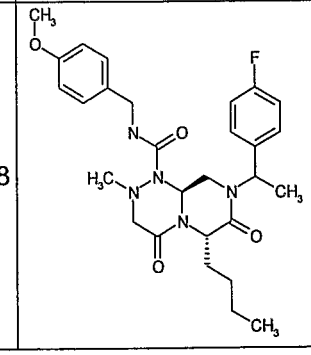
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2769		593	594
2770		586	587
2771		536	537
2772		522	523
2773		570	571
2774		536	537

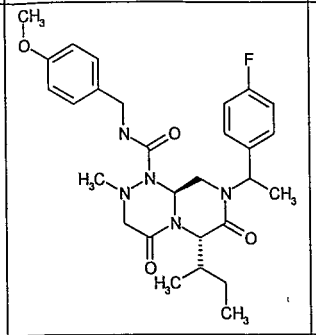
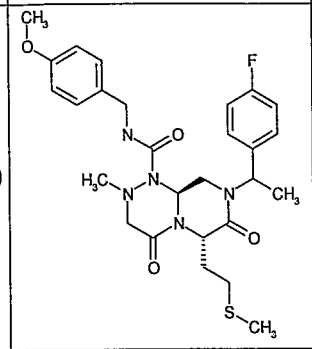
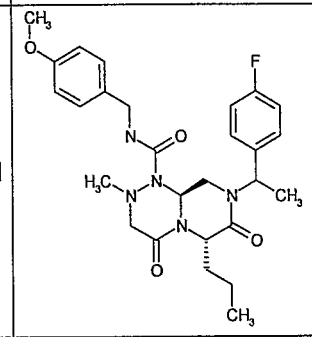
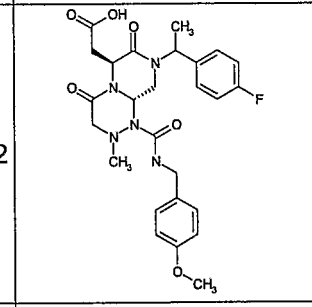
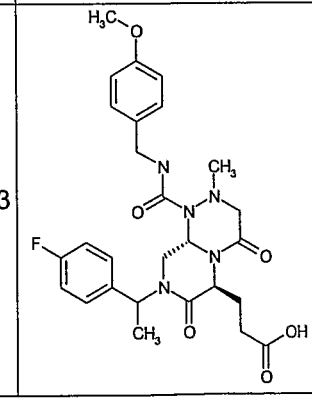
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2776		554	555
2777		522	523
2778		538	539
2779		552	553
2780		556	557

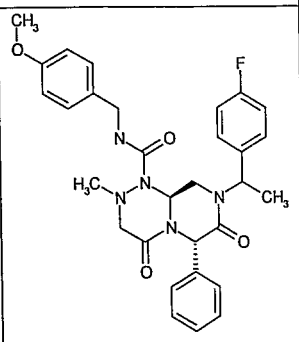
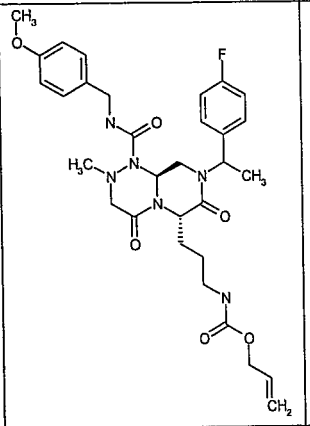
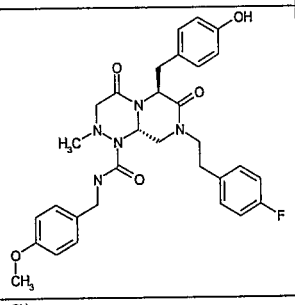
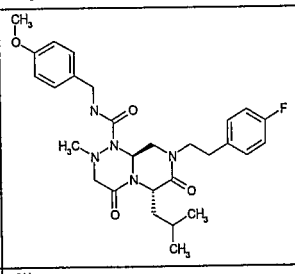
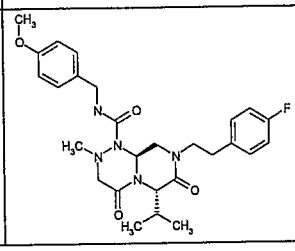
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2781		621	622
2782		558	559
2783		508	509
2784		494	495
2785		542	543

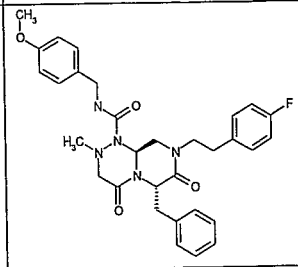
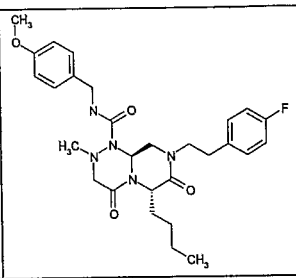
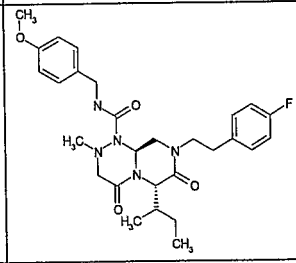
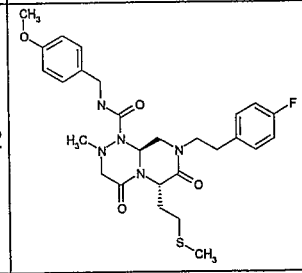
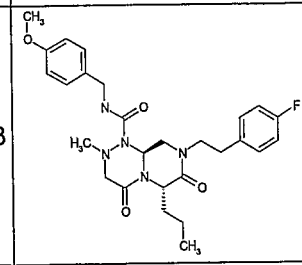
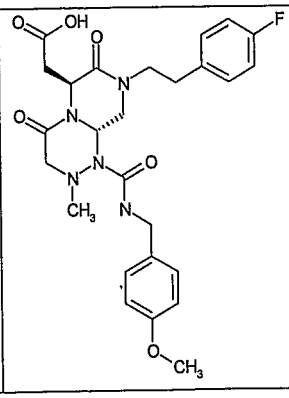
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2786		508	509
2787		508	509
2788		526	527
2789		494	495

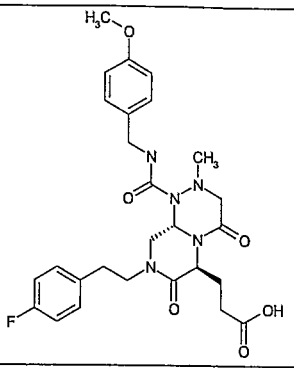
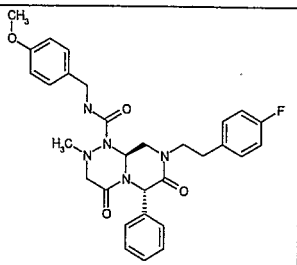
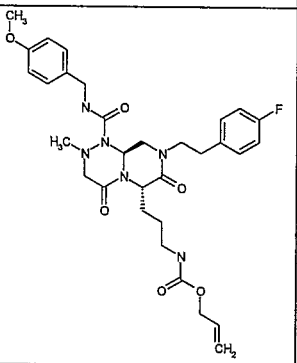
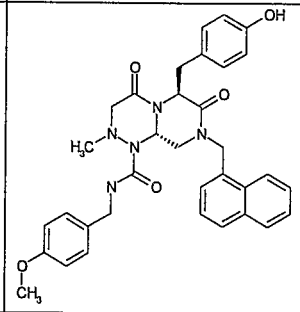
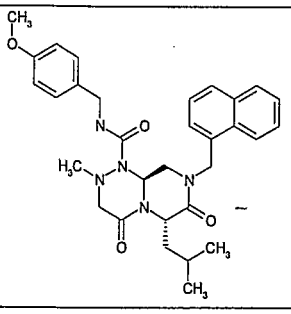
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2790		510	511
2791		524	525
2792		528	529
2793		593	594

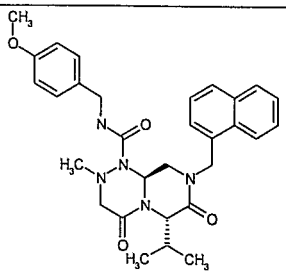
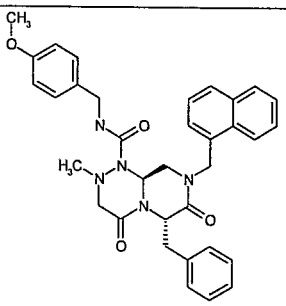
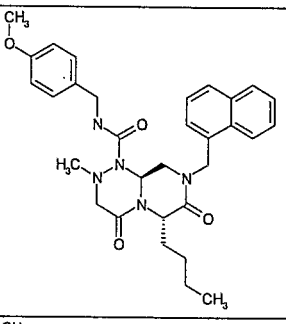
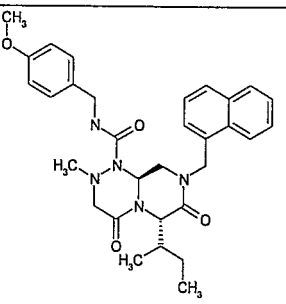
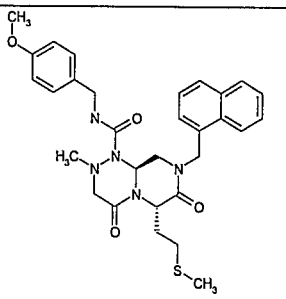
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2794		576	577
2795		526	527
2796		512	513
2797		560	561
2798		526	527

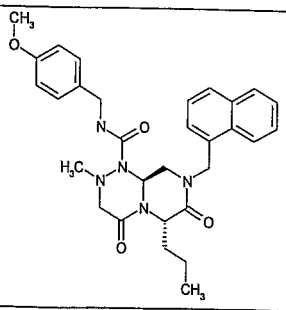
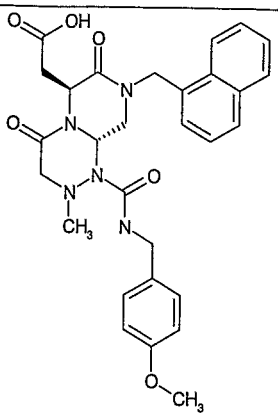
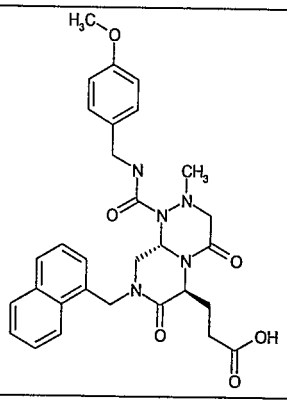
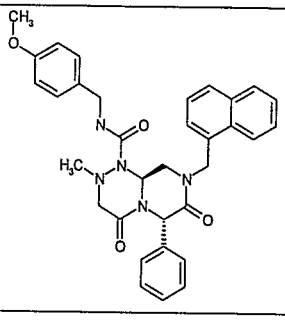
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2799		526	527
2800		544	545
2801		512	513
2802		528	529
2803		542	543

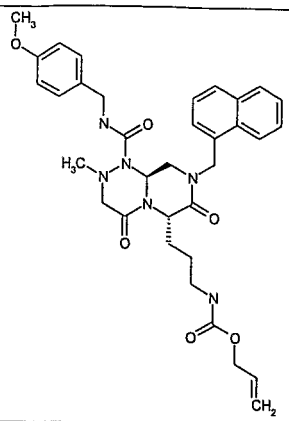
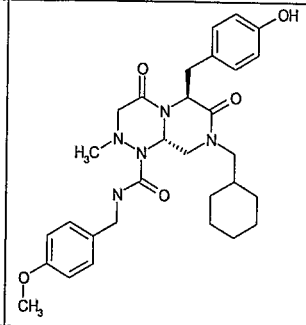
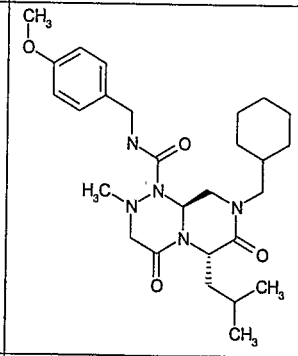
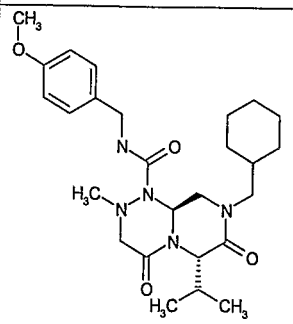
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2804		546	547
2805		611	612
2806		576	577
2807		526	527
2808		512	513

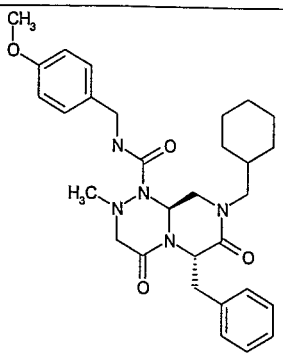
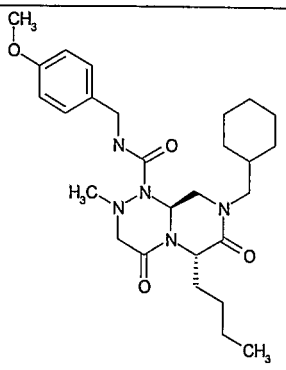
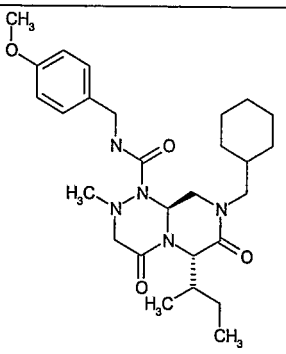
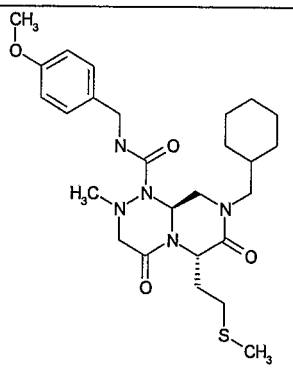
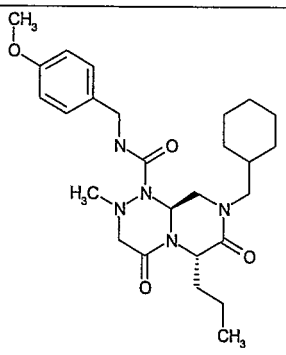
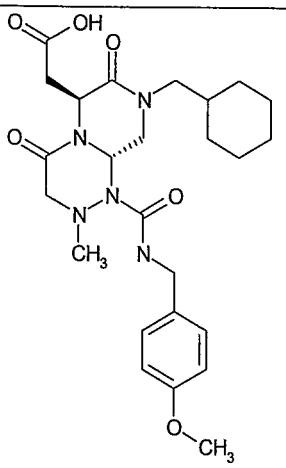
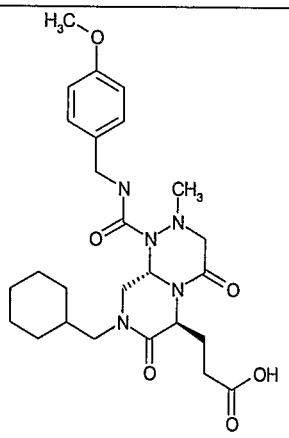
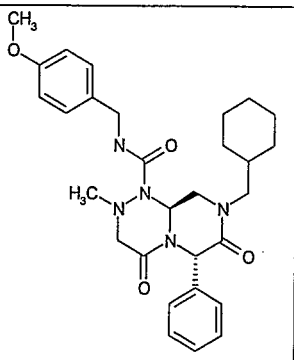
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2809		560	561
2810		526	527
2811		526	527
2812		544	545
2813		512	513
2814		528	529

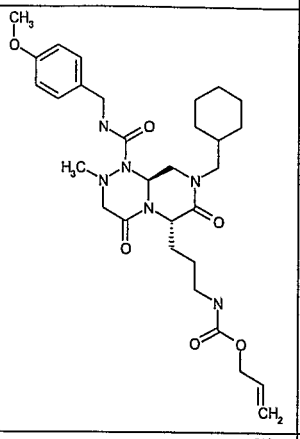
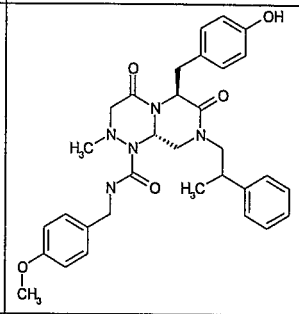
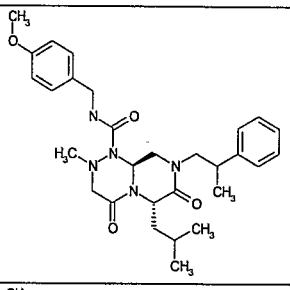
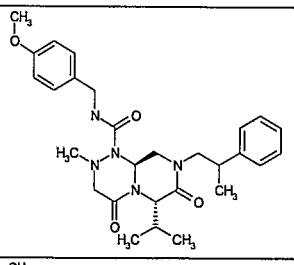
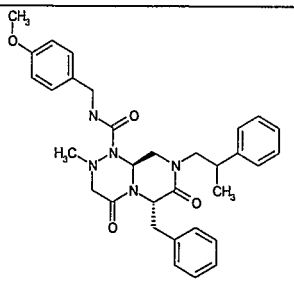
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2815		542	543
2816		546	547
2817		611	612
2818		594	595
2819		544	545

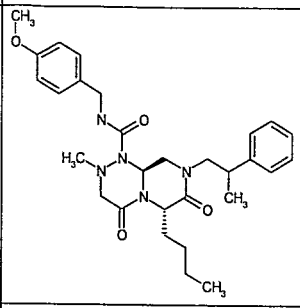
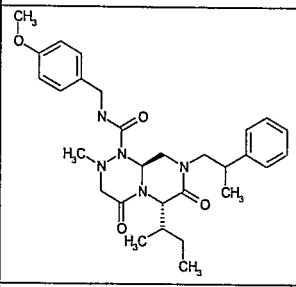
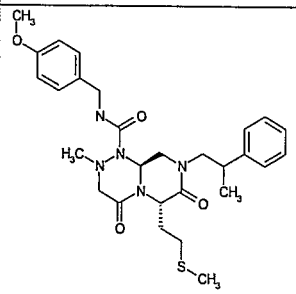
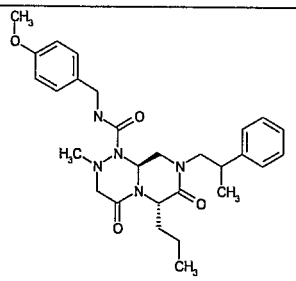
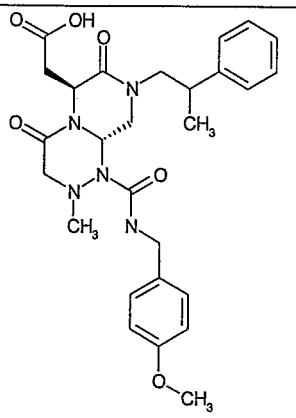
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2820		530	531
2821		578	579
2822		544	545
2823		544	545
2824		562	563

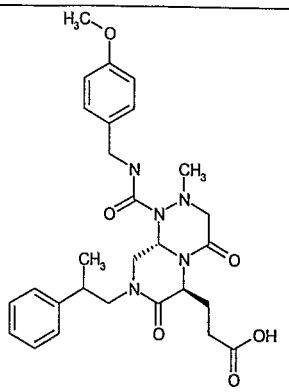
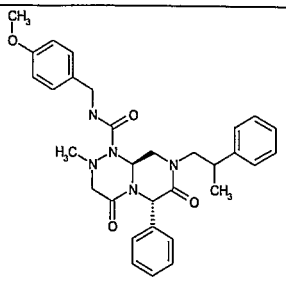
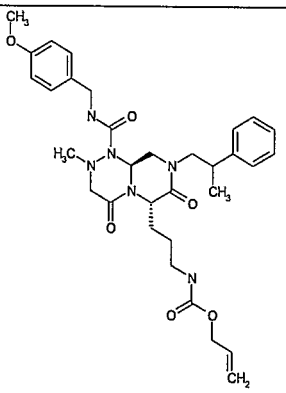
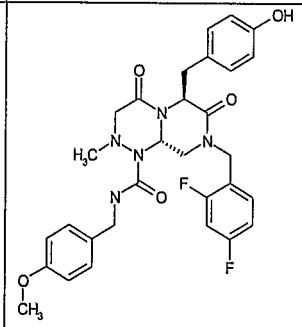
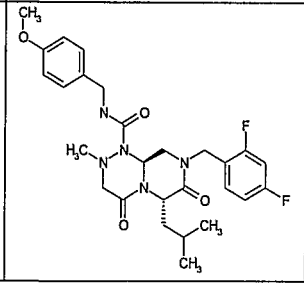
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2825		530	531
2826		546	547
2827		560	561
2828		564	565

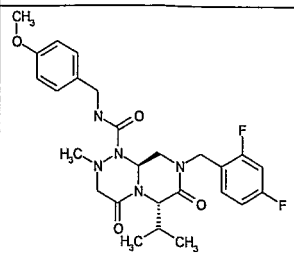
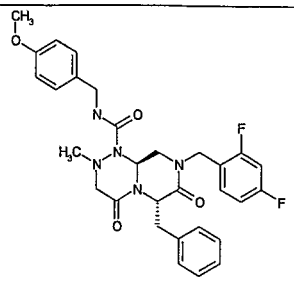
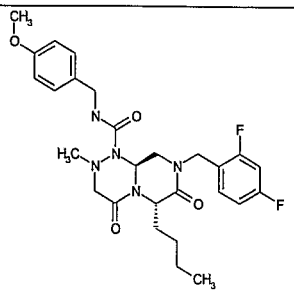
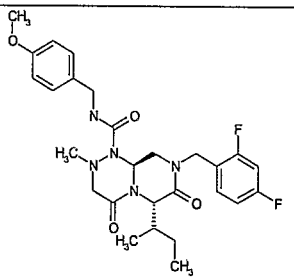
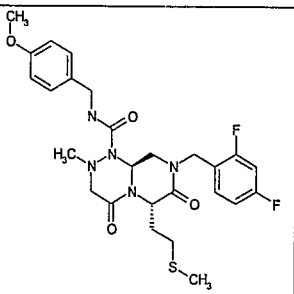
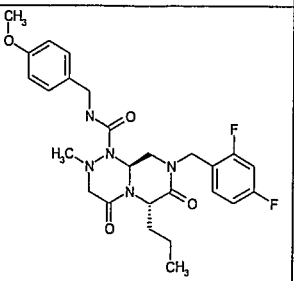
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2829		629	630
2830		550	551
2831		500	501
2832		486	487

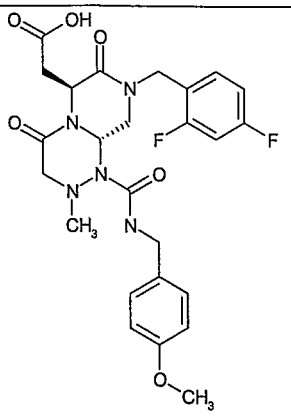
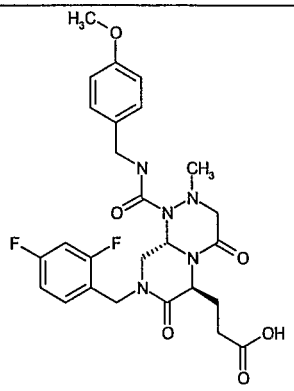
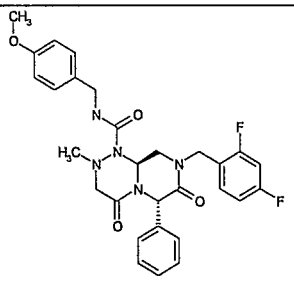
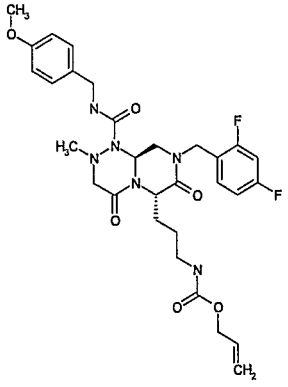
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2833		534	535
2834		500	501
2835		500	501
2836		518	519
2837		486	487
2838		502	503
2839		516	517
2840		520	521

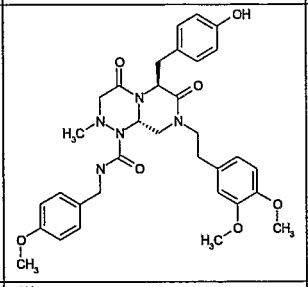
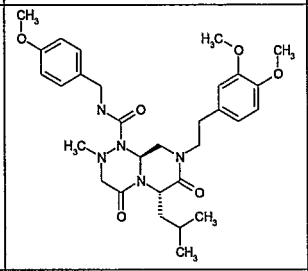
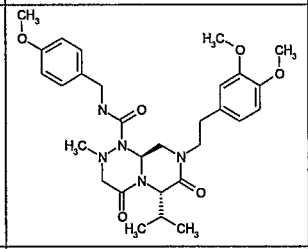
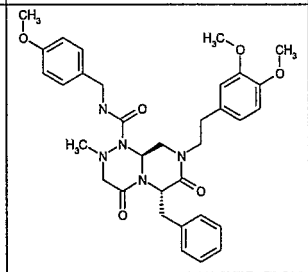
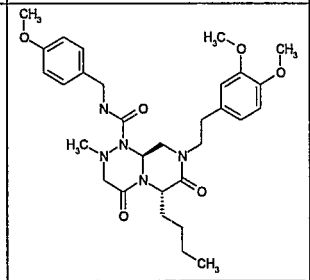
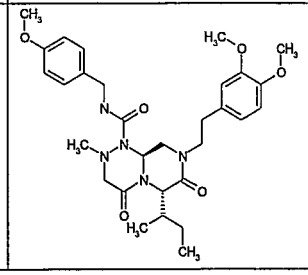
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2841		585	586
2842		572	573
2843		522	523
2844		508	509
2845		556	557

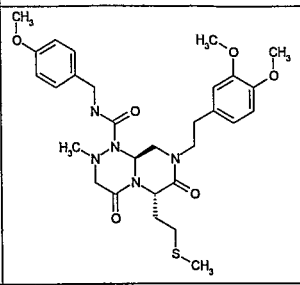
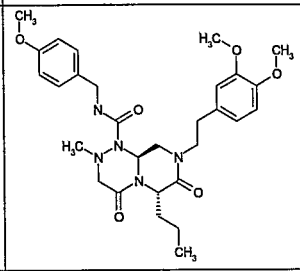
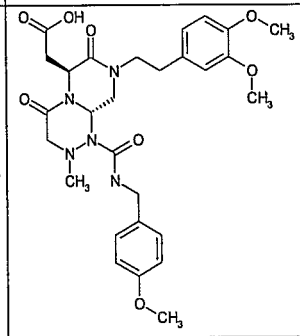
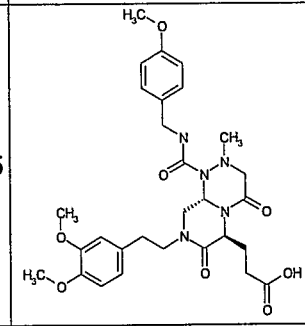
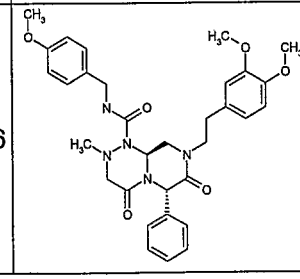
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2846		522	523
2847		522	523
2848		540	541
2849		508	509
2850		524	525

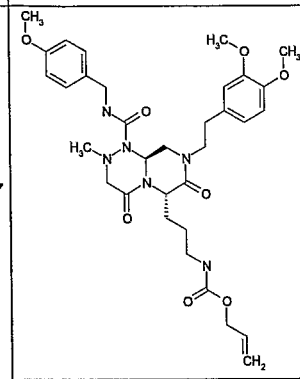
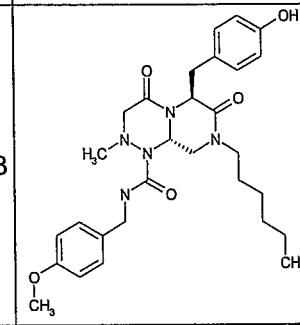
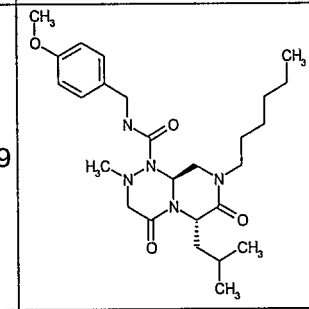
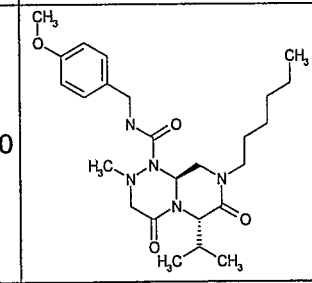
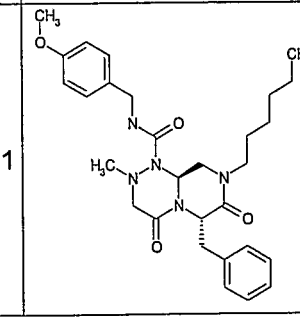
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2851		538	539
2852		542	543
2853		607	608
2854		580	581
2855		530	531

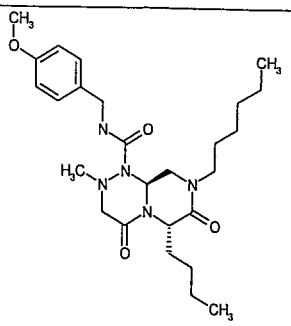
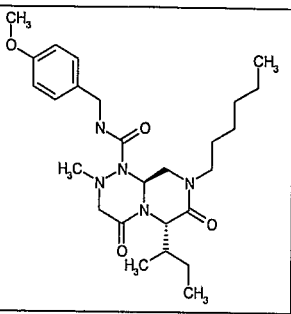
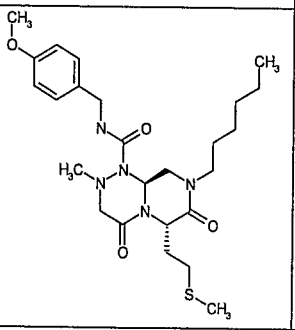
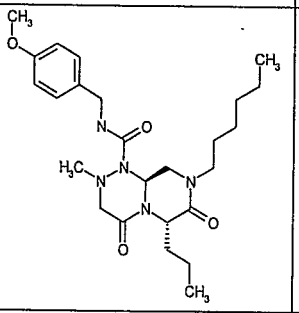
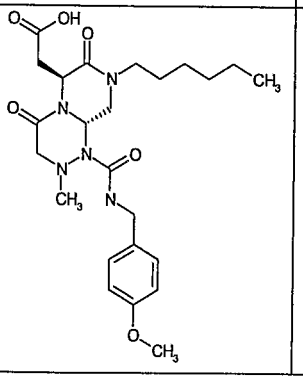
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2856		516	517
2857		564	565
2858		530	531
2859		530	531
2860		548	549
2861		516	517

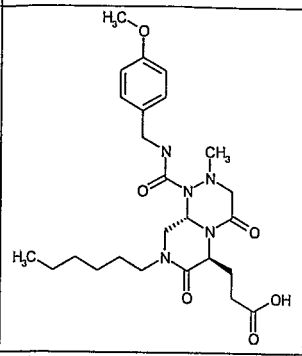
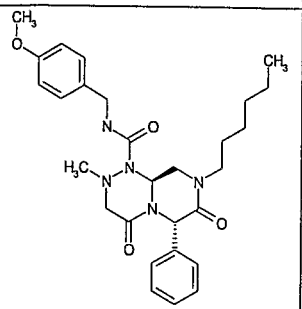
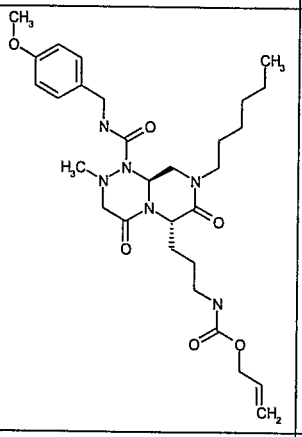
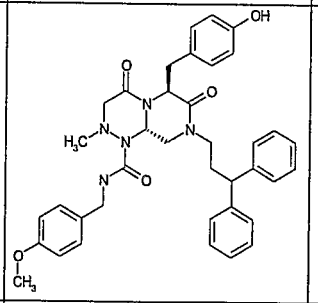
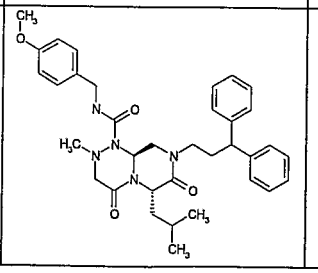
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2862		532	533
2863		546	547
2864		550	551
2865		615	616

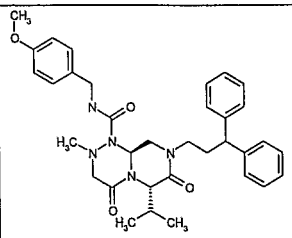
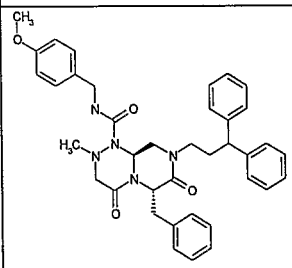
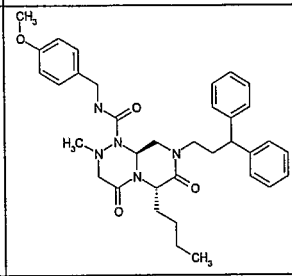
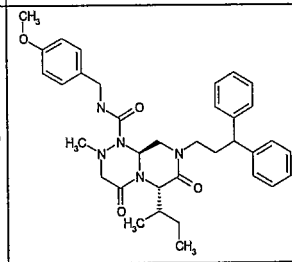
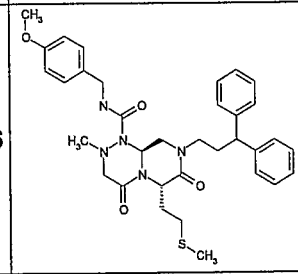
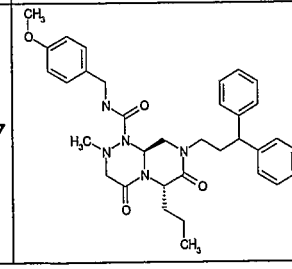
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2866		618	619
2867		568	569
2868		554	555
2869		602	603
2870		568	569
2871		568	569

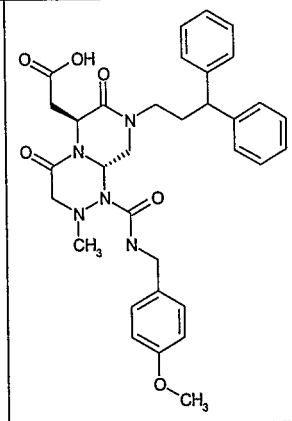
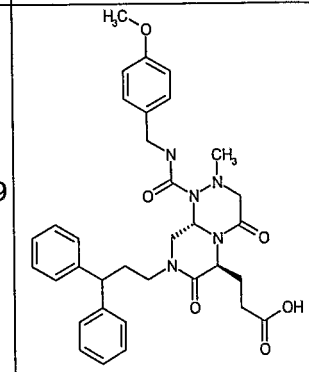
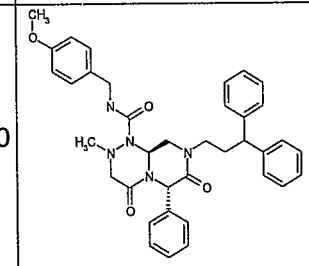
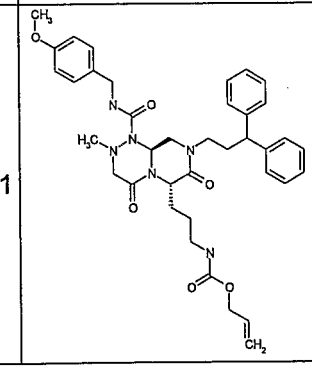
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2872		586	587
2873		554	555
2874		570	571
2875		584	585
2876		588	589

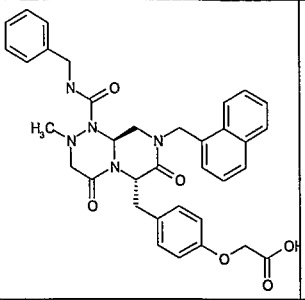
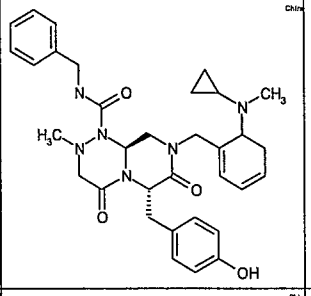
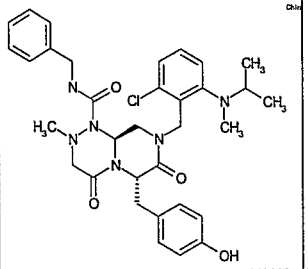
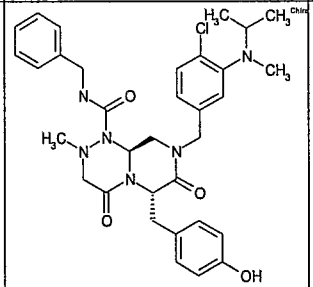
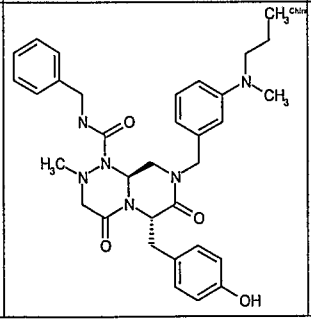
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2877		653	654
2878		538	539
2879		488	489
2880		474	475
2881		522	523

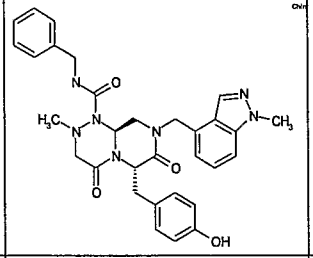
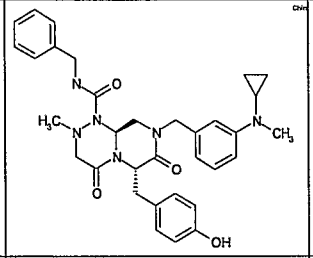
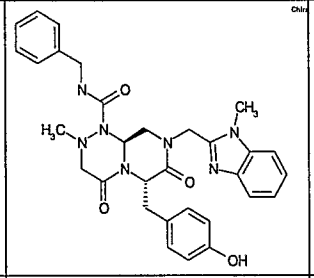
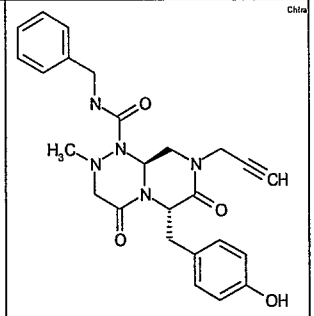
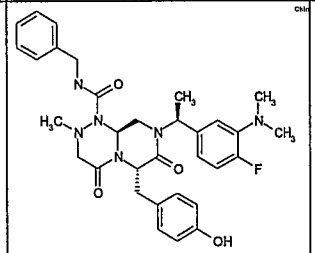
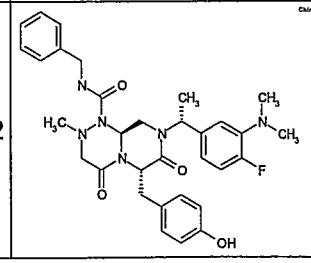
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2882		488	489
2883		488	489
2884		506	507
2885		474	475
2886		490	491

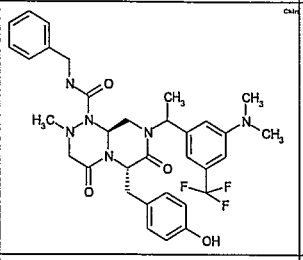
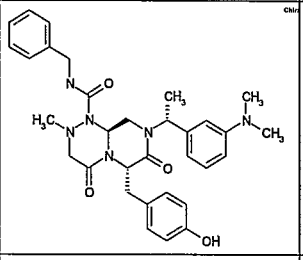
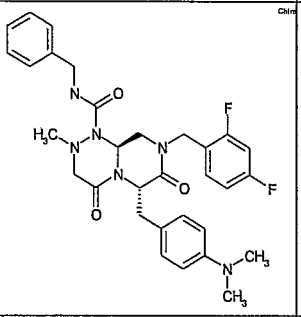
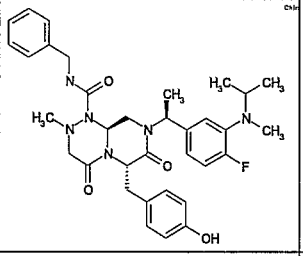
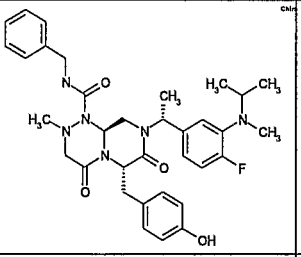
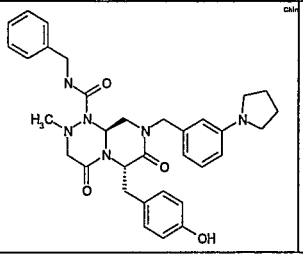
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2888		508	509
2889		573	574
2890		648	649
2891		598	599

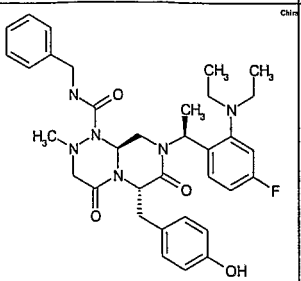
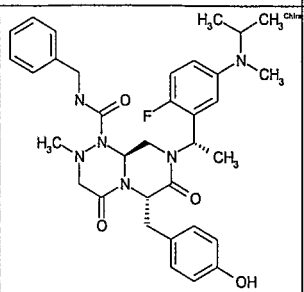
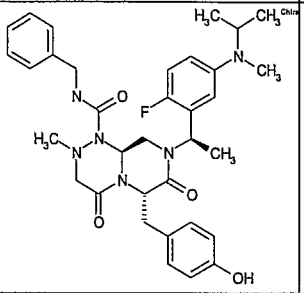
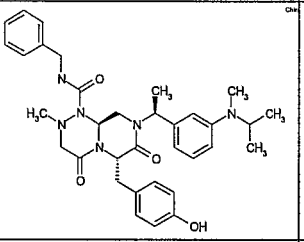
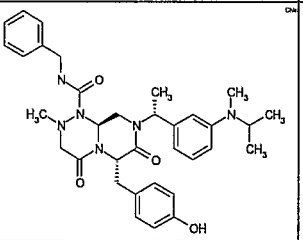
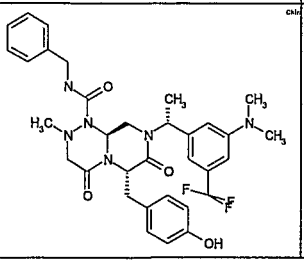
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2892		584	585
2893		632	633
2894		598	599
2895		598	599
2896		616	617
2897		584	585

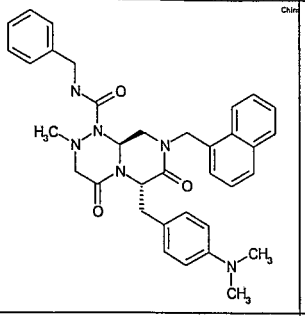
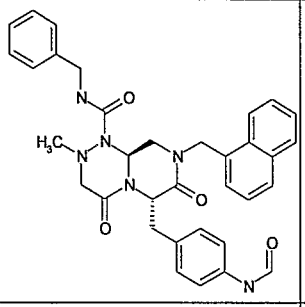
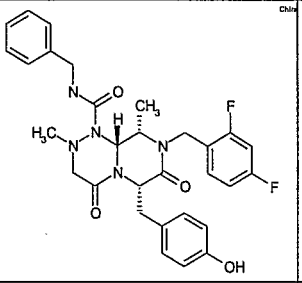
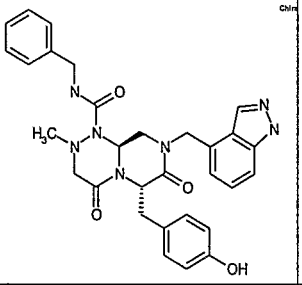
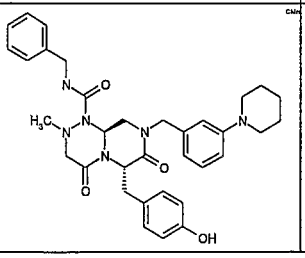
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2898		600	601
2899		614	615
2900		618	619
2901		683	684

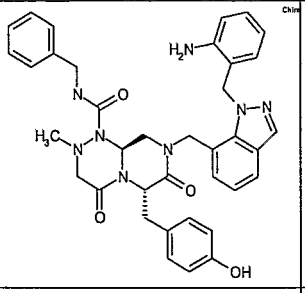
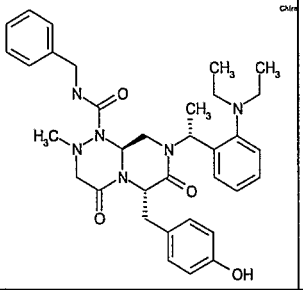
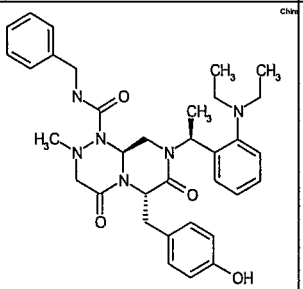
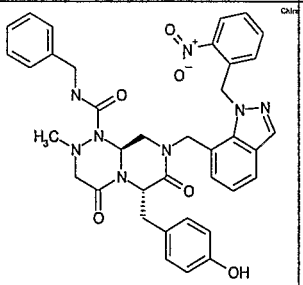
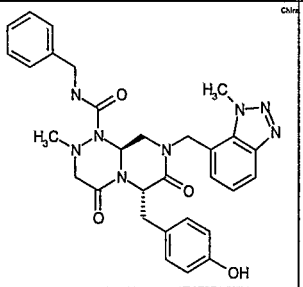
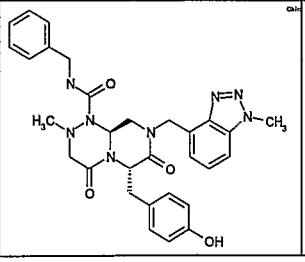
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2902		622	623
2903		585	586
2904		619	620
2905		619	620
2906		585	586

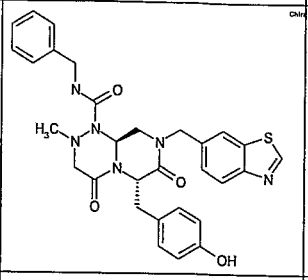
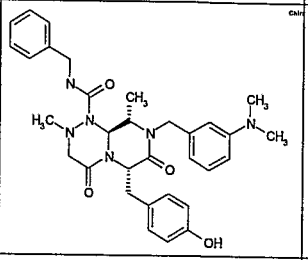
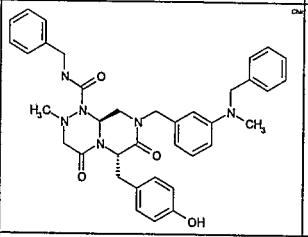
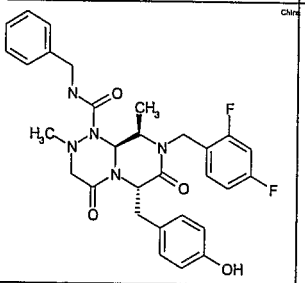
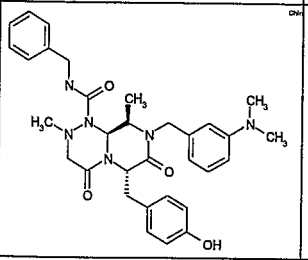
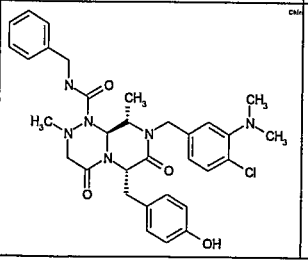
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2908		583	584
2909		568	569
2910		462	463
2911		589	590
2912		589	590

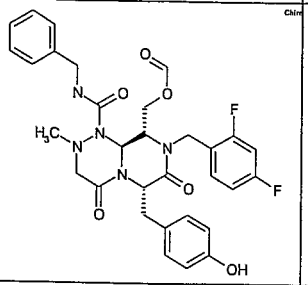
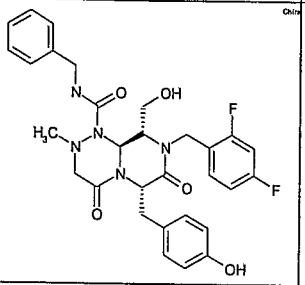
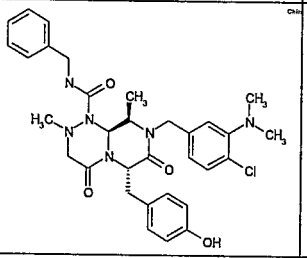
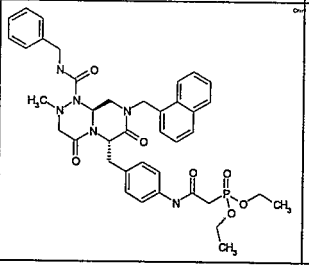
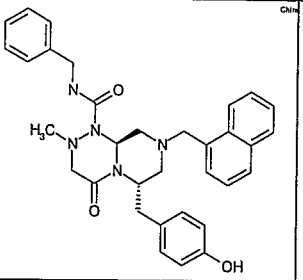
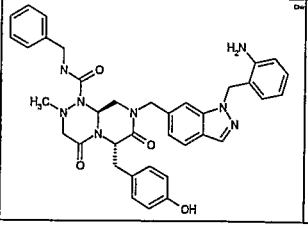
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2914		571	572
2915		577	578
2916		617	618
2917		617	618
2918		583	584

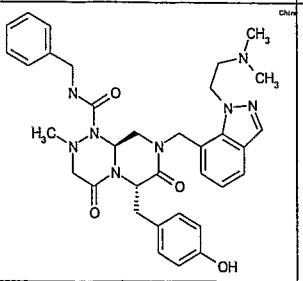
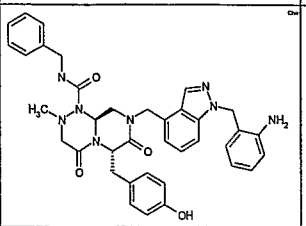
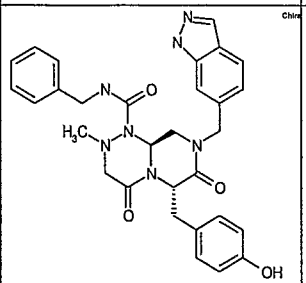
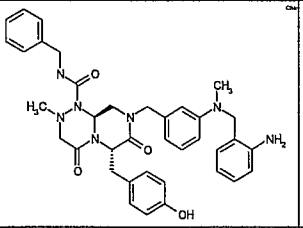
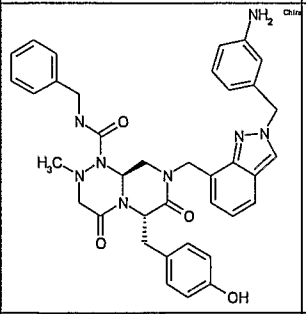
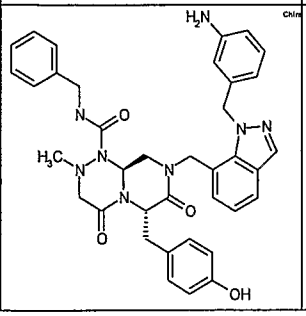
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2920		617	618
2921		617	618
2922		599	600
2923		599	600
2924		639	640

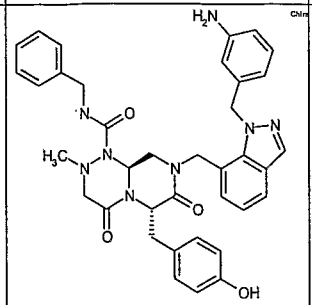
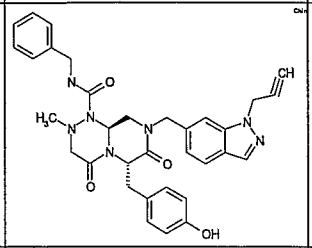
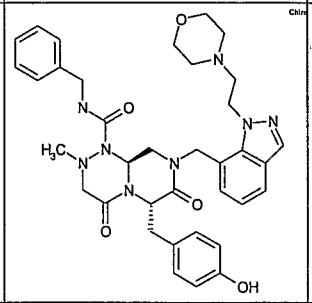
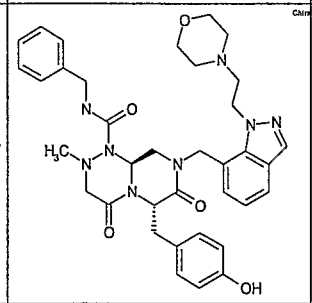
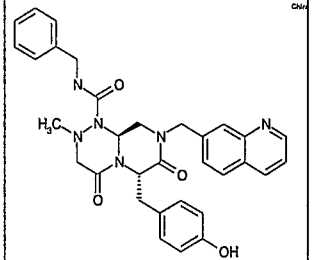
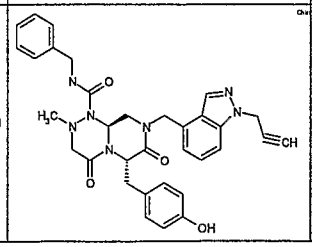
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2926		591	592
2927		564	565
2928		554	555
2929		597	598

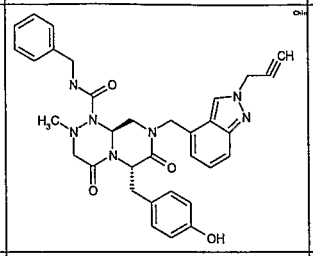
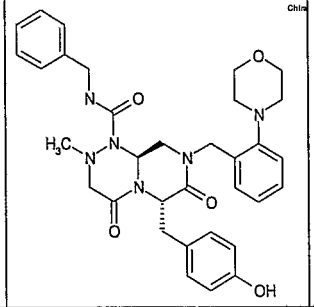
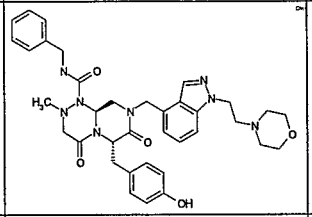
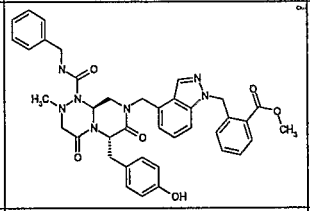
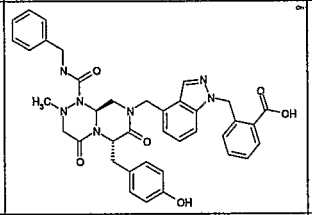
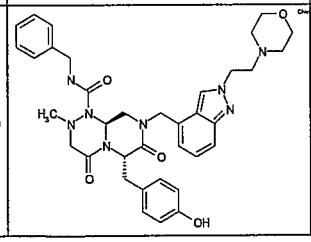
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2930		659	660
2931		599	600
2932		599	600
2933		689	690
2934		569	570
2935		569	570

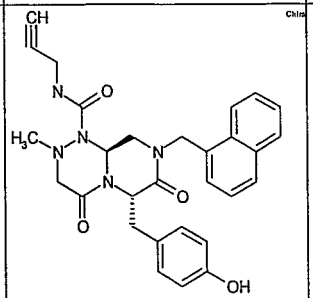
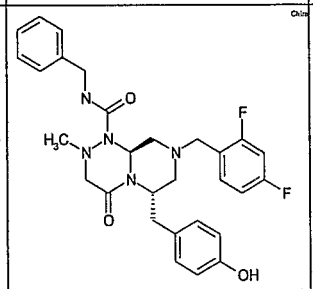
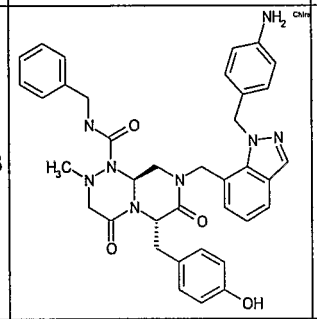
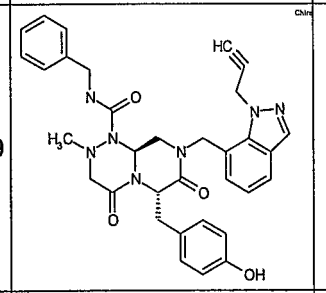
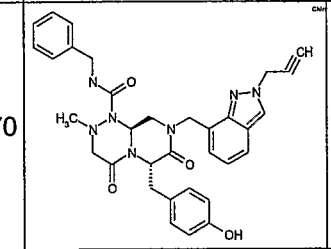
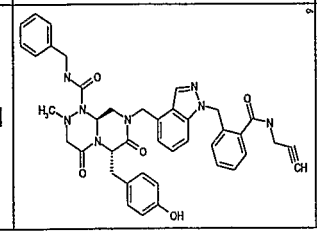
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2937		571	572
2938		633	634
2939		564	565
2940		571	572
2941		605	606

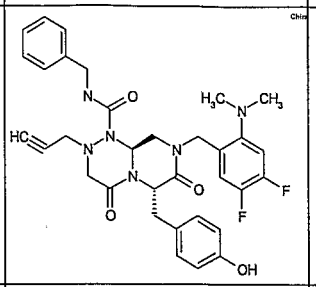
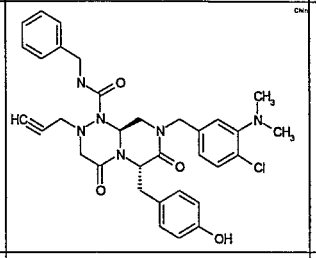
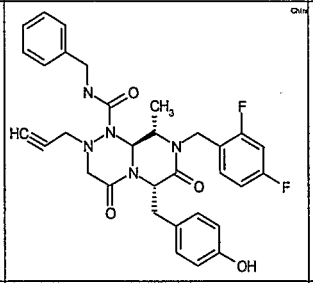
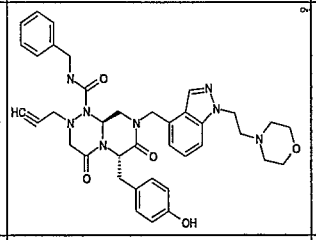
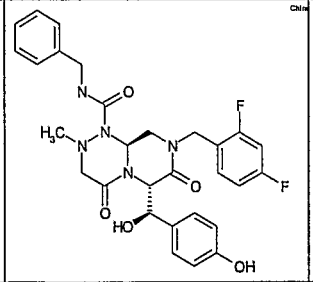
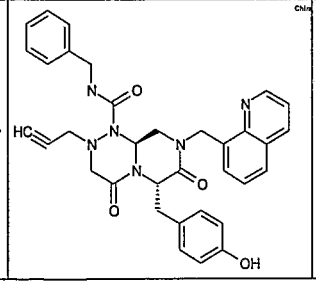
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2943		580	581
2944		605	606
2945		741	742
2946		550	551
2947		659	660

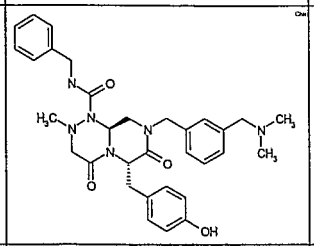
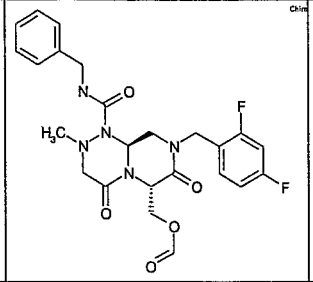
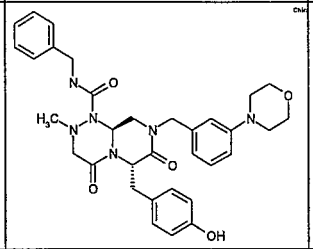
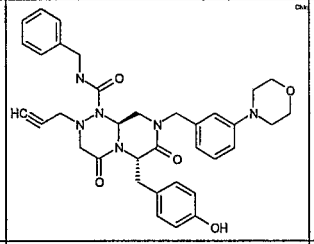
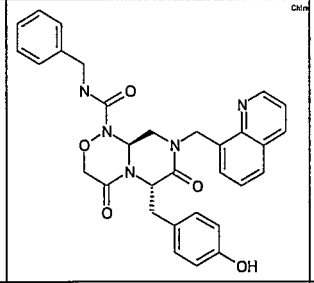
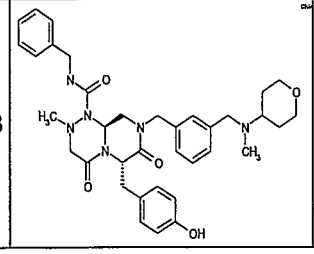
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2949		659	660
2950		554	555
2951		648	649
2952		659	660
2953		659	660

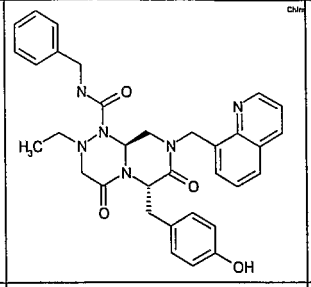
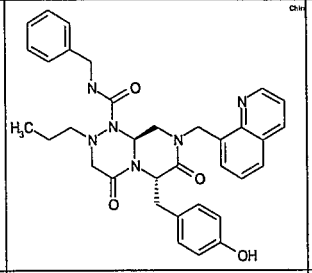
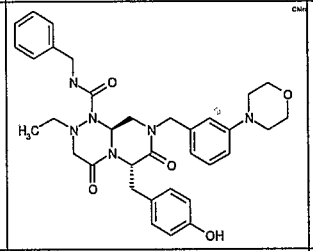
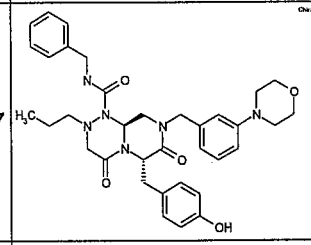
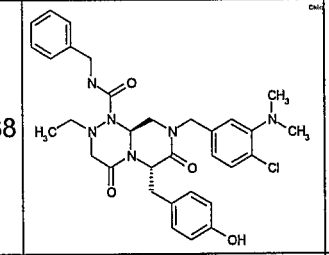
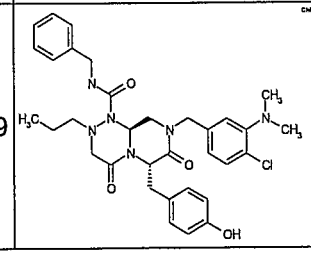
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2955		592	593
2956		667	668
2957		667	668
2958		565	566
2959		592	593

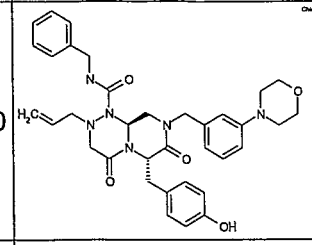
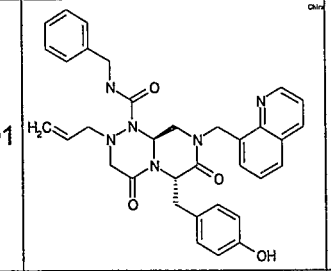
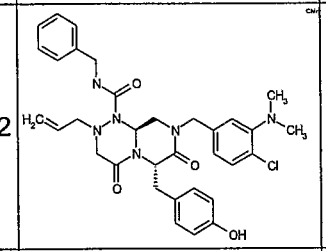
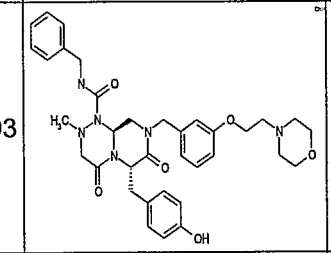
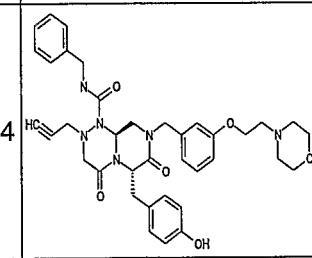
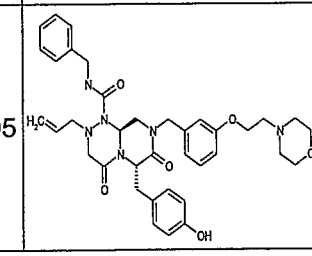
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2961		599	600
2962		667	668
2963		702	703
2964		688	689
2965		667	668

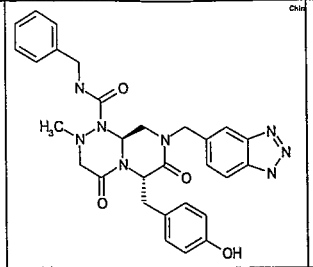
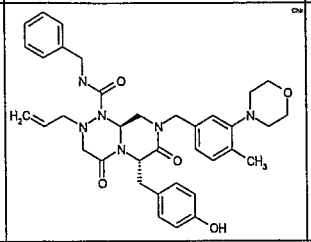
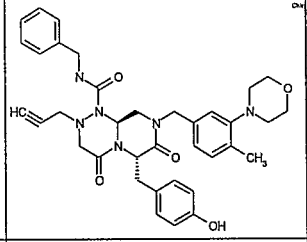
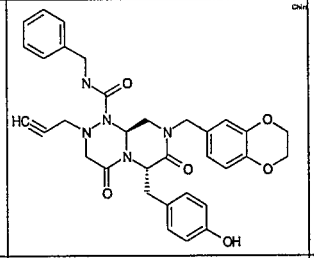
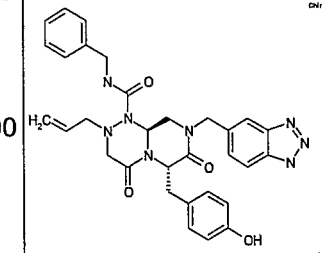
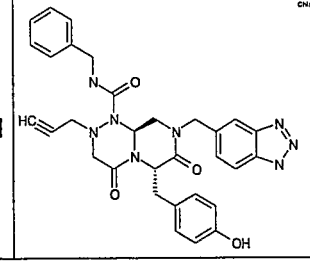
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2967		536	537
2968		659	660
2969		592	593
2970		592	593
2971		725	726

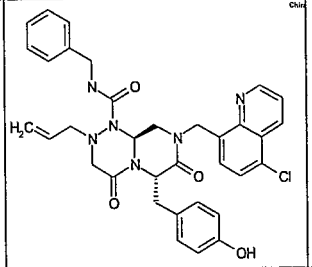
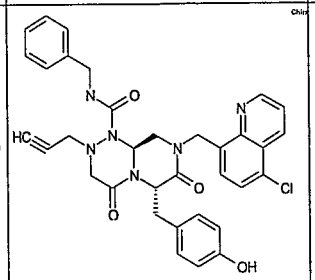
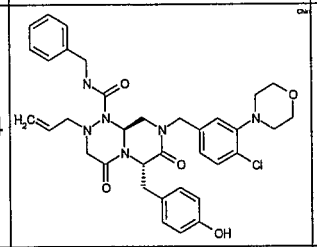
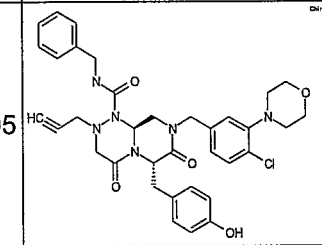
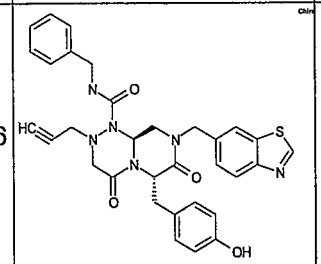
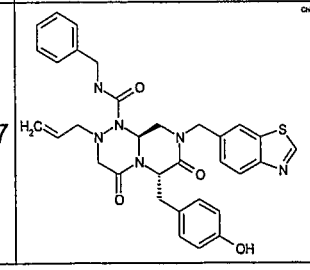
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2973		615	616
2974		588	589
2975		691	692
2976		566	567
2977		589	590

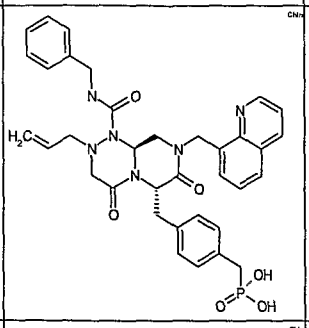
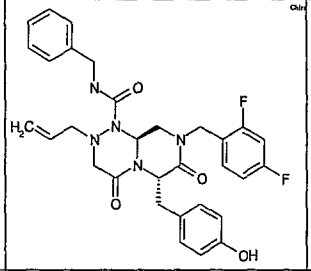
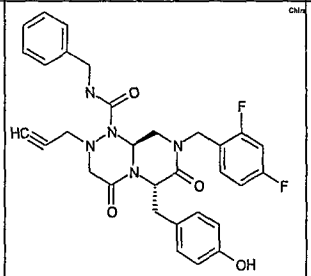
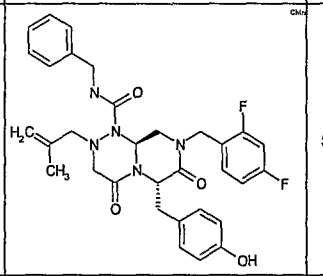
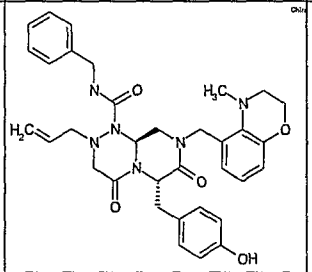
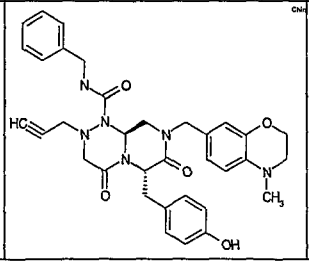
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2979		501	502
2980		599	600
2981		623	624
2982		552	553
2983		641	642

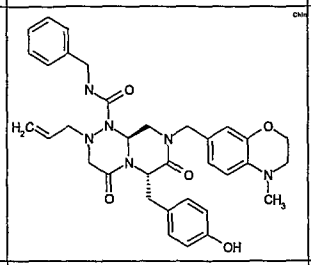
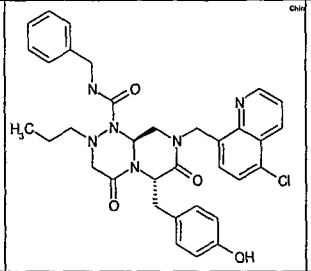
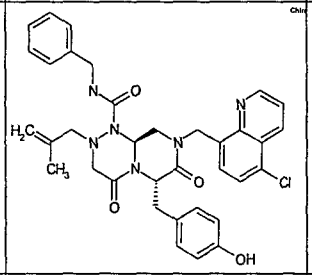
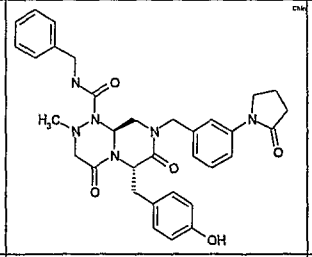
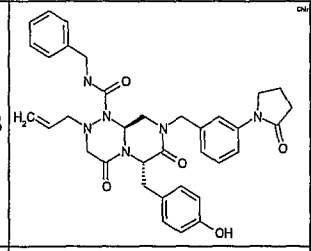
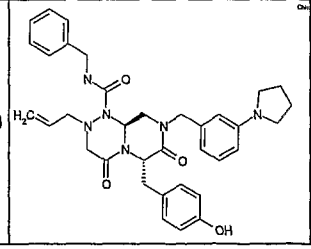
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
2984		579	580
2985		593	594
2986		613	614
2987		627	628
2988		605	606
2989		619	620

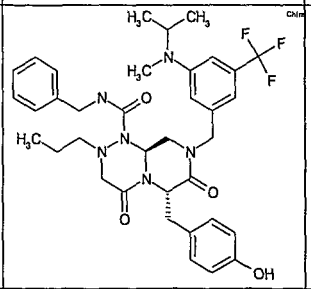
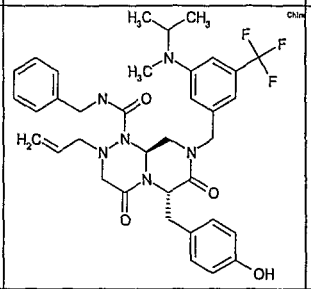
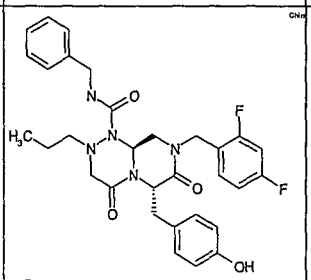
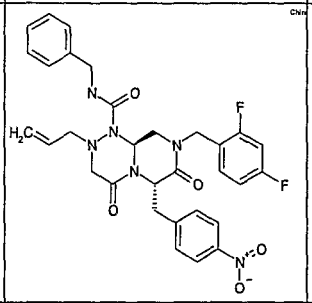
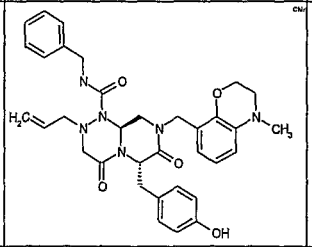
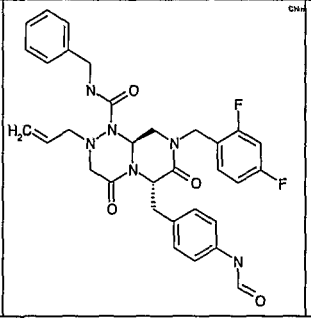
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2991		591	592
2992		617	618
2993		643	644
2994		667	668
2995		669	670

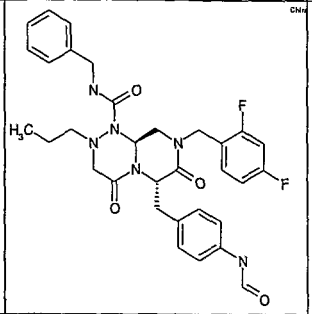
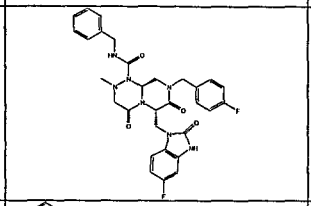
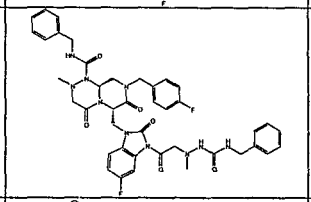
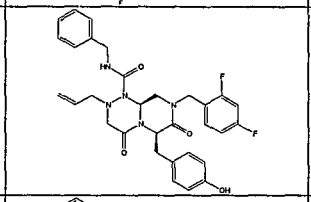
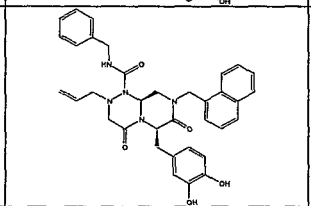
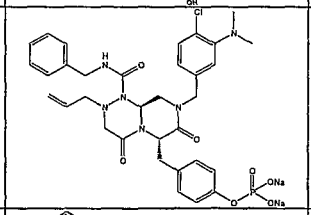
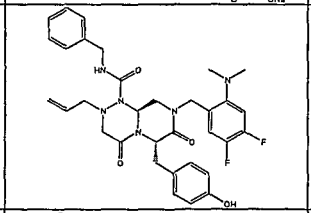
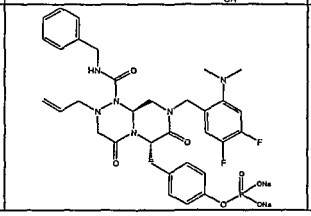
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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2997		639	640
2998		637	638
2999		596	597
3000		581	582
3001		579	580

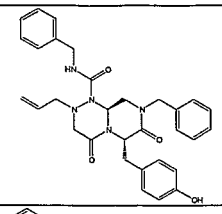
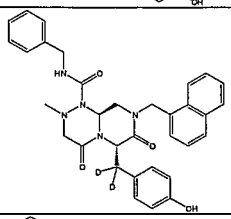
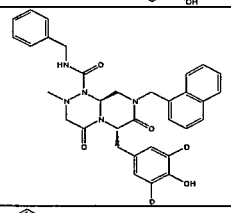
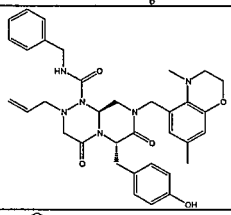
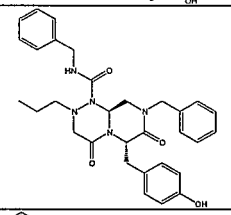
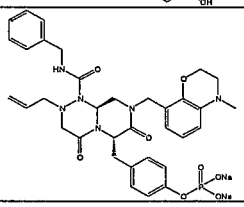
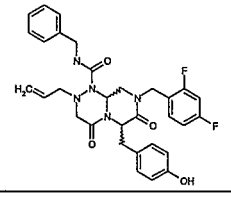
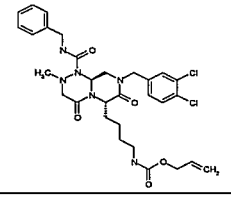
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3003		623	624
3004		659	660
3005		657	658
3006		595	596
3007		597	598

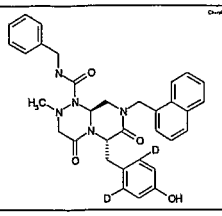
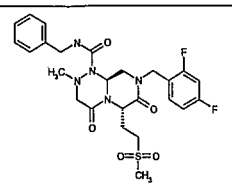
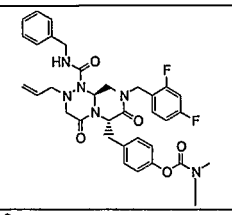
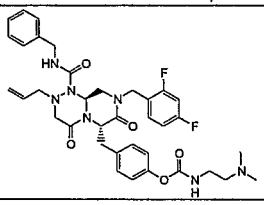
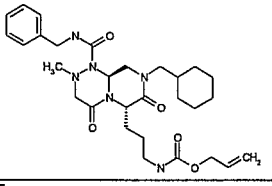
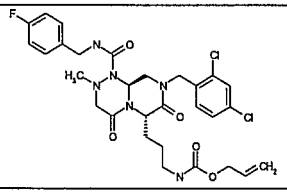
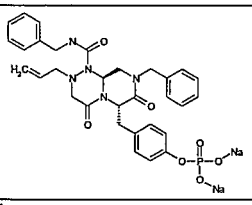
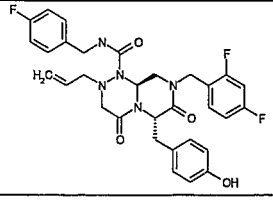
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3009		576	577
3010		574	575
3011		590	591
3012		611	612
3013		609	610

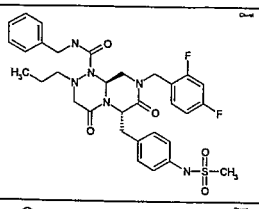
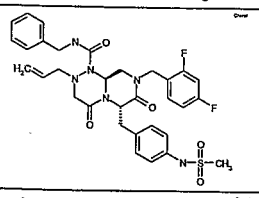
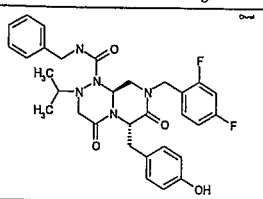
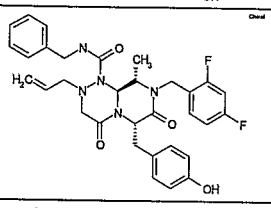
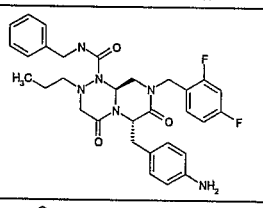
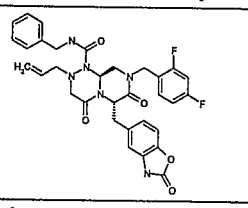
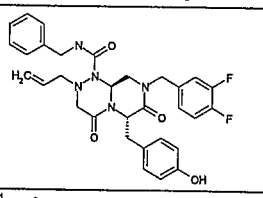
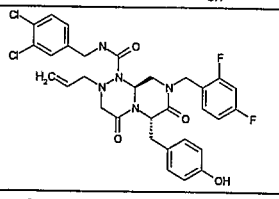
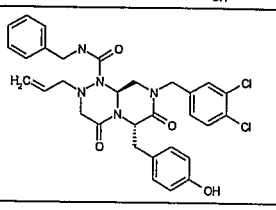
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3019		609	610

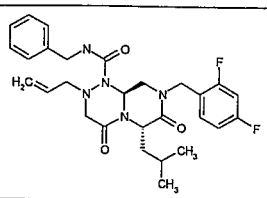
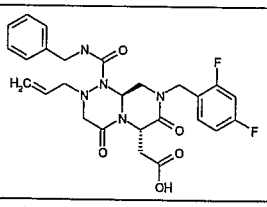
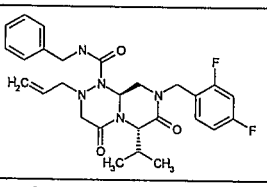
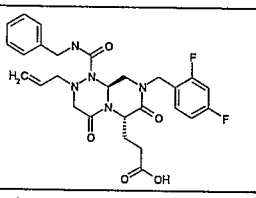
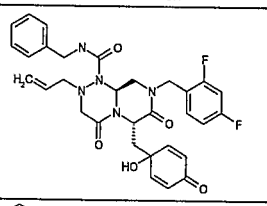
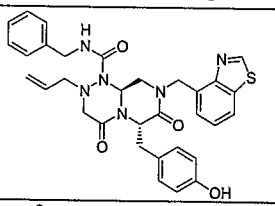
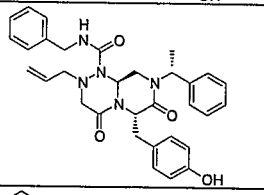
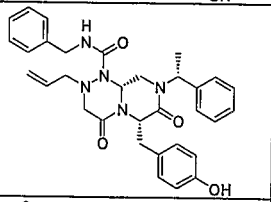
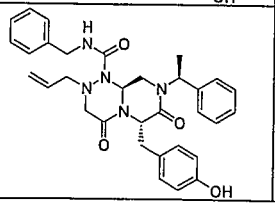
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3022		578	579
3023		605	606
3024		611	612
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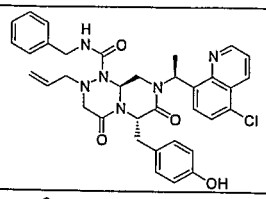
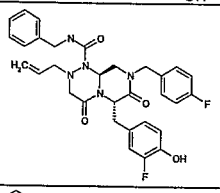
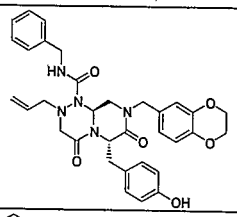
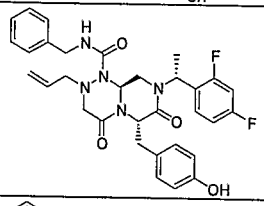
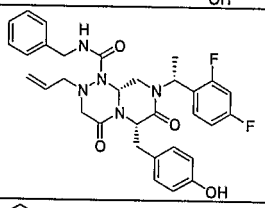
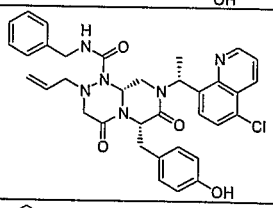
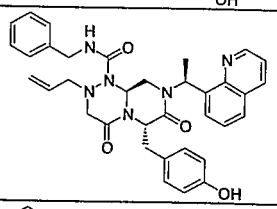
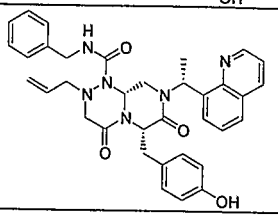
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3027		589	590
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3029		575	576
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3031		741	742
3032		618	619
3033		742	743

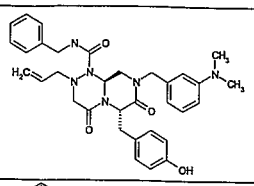
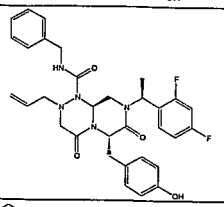
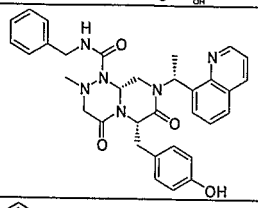
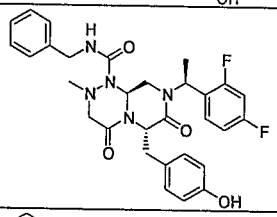
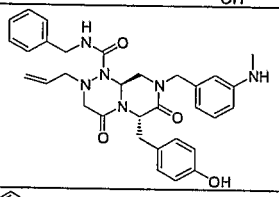
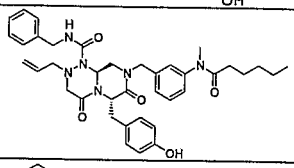
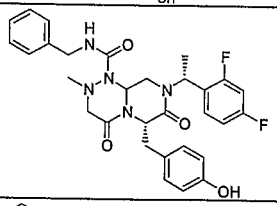
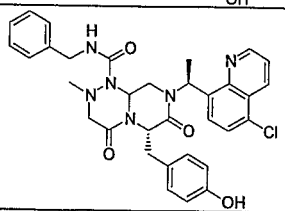
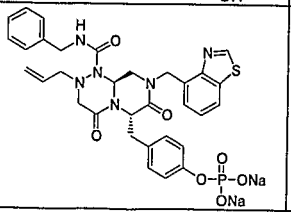
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3037		624	625
3038		541	542
3039		734	735
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3041		617	618

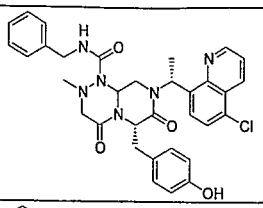
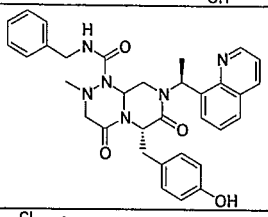
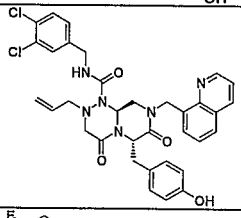
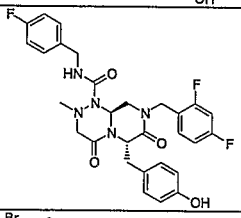
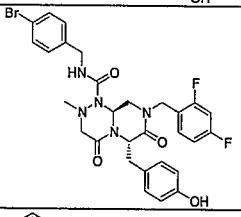
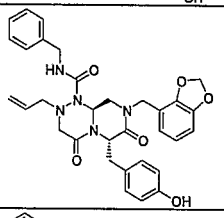
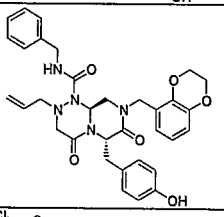
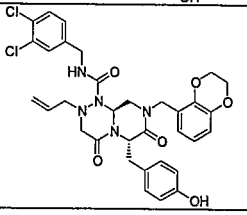
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3045		690	691
3046		555	556
3047		636	637
3048		664	665
3049		594	595

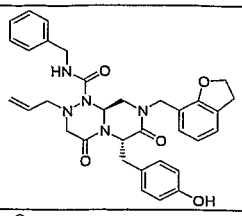
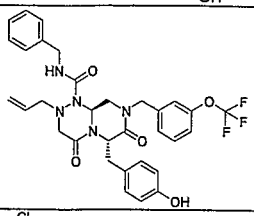
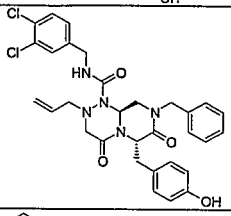
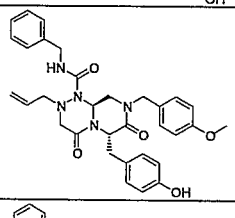
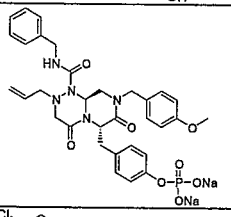
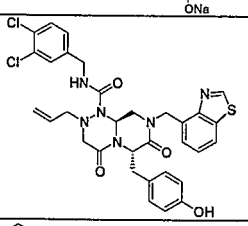
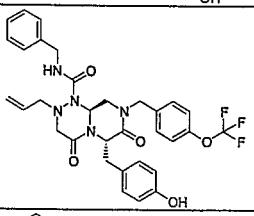
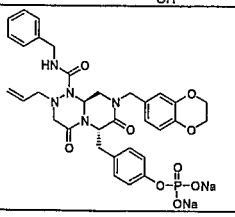
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3054		577	578
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3058		609	610

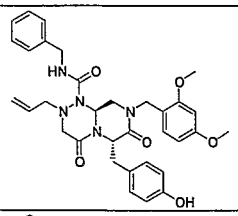
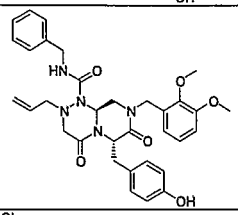
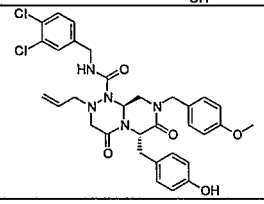
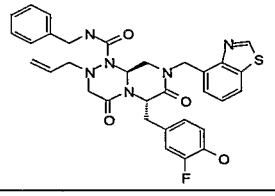
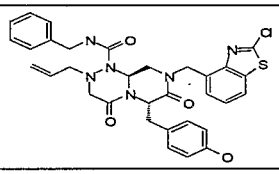
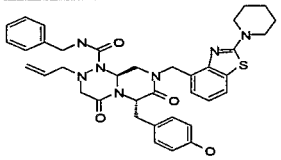
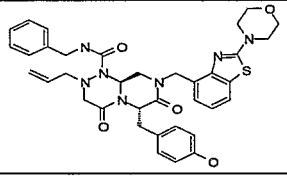
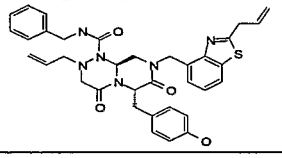
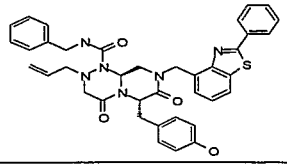
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3063		592	593
3064		597	598
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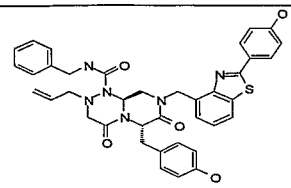
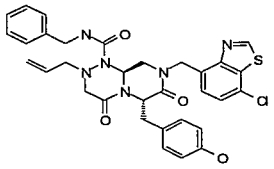
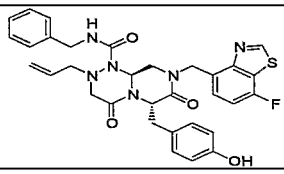
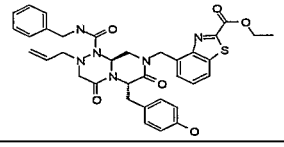
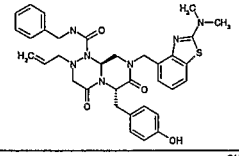
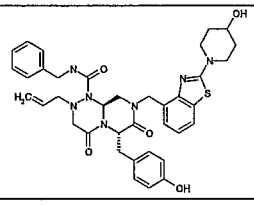
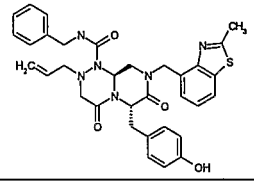
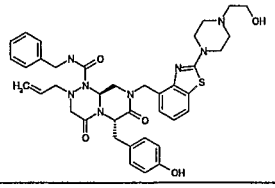
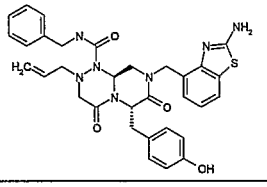
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3075		639	640

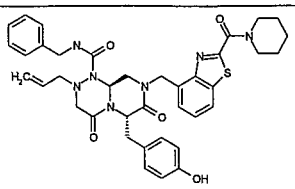
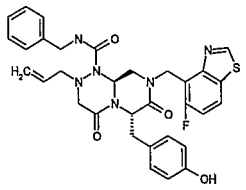
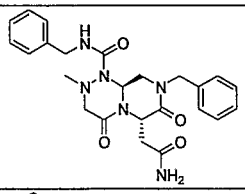
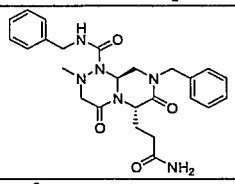
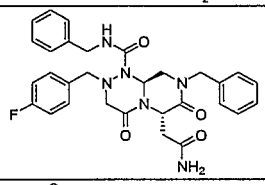
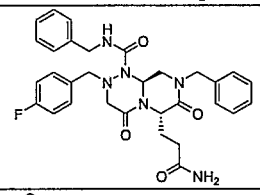
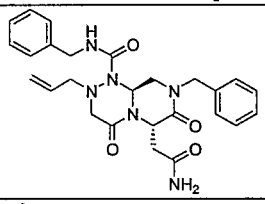
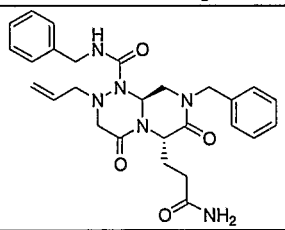
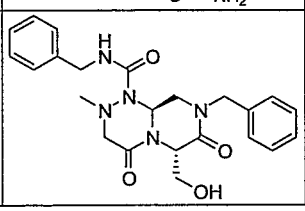
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
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3078		579	580
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3080		569	570
3081		667	668
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3083		613	614
3084		721	722

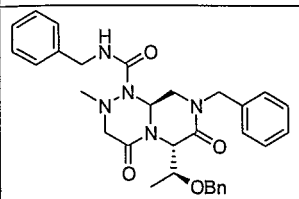
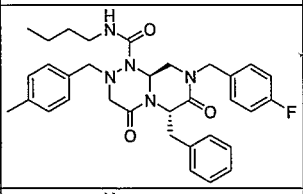
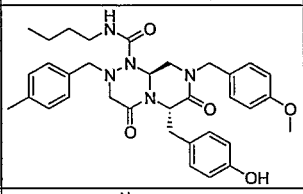
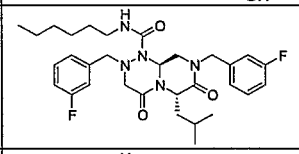
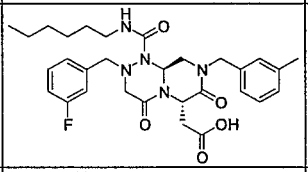
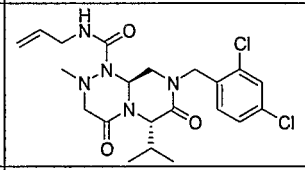
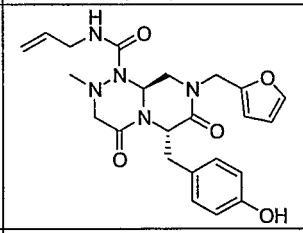
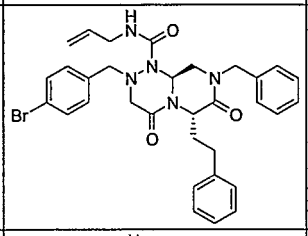
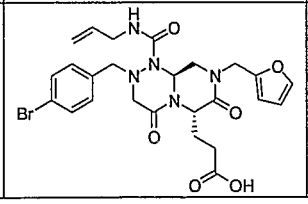
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3085		613	614
3086		579	580
3087		660	661
3088		568	569
3089		628	629
3090		584	585
3091		598	599
3092		667	668

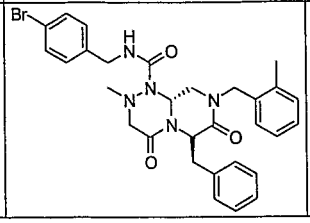
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3093		582	583
3094		624	625
3095		609	610
3096		570	571
3097		694	695
3098		694	695
3099		694	695
3100		694	695

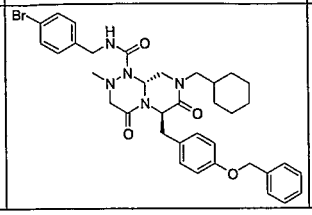
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3101		694	695
3102		694	695
3103		639	640
3104		615	616
3105		631	632
3106		680	681
3107		682	683
3108		637	638
3109		673	674

No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3110		689	690
3111		631	632
3112		615	616
3113		669	670
3114		640	641
3115		696	697
3116		611	612
3117		725	726
3118		612	613

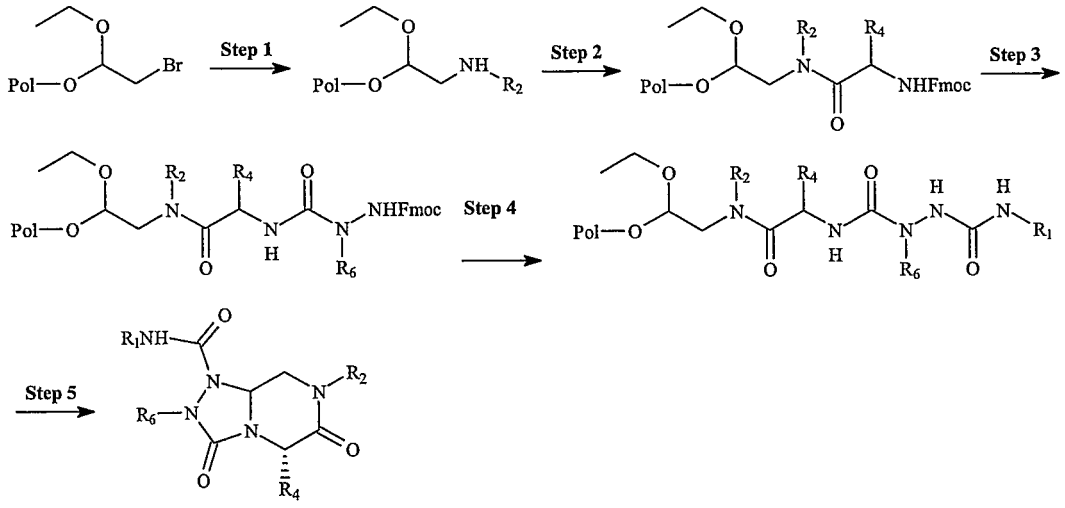
No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3119		708	709
3120		615	616
3121		464	465
3122		478	479
3123		558	559
3124		572	573
3125		490	491
3126		504	505
3127		437	438

No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3128		541	542
3129		571	572
3130		599	600
3131		569	570
3132		567	568
3133		468	469
3134		453	454
3135		616	617
3136		574	575

No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3137		590	591

No	MOLSTRUCTURE	Mol. Wgt	M+H (MS)
3138		688	689

In addition, synthesis of the peptide mimetics of the library of the present invention may be accomplished using the General Scheme of [4,3,0] Reverse-Turn Mimetic Library as follows:



Synthesis of the peptide mimetics of the bicyclic template libraries of the present invention was accomplished using FlexChem Reactor Block which has 96 well plate by known techniques. In the above scheme 'Pol' represents Bromoacetal resin (Advanced ChemTech) and detailed procedure is illustrated below.

Step 1

The bromoacetal resin (1.6mmol/g) and a solution of R1 amine in DMSO (2M solution) were placed in 96 well Robbins block (FlexChem). The reaction mixture was shaken at 60°C using rotating oven [Robbins Scientific] for 12 hours. The resin was washed with DMF, MeOH, and then DCM

Step 2

A solution of commercial available Fmoc-Amino Acids (4 equiv.), PyBob (4 equiv.), HOAt (4 equiv.), and DIEA (12 equiv.) in DMF was added to the resin. After the reaction mixture was shaken for 12 hours at room temperature, the resin was washed with DMF, MeOH, and then DCM.

Step 3

To the resin swollen by DMF before reaction was added 25% piperidine in DMF. After the reaction mixture was shaken for 30 min at room temperature. This deprotection step was repeated again and then washed with DMF, Methanol, then DCM. A solution of hydrazine carbamoyl chloride (4 equiv.), HOBt (4 equiv.), and DIC (4 equiv.) in DMF was added to the resin. After the reaction mixture was shaken for 12 hours at room temperature, the resin was washed with DMF, MeOH, and then DCM.

Step 4

To the resin swollen by DMF before reaction was added 25% piperidine in DMF. After the reaction mixture was shaken for 30 min at room temperature. This deprotection step was repeated again and then washed with DMF, Methanol, then DCM. To the resin swollen by DCM before reaction was added R_1-isocynate (5 equiv.) in DCM. After the reaction mixture was shaken for 12 hours at room temperature the resin was washed with DMF, MeOH, then DCM.

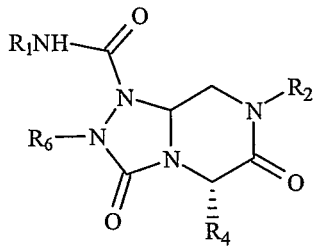
Step 5

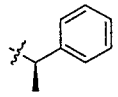
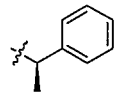
The resin was treated with formic acid (1.2 mL each well) for 18 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under reduced pressure using SpeedVac [SAVANT] to give the product as oil. These products were diluted with 50% water/acetonitrile and then lyophilized after freezing.

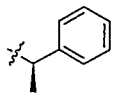
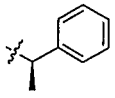
Table 3 shows a [4,3,0] reverse turn mimetics library which can be prepared according to the present invention, of which representative preparation is given in Example 5.

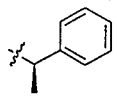
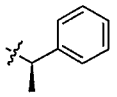
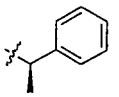
TABLE 3

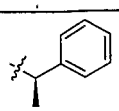
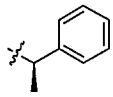
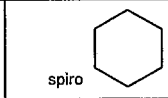
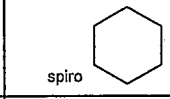
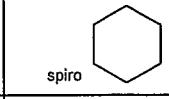
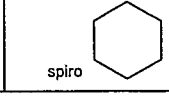
THE [4,3,0] REVERSE TURN MIMETICS LIBRARY

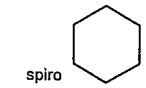
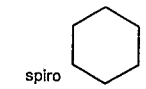
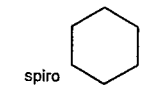
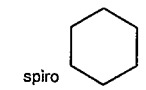
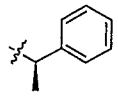
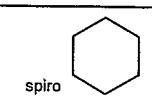
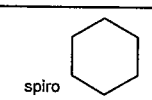
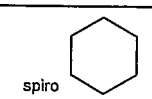
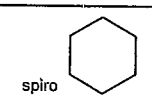
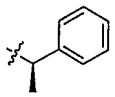


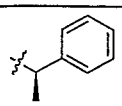
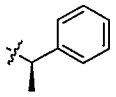
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610	Isoamyl	4-HO-phenyl	Methyl	Phenyl	466	467
611	Isoamyl	4-HO-phenyl	Methyl	4-Me-phenyl	480	481
612	Isoamyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	494	495
613	Isoamyl	4-HO-phenyl	Methyl	4-MeO-phenyl	496	497
614	Isoamyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	534	535
615	Isoamyl	4-HO-phenyl	Methyl	Cyclohexyl	472	473
616	Isoamyl	4-HO-phenyl	Methyl	Benzyl	480	481
617	Isoamyl	4-HO-phenyl	Methyl		494	495
618	Isoamyl	4-HO-phenyl	Methyl	4-MeO-benzyl	510	511
619	Isoamyl	4-HO-phenyl	Methyl	Phenethyl	494	495
620	Isoamyl	4-HO-phenyl	Methyl	Pentyl	460	461
621	Isoamyl	4-HO-phenyl	Methyl	Hexyl	474	475
622	Benzyl	4-HO-phenyl	Methyl	Phenyl	486	487
623	Benzyl	4-HO-phenyl	Methyl	4-Me-phenyl	500	501
624	Benzyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	514	515
625	Benzyl	4-HO-phenyl	Methyl	4-MeO-phenyl	516	517
626	Benzyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	554	555
627	Benzyl	4-HO-phenyl	Methyl	Cyclohexyl	492	493
628	Benzyl	4-HO-phenyl	Methyl	Benzyl	500	501
629	Benzyl	4-HO-phenyl	Methyl		514	515
630	Benzyl	4-HO-phenyl	Methyl	4-MeO-benzyl	530	531
631	Benzyl	4-HO-phenyl	Methyl	Phenethyl	514	515
632	Benzyl	4-HO-phenyl	Methyl	Pentyl	480	481
633	Benzyl	4-HO-phenyl	Methyl	Hexyl	494	495

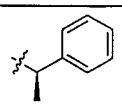
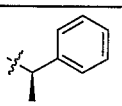
No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
634	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Phenyl	536	537
635	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	4-Me-phenyl	550	551
636	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	564	565
637	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	4-MeO-phenyl	566	567
638	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	604	605
639	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Cyclohexyl	542	543
640	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Benzyl	550	551
641	Naphth-1-ylmethyl	4-HO-phenyl	Methyl		564	565
642	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	4-MeO-benzyl	580	581
643	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Phenethyl	564	565
644	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Pentyl	530	531
645	Naphth-1-ylmethyl	4-HO-phenyl	Methyl	Hexyl	544	545
646	Cyclohexylmethyl	4-HO-phenyl	Methyl	Phenyl	492	493
647	Cyclohexylmethyl	4-HO-phenyl	Methyl	4-Me-phenyl	506	507
648	Cyclohexylmethyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	520	521
649	Cyclohexylmethyl	4-HO-phenyl	Methyl	4-MeO-phenyl	522	523
650	Cyclohexylmethyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	560	561
651	Cyclohexylmethyl	4-HO-phenyl	Methyl	Cyclohexyl	468	469
652	Cyclohexylmethyl	4-HO-phenyl	Methyl	Benzyl	506	507
653	Cyclohexylmethyl	4-HO-phenyl	Methyl		520	521
654	Cyclohexylmethyl	4-HO-phenyl	Methyl	4-MeO-benzyl	536	537
655	Cyclohexylmethyl	4-HO-phenyl	Methyl	Phenethyl	520	521
656	Cyclohexylmethyl	4-HO-phenyl	Methyl	Pentyl	486	487
657	Cyclohexylmethyl	4-HO-phenyl	Methyl	Hexyl	500	501
658	4-methylbenzyl	4-HO-phenyl	Methyl	Phenyl	500	501
659	4-methylbenzyl	4-HO-phenyl	Methyl	4-Me-phenyl	514	515
660	4-methylbenzyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	528	529

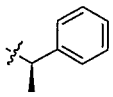
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662	4-methylbenzyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	568	569
663	4-methylbenzyl	4-HO-phenyl	Methyl	Cyclohexyl	506	507
664	4-methylbenzyl	4-HO-phenyl	Methyl	Benzyl	514	515
665	4-methylbenzyl	4-HO-phenyl	Methyl		528	529
666	4-methylbenzyl	4-HO-phenyl	Methyl	4-MeO-benzyl	544	545
667	4-methylbenzyl	4-HO-phenyl	Methyl	Phenethyl	528	529
668	4-methylbenzyl	4-HO-phenyl	Methyl	Pentyl	494	495
669	4-methylbenzyl	4-HO-phenyl	Methyl	Hexyl	508	509
670	Methoxypropyl	4-HO-phenyl	Methyl	Phenyl	468	469
671	Methoxypropyl	4-HO-phenyl	Methyl	4-Me-phenyl	482	483
672	Methoxypropyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	496	497
673	Methoxypropyl	4-HO-phenyl	Methyl	4-MeO-phenyl	498	499
674	Methoxypropyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	536	537
675	Methoxypropyl	4-HO-phenyl	Methyl	Cyclohexyl	474	475
676	Methoxypropyl	4-HO-phenyl	Methyl	Benzyl	482	483
677	Methoxypropyl	4-HO-phenyl	Methyl		496	497
678	Methoxypropyl	4-HO-phenyl	Methyl	4-MeO-benzyl	512	513
679	Methoxypropyl	4-HO-phenyl	Methyl	Phenethyl	496	497
680	Methoxypropyl	4-HO-phenyl	Methyl	Pentyl	462	463
681	Methoxypropyl	4-HO-phenyl	Methyl	Hexyl	476	477
682	Phenethyl	4-HO-phenyl	Methyl	Phenyl	500	501
683	Phenethyl	4-HO-phenyl	Methyl	4-Me-phenyl	514	515
684	Phenethyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	528	529
685	Phenethyl	4-HO-phenyl	Methyl	4-MeO-phenyl	530	531
686	Phenethyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	568	569
687	Phenethyl	4-HO-phenyl	Methyl	Cyclohexyl	506	507
688	Phenethyl	4-HO-phenyl	Methyl	Benzyl	514	515
689	Phenethyl	4-HO-phenyl	Methyl		528	529
690	Phenethyl	4-HO-phenyl	Methyl	4-MeO-benzyl	544	545
691	Phenethyl	4-HO-phenyl	Methyl	Phenethyl	528	529
692	Phenethyl	4-HO-phenyl	Methyl	Pentyl	494	495
693	Phenethyl	4-HO-phenyl	Methyl	Hexyl	508	509
694	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Phenyl	576	577
695	2,2-bisphenylethyl	4-HO-phenyl	Methyl	4-Me-phenyl	590	591
696	2,2-bisphenylethyl	4-HO-phenyl	Methyl	3,5-Me_2-phenyl	604	605
697	2,2-bisphenylethyl	4-HO-phenyl	Methyl	4-MeO-phenyl	606	607
698	2,2-bisphenylethyl	4-HO-phenyl	Methyl	4-CF_3-phenyl	644	645

No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
699	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Cyclohexyl	582	583
700	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Benzyl	586	587
701	2,2-bisphenylethyl	4-HO-phenyl	Methyl		604	605
702	2,2-bisphenylethyl	4-HO-phenyl	Methyl	4-MeO-benzyl	620	621
703	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Phenethyl	604	605
704	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Pentyl	570	571
705	2,2-bisphenylethyl	4-HO-phenyl	Methyl	Hexyl	584	585
706	Naphth-1-ylmethyl	Benzyl	Methyl	Phenyl	520	521
707	Naphth-1-ylmethyl	Benzyl	Methyl	4-Me-phenyl	534	535
708	Naphth-1-ylmethyl	Benzyl	Methyl	3,5-Me_2-phenyl	548	549
709	Naphth-1-ylmethyl	Benzyl	Methyl	4-MeO-phenyl	550	551
710	Naphth-1-ylmethyl	Benzyl	Methyl	4-CF_3-phenyl	588	589
711	Naphth-1-ylmethyl	Benzyl	Methyl	Cyclohexyl	526	527
712	Naphth-1-ylmethyl	Benzyl	Methyl	Benzyl	534	535
713	Naphth-1-ylmethyl	Benzyl	Methyl		548	549
714	Naphth-1-ylmethyl	Benzyl	Methyl	4-MeO-benzyl	564	565
715	Naphth-1-ylmethyl	Benzyl	Methyl	Phenethyl	548	549
716	Naphth-1-ylmethyl	Benzyl	Methyl	Pentyl	514	515
717	Naphth-1-ylmethyl	Benzyl	Methyl	Hexyl	528	529
718	Naphth-1-ylmethyl		Methyl	Phenyl	498	499
719	Naphth-1-ylmethyl		Methyl	4-Me-phenyl	512	513
720	Naphth-1-ylmethyl		Methyl	3,5-Me_2-phenyl	526	527
721	Naphth-1-ylmethyl		Methyl	4-MeO-phenyl	528	529

No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
722	Naphth-1-ylmethyl		Methyl	4-CF_3-phenyl	566	567
723	Naphth-1-ylmethyl		Methyl	Cyclohexyl	504	505
724	Naphth-1-ylmethyl		Methyl	Benzyl	512	513
725	Naphth-1-ylmethyl		Methyl		526	527
726	Naphth-1-ylmethyl		Methyl	4-MeO-benzyl	542	543
727	Naphth-1-ylmethyl		Methyl	Phenethyl	526	527
728	Naphth-1-ylmethyl		Methyl	Pentyl	492	493
729	Naphth-1-ylmethyl		Methyl	Hexyl	506	507
730	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Phenyl	570	571
731	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	4-Me-phenyl	584	585
732	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	3,5-Me_2-phenyl	598	599
733	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	4-MeO-phenyl	600	601
734	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	4-CF_3-phenyl	638	639
735	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Cyclohexyl	576	577
736	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Benzyl	584	585
737	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl		598	599
738	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	4-MeO-benzyl	614	615
739	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Phenethyl	598	599
740	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Pentyl	564	565
741	Naphth-1-ylmethyl	Naphth-1-ylmethyl	Methyl	Hexyl	578	579
742	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Phenyl	526	527
743	Naphth-1-	Cyclohexylmethyl	Methyl	4-Me-phenyl	540	541

No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
	ylmethyl					
744	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	3,5-Me_2-phenyl	554	555
745	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	4-MeO-phenyl	556	557
746	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	4-CF_3-phenyl	594	595
747	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Cyclohexyl	532	533
748	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Benzyl	540	541
749	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl		554	555
750	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	4-MeO-benzyl	570	571
751	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Phenethyl	554	555
752	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Pentyl	520	521
753	Naphth-1-ylmethyl	Cyclohexylmethyl	Methyl	Hexyl	534	535
754	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Phenyl	554	555
755	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	4-Me-phenyl	568	569
756	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	3,5-Me_2-phenyl	582	583
757	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	4-MeO-phenyl	584	585
758	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	4-CF_3-phenyl	622	623
759	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Cyclohexyl	560	561
760	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Benzyl	568	569
761	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl		582	583
762	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	4-MeO-benzyl	598	599
763	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Phenethyl	582	583
764	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Pentyl	548	549
765	Naphth-1-ylmethyl	4-chlorobenzyl	Methyl	Hexyl	562	563
766	Naphth-1-ylmethyl	Methyl	Methyl	Phenyl	444	445
767	Naphth-1-ylmethyl	Methyl	Methyl	4-Me-phenyl	458	459
768	Naphth-1-ylmethyl	Methyl	Methyl	3,5-Me_2-phenyl	472	473

No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
769	Naphth-1-ylmethyl	Methyl	Methyl	4-MeO-phenyl	474	475
770	Naphth-1-ylmethyl	Methyl	Methyl	4-CF_3-phenyl	512	513
771	Naphth-1-ylmethyl	Methyl	Methyl	Cyclohexyl	450	451
772	Naphth-1-ylmethyl	Methyl	Methyl	Benzyl	458	459
773	Naphth-1-ylmethyl	Methyl	Methyl		472	473
774	Naphth-1-ylmethyl	Methyl	Methyl	4-MeO-benzyl	488	489
775	Naphth-1-ylmethyl	Methyl	Methyl	Phenethyl	472	473
776	Naphth-1-ylmethyl	Methyl	Methyl	Pentyl	438	439
777	Naphth-1-ylmethyl	Methyl	Methyl	Hexyl	452	453
778	Naphth-1-ylmethyl	Isobutyl	Methyl	Phenyl	486	487
779	Naphth-1-ylmethyl	Isobutyl	Methyl	4-Me-phenyl	500	501
780	Naphth-1-ylmethyl	Isobutyl	Methyl	3,5-Me_2-phenyl	514	515
781	Naphth-1-ylmethyl	Isobutyl	Methyl	4-MeO-phenyl	516	517
782	Naphth-1-ylmethyl	Isobutyl	Methyl	4-CF_3-phenyl	554	555
783	Naphth-1-ylmethyl	Isobutyl	Methyl	Cyclohexyl	492	493
784	Naphth-1-ylmethyl	Isobutyl	Methyl	Benzyl	500	501
785	Naphth-1-ylmethyl	Isobutyl	Methyl		514	515
786	Naphth-1-ylmethyl	Isobutyl	Methyl	4-MeO-benzyl	530	531
787	Naphth-1-ylmethyl	Isobutyl	Methyl	Phenethyl	514	515
788	Naphth-1-ylmethyl	Isobutyl	Methyl	Pentyl	480	481
789	Naphth-1-ylmethyl	Isobutyl	Methyl	Hexyl	494	495
790	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Phenyl	504	505
791	Naphth-1-ylmethyl	Methylthioethyl	Methyl	4-Me-phenyl	518	519
792	Naphth-1-ylmethyl	Methylthioethyl	Methyl	3,5-Me_2-phenyl	532	533
793	Naphth-1-ylmethyl	Methylthioethyl	Methyl	4-MeO-phenyl	534	535
794	Naphth-1-	Methylthioethyl	Methyl	4-CF_3-phenyl	572	573

No	R_2	R_4	R_6	R_1	Mol. Weight	M+H
	ylmethyl					
795	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Cyclohexyl	510	511
796	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Benzyl	518	519
797	Naphth-1-ylmethyl	Methylthioethyl	Methyl		532	533
798	Naphth-1-ylmethyl	Methylthioethyl	Methyl	4-MeO-benzyl	548	549
799	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Phenethyl	532	533
800	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Pentyl	498	499
801	Naphth-1-ylmethyl	Methylthioethyl	Methyl	Hexyl	512	513

In a further aspect of this invention, the present invention provides methods for screening the libraries for bioactivity and isolating bioactive library members.

In yet another aspect, the present invention provides a method for carrying out a binding assay. The method includes providing a composition that includes a first co-activator, an interacting protein, and a test compound. The amino acid structure of the first co-activator includes a binding motif of LXXLL, LXXLI or FxxFF wherein X is any amino acid. The method further includes detecting an alteration in binding between the first co-activator and the interacting protein due to the presence of the compound, and then characterizing the test compound in terms of its effect on the binding.

The assay may be carried out by any means that can measure the effect of a test compound on the binding between two proteins. Many such assays are known in the art and can be utilized in the method of the present invention, including the so-called Two-Hybrid and Split-Hybrid systems.

The Two-Hybrid system, and various means to carry out an assay using this system, are described in, *e.g.,* U.S. Patent 6,410,245. The Split-Hybrid system has been described by, *e.g.,* Hsiu-Ming Shiu et al. *Proc. Natl. Acad. Sci. USA,* 93:13896-13901, November 1996; and John D. Crispino, et al.

Molecular Cell, 3:1-20, February 1999. In the Split-Hybrid system, a fusion protein is utilized where protein X is fused to the lexA DNA binding domains (pLexA) and protein Y is fused to the transcription activator VP16 (pSHM.1-LacZ). Interaction between lexA-X and VP16-Y leads to the expression of the Tetracycline repressor protein (TetR). TetR prevents transcription of the HIS3 reporter gene, making the cells unable to grow on media lacking histidine. Disruption of protein-protein interaction will restore the ability of the cells to grow on such media by shutting down expression of the tetracycline repressor. Accordingly, compounds of the present invention may be added to the growing cells, and if the addition of the compound restores the ability of the cells to grow on the media, the compound may be seen as an effective disruptor of the protein-protein interaction.

The yeast strains required to make the Split-Hybrid system work can be employed with two hybrid LexA/VP16 constructs such as those described by Stanley M. Hollenberg, et al. *Molecular and Cellular Biology* 15(7):3813-3822, July 1995. A useful modification of the Split-Hybrid system was utilized by Takemaru, K. I. and Moon, R. T. *J. of Cell Biol.* 149:249-254, 2000.

Other assay formats are also suitable. For example, reporter gene assays for AP-1, ELISA, for example, blocking the production of IL-2 by a T-cell line after stimulation with CD3 and CD28 to look for inhibitors of IL-2 transcription. Direct binding assays (between coactivators and their partners) can be performed by surface plasmon resonance spectroscopy (Biacore, Sweden, manufactures suitable instruments) or ELISA.

Exemplary transcriptional regulators include, without limitation, VP16, VP64, p300, CBP, PCAF,SRC1 PvALF, AtHD2A and ERF-2. See, for example, Robyr et al. (2000) *Mol. Endocrinol.* 14:329-347; Collingwood et al. (1999) J. *Mol. Endocrinol.* 23:255-275; Leo et al. (2000) *Gene* 245:1-11; Manteuffel-Cymborowska (1999) *Acta Biochim. Pol.* 46:77-89; McKenna et al. (1999) *J. Steroid Biochem. Mol. Biol.* 69:3-12; Malik et al. (2000) *Trends*

Biochem. Sci. 25:277-283; and Lemon et al. (1999) *Curr. Opin. Genet. Dev.* 9:499-504. Other exemplary transcription factors include, without limitation, OsGAI, HALF-1, C1, AP1, ARF-5, -6, -7, and -8, CPRF1, CPRF4, MYC-RP/GP, and TRAB1. See, for example, Ogawa et al. (2000) *Gene* 245:21 -29; Okanami et al. (1996) *Genes Cells* 1:87-99; Goff et al. (1991) *Genes Dev.* 5:298 -309; Cho et al. (1999) *Plant Mol. Biol.* 40:419-429; Ulmason et al. (1999) *Proc. Natl. Acad. Sci. USA* 96:5844-5849; Sprenger-Haussels et al. (2000) *Plant J.* 22:1-8; Gong et al. (1999) *Plant Mol. Biol.* 41:33-44; and Hobo et al. (1999) *Proc. Natl. Acad. Sci. USA* 96:15,348-15,353.

In a preferred embodiment, the transcriptional coactivator is a human transcriptional coactivator. In another preferred embodiment, the transcriptional coactivator is a member of the p300/CBP family of co-activators which have histone acetyltransferase activity. p300 is described for example by Eckner et al, 1994 and CBP by Bannister and Kouzarides, 1996. For the purposes of the present invention, reference to p300/CBP refers to human allelic and synthetic variants of p300, and to other mammalian variants and allelic and synthetic variants thereof, as well as fragments of said human and mammalian forms of p300. In one aspect of the assay, the interacting protein is a transcription factor or a second co-activator.

In one aspect of the assay, the interacting protein is any one of RIP140; SRC-1 (NCoA-1); TIF2 (GRIP-1; SRC-2); p (CIP; RAC3; ACTR; AIB-1; TRAM-1; SRC-3); CBP (p300); TRAPs (DRIPs); PGC-1; CARM-1; PRIP (ASC-2; AIB3; RAP250; NRC); GT-198; and SHARP (CoAA; p68; p72). In another aspect of the assay, the interacting protein is any one of TAL 1; p73; MDm2; TBP; HIF-1; Ets-1; RXR; p65; AP-1; Pit-1; HNF-4; Stat2; HPV E2; BRCA1; p45 (NF-E2); c-Jun; c-myb; Tax; Sap 1; YY1; SREBP; ATF-1; ATF-4; Cubitus; Interruptus; Gli3; MRF; AFT-2; JMY; dMad; PyLT: HPV E6; CITTA; Tat; SF-1; E2F; junB; RNA helicase A; C/EBP β; GATA-1; Neuro D; Microphthalimia; E1A; TFIIB; p53; P/CAF; Twist; Myo D; pp9O RSK; c-Fos; and SV40 Large T. In another aspect of the assay, the interacting protein is any one of ERAP140;

RIP140; RIP160; Trip1; SWI1 (SNF); ARA70; RAP46; TIF1; TIF2; GRIP1; and TRAP. In another aspect of the invention, the interacting protein is any one of VP16; VP64; p300; CBP; PCAF; SRC1 PvALF; AtHD2A; ERF-2; OsGAI; HALF-1; C1; AP-1; ARF-5; ARF-6; ARF-7; ARF-8; CPRF1; CPRF4; MYC-RP/GP; and TRAB1. In another aspect of the invention, the first co-activator is CBP or p300.

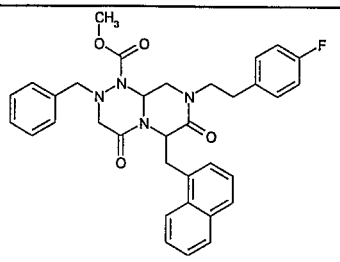
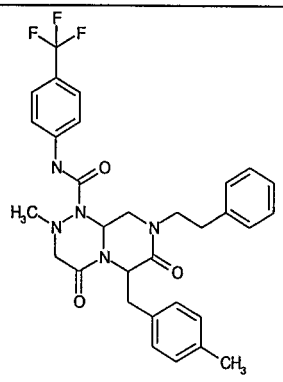
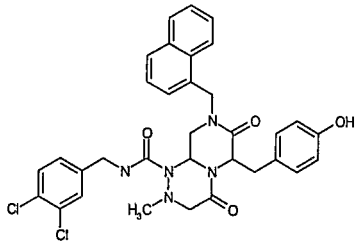
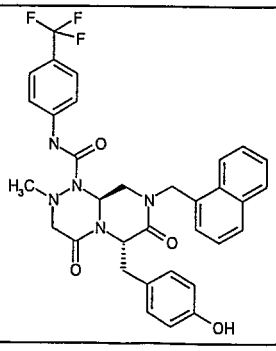
The test compound is selected from compounds as described herein. For example, compounds having the formula (I), (II), (III), (IV), (VI) and (VIa). Typically, a test compound will be evaluated at several different concentrations, where these concentrations will be selected, in part, based on the conditions of the assay, *e.g.,* the concentrations of the first co-activator and the interacting protein. Concentrations in the range of about 0.1 to 10 μM are typical. In one aspect, the assay evaluates the relative efficacy of two compounds to affect the binding interaction between two proteins, where at least one of those two compounds is a compound of the present invention. The more effective compound can than serve as a reference compound in a study of the relationship between compound structure and compound activity.

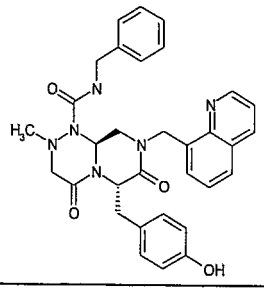
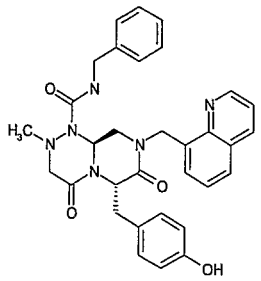
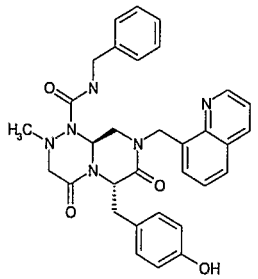
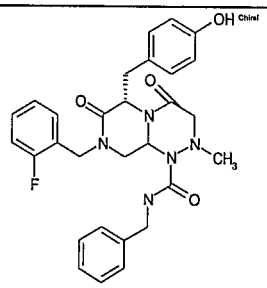
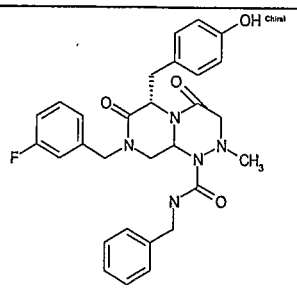
The libraries of the present invention were screened for bioactivity by various techniques and methods. In general, the screening assay may be performed by (1) contacting the mimetics of a library with a biological target of interest, such as a receptor, to allow binding between the mimetics of the library and the target to occur, and (2) detecting the binding event by an appropriate assay, such as the calorimetric assay disclosed by Lam et al. (*Nature* 354:82-84, 1991) or Griminski et al. (*Biotechnology* 12:1008-1011, 1994) (both of which are incorporated herein by reference). In a preferred embodiment, the library members are in solution and the target is immobilized on a solid phase. Alternatively, the library may be immobilized on a solid phase and may be probed by contacting it with the target in solution.

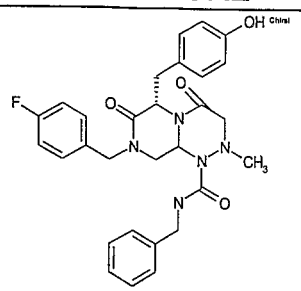
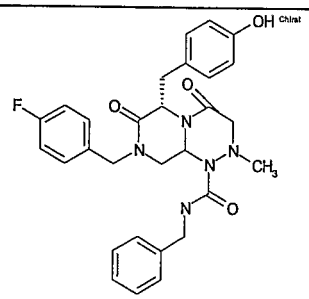
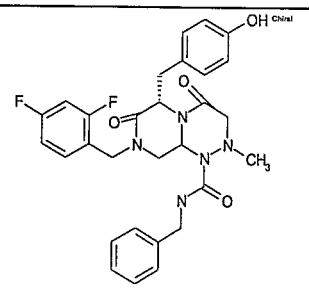
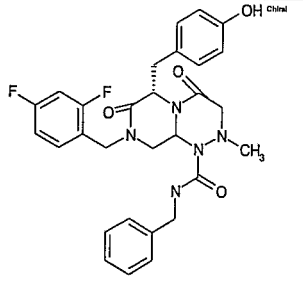
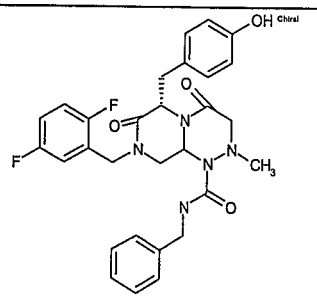
Table 4 below shows compounds for bioactivity test selected from the library of the present invention and IC_{50} values thereof, which are measured by the Reporter gene assay as described in Example 6.

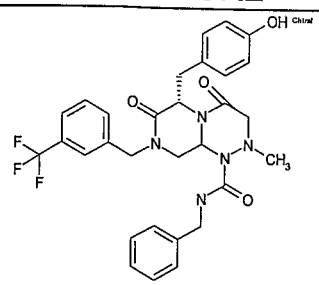
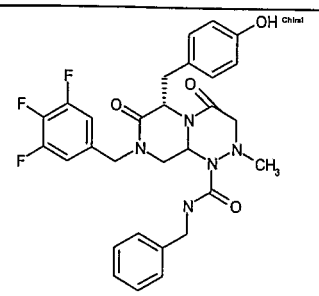
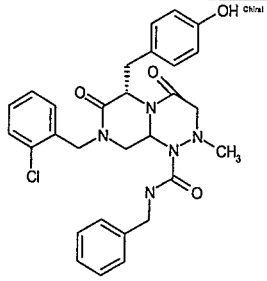
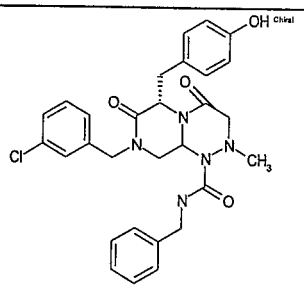
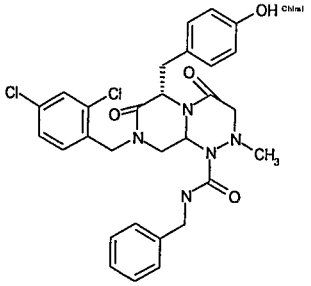
TABLE 4

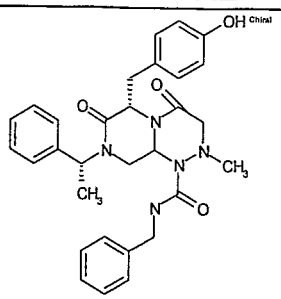
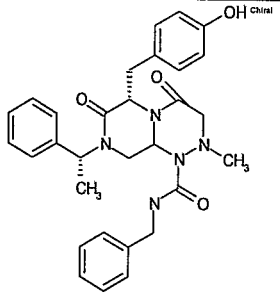
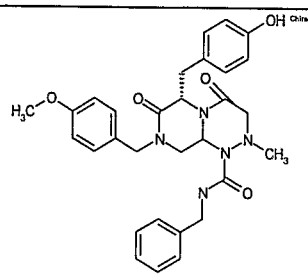
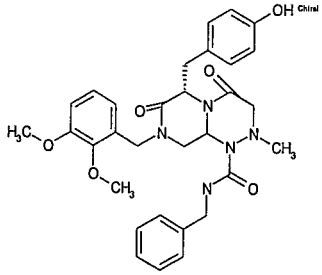
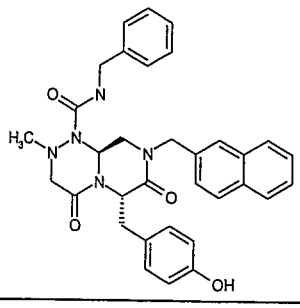
$IC_{50}(\mu M)$ OF SELECTED LIBRARY COMPOUNDS

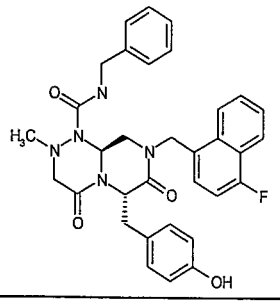
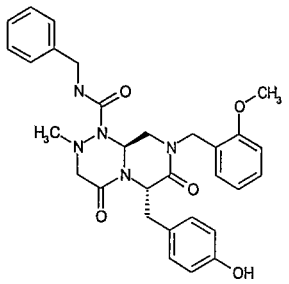
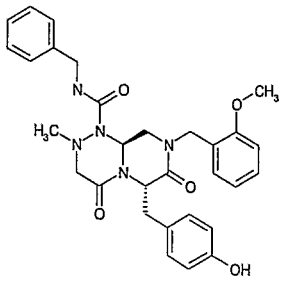
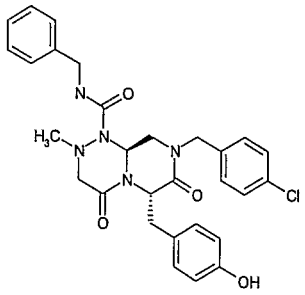
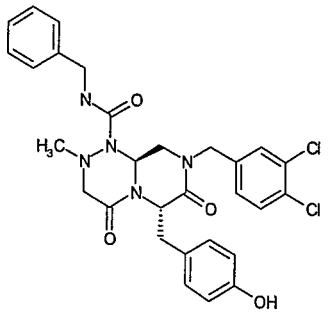
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
1		580.7	12.8
2		579.6	12.6
3		632.5	13.9
4		617.6	11.8

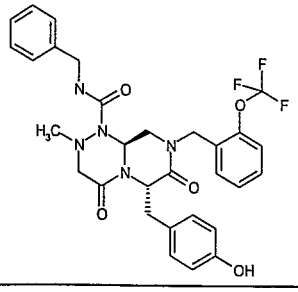
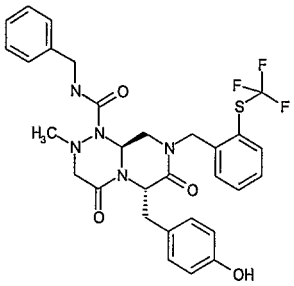
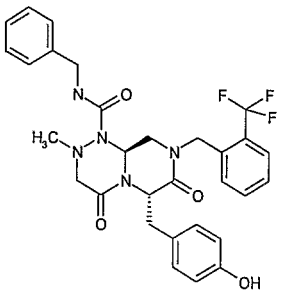
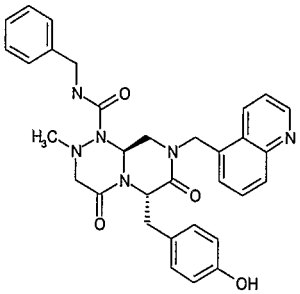
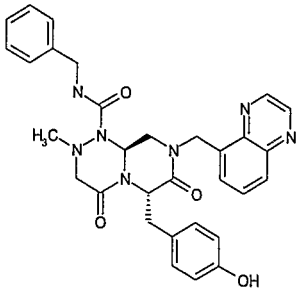
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
5		564.6	6.8
6		564.6	6.1
7		564.6	2.2
8		531.6	14.5
9		531.6	6.7

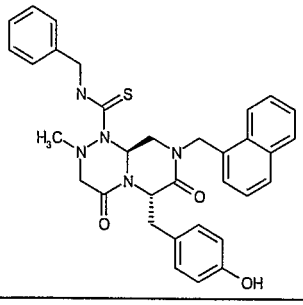
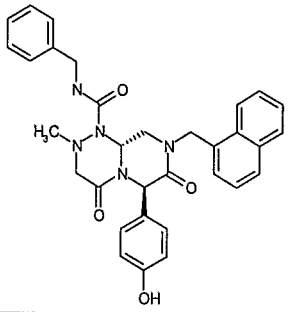
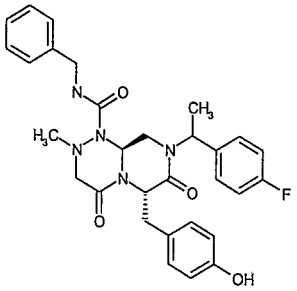
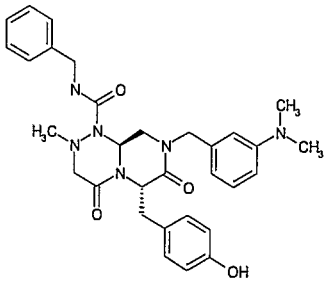
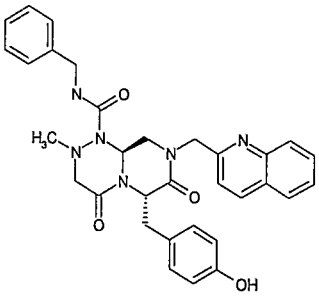
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
10		531.6	4.0
11		531.6	4.6
12		549.6	9.0
13		549.6	6.4
14		549.6	17.7

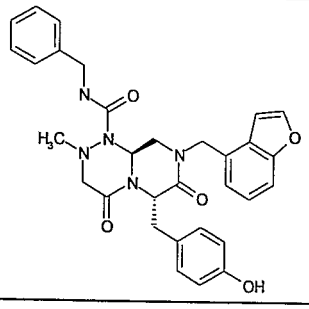
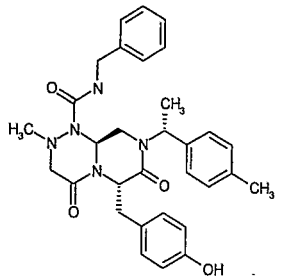
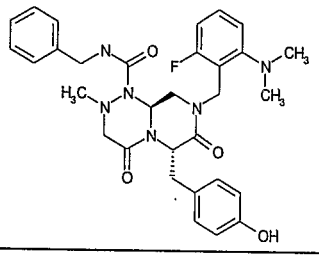
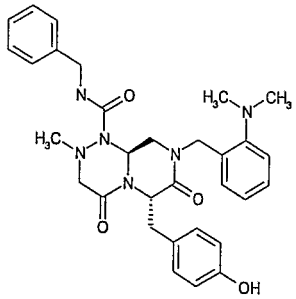
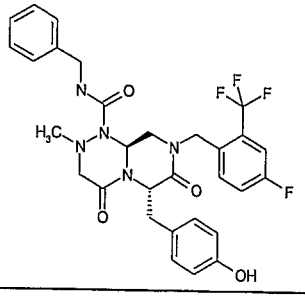
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
15		581.6	4.2
16		567.6	3.8
17		548.0	14.3
18		548.0	3.3
19		582.5	11.5

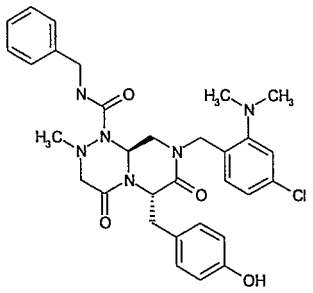
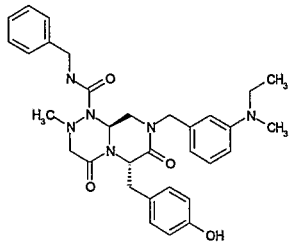
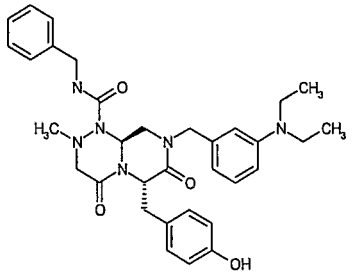
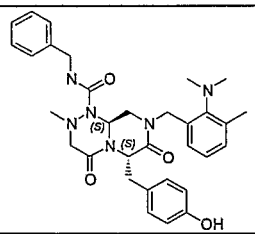
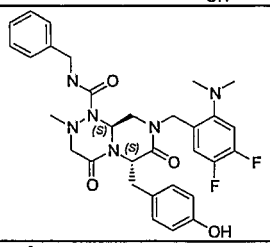
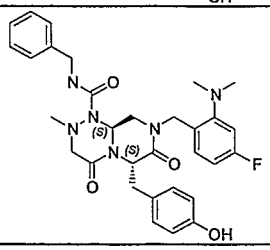
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
20		527.6	5.1
21		527.6	5.0
22		543.6	10.4
23		573.6	10.7
24		563.7	5.0

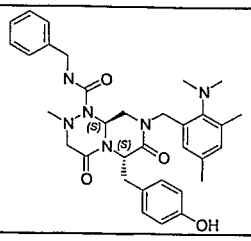
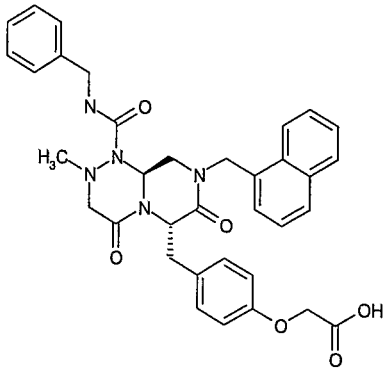
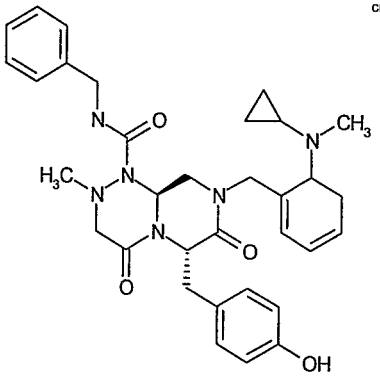
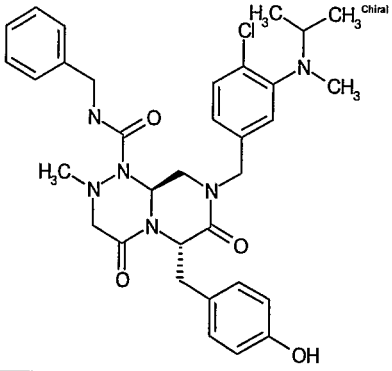
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
25		581.6	3.0
26		543.6	7.1
27		543.6	5.2
28		548.0	7.5
29		582.5	3.8

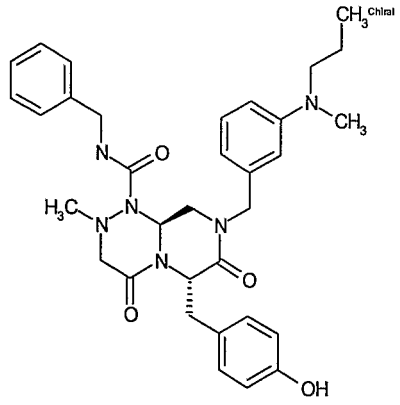
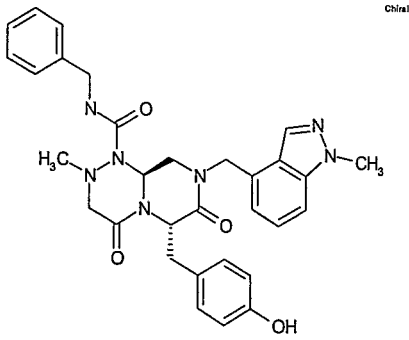
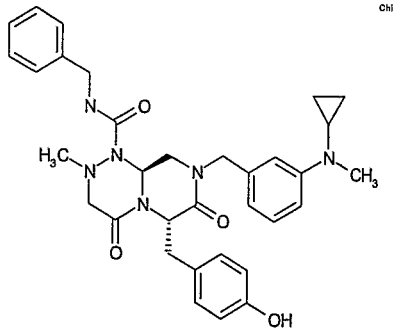
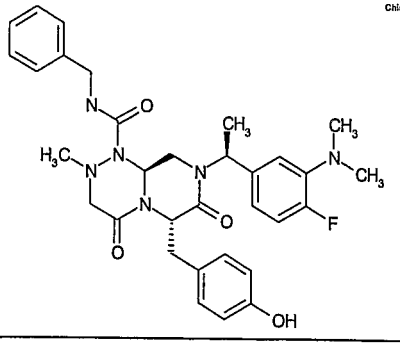
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
30		597.6	7.5
31		613.7	11.9
32		581.6	4.1
33		564.6	13.0
34		565.6	4.4

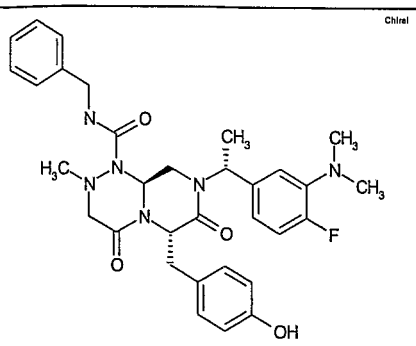
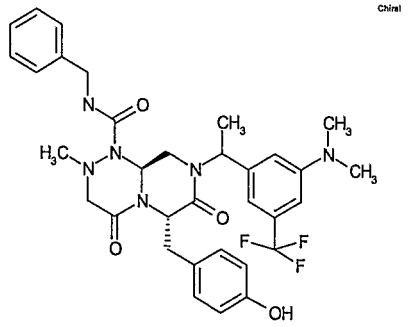
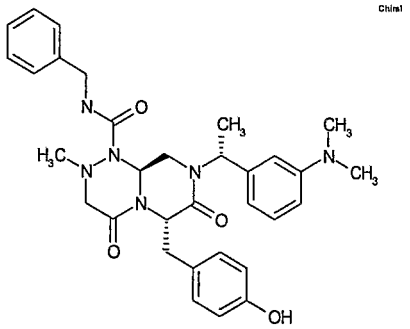
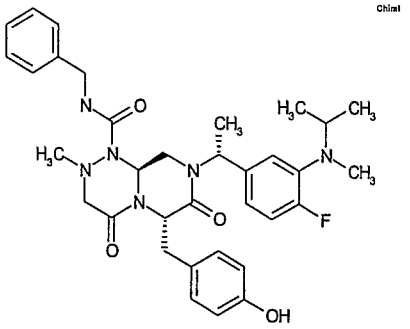
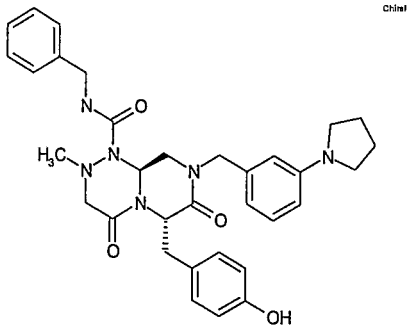
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
35		579.7	11.4
36		549.6	12.5
37		545.6	2.3
38		556.7	7.1
39		564.6	9.7

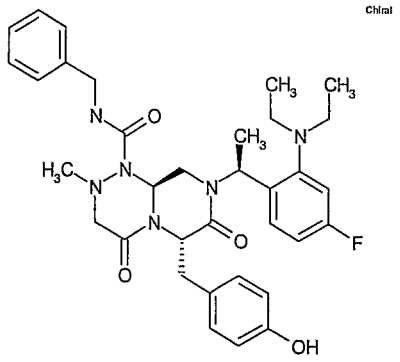
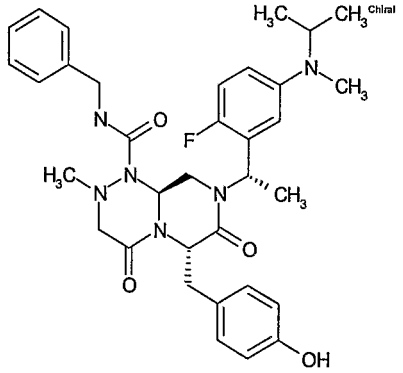
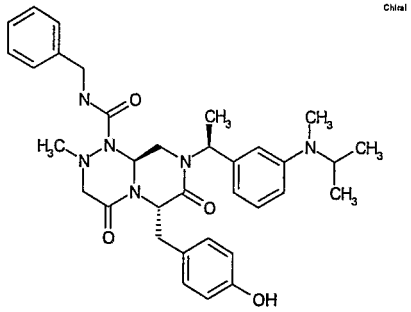
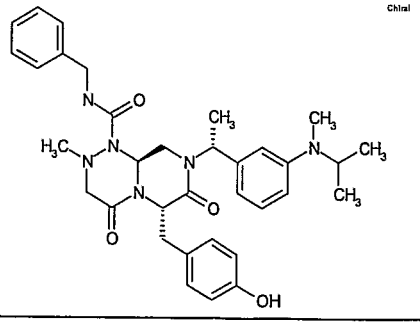
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
40		553.6	7.0
41		541.6	13.6
42		574.7	18.2
43		556.7	5.2
44		599.6	1.3

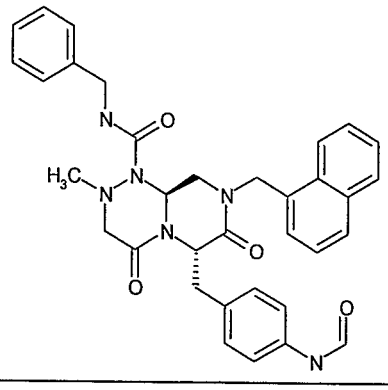
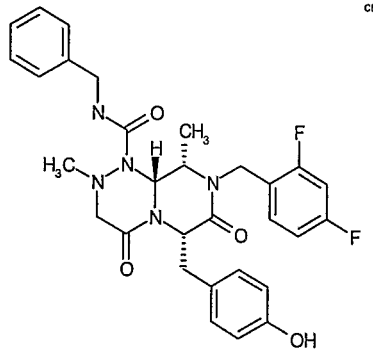
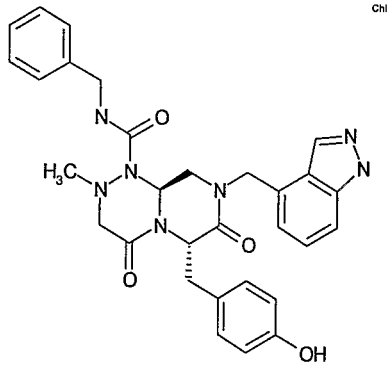
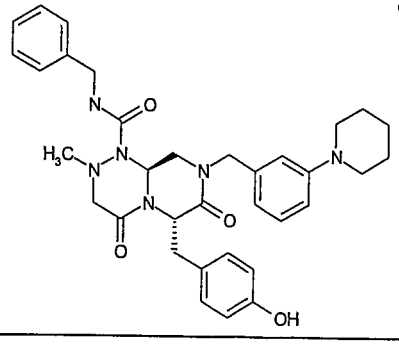
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
45		591.1	2.2
46		570.7	4.4
47		584.7	3.5
48		570.7	10.9
49		592.6	1.4
50		574.6	1.3

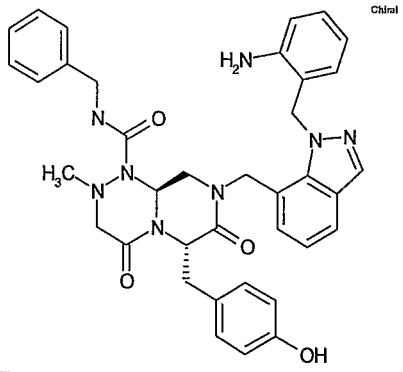
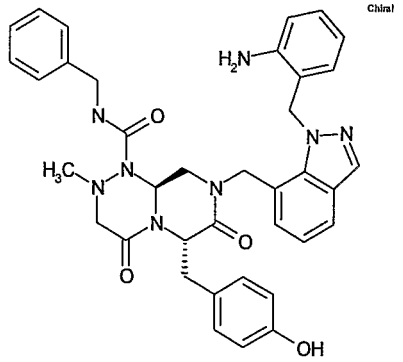
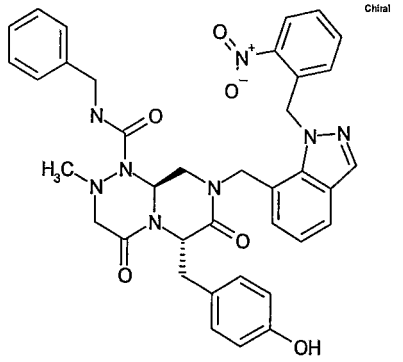
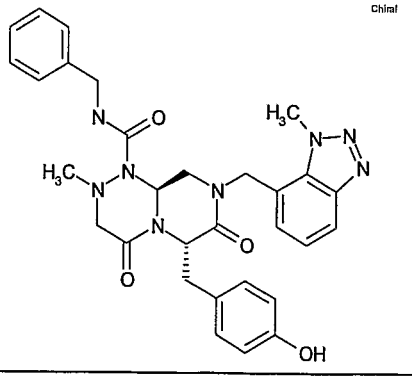
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
51		584.7	4.8
52		621.69	25
53		584.72	9.0 ± 1.5
54		619.16	23.6 ± 5.6

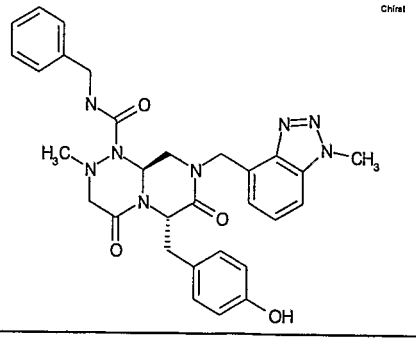
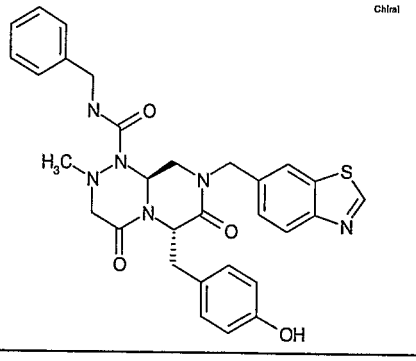
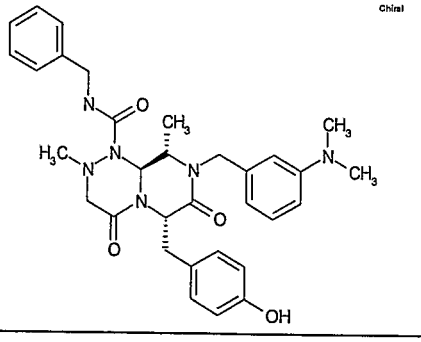
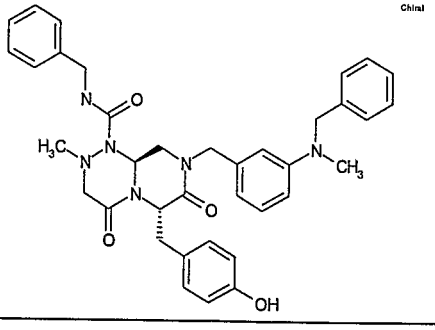
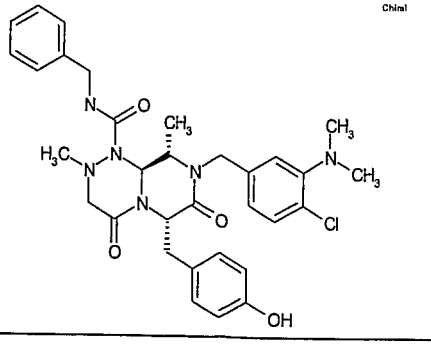
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
55		584.72	7.2 ± 1.4
56		567.65	9.3 ± 1.6
57		582.70	9.4 ± 1.5
58		588.68	49.1 ± 8.1

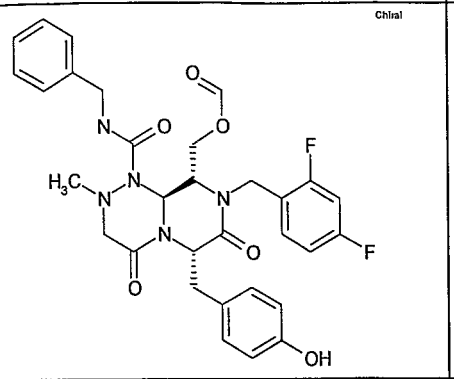
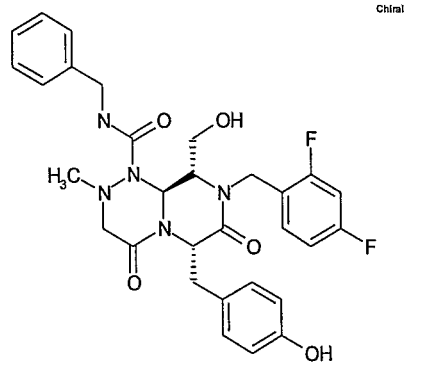
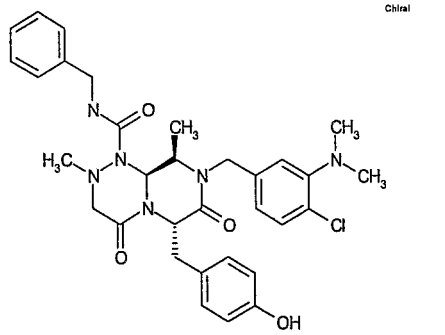
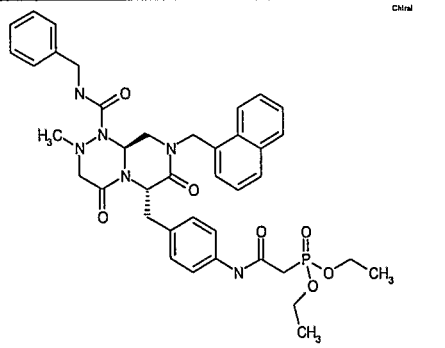
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
59		588.68	5.3 ± 1.3
60		638.69	6.9 ± 1.7
61		570.69	25.8
62		616.73	9.7 ± 1.7
63		582.70	4.1 ± 0.5

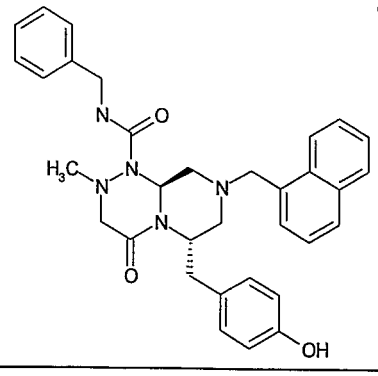
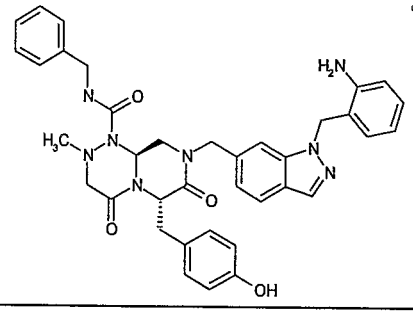
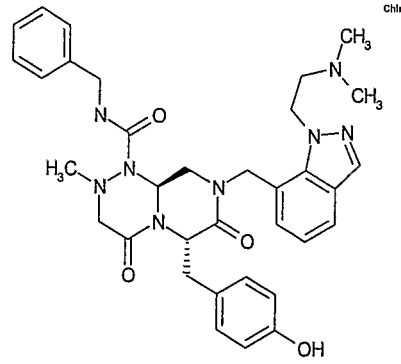
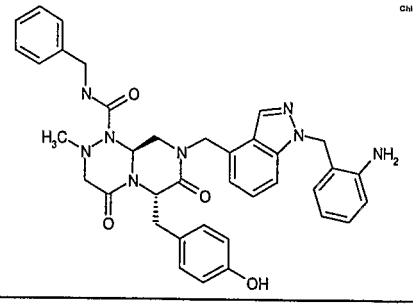
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
64		616.73	25.3 ± 6.6
65		616.73	19 ± 7.1
66		598.74	11.8
67		598.74	6.8

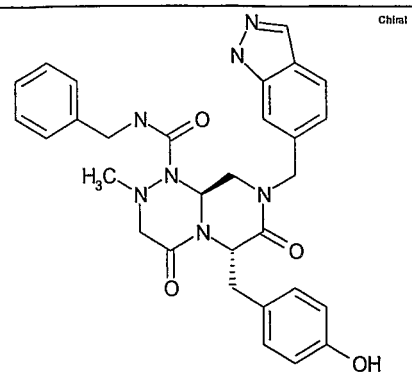
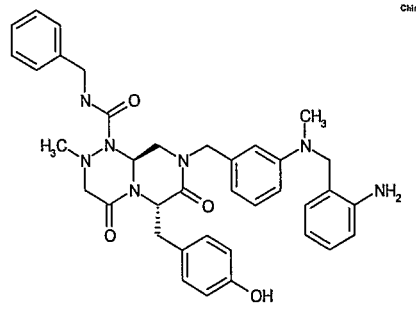
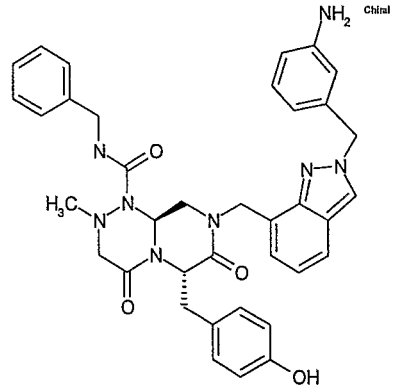
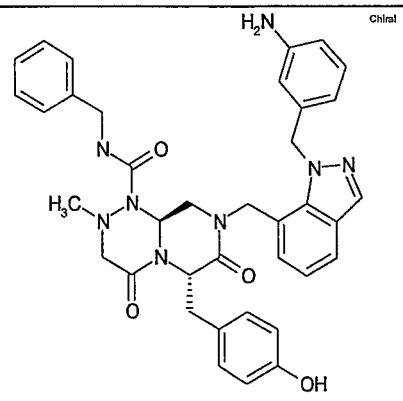
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
68		590.68	4.3 ± 0.8
69		563.60	1.4 ± 0.7
70		553.62	8.8 ± 1.9
71		596.73	6.5 ± 0.7

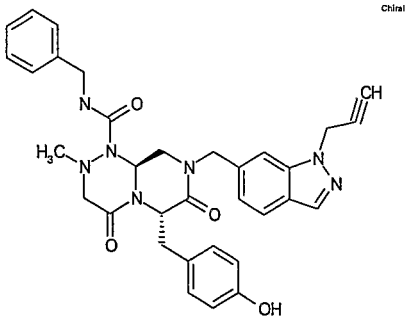
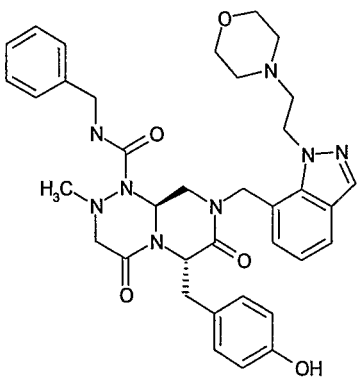
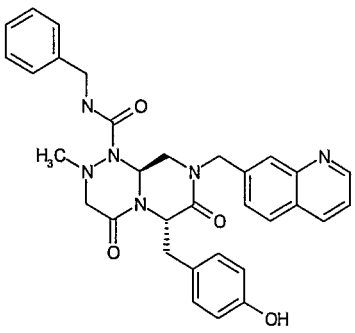
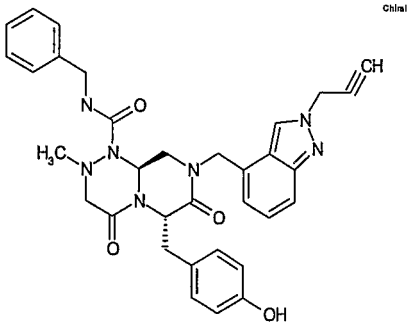
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
72		658.76	1.6 ± 0.1
73		658.76	3.6
74		688.74	2.1 ± 0.2
75		568.64	50.5 ± 18.4

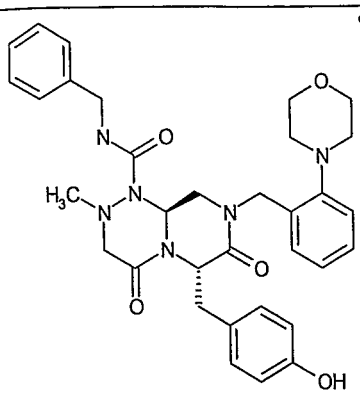
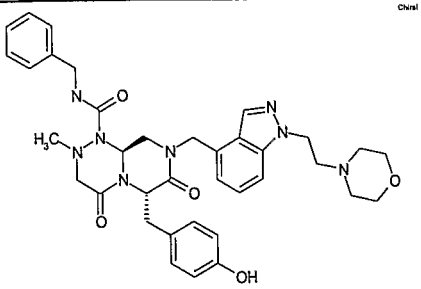
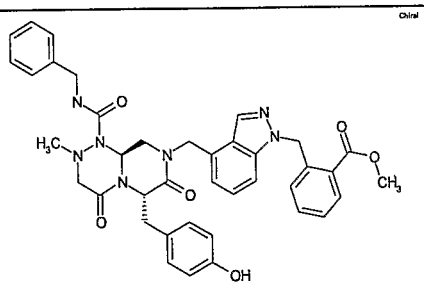
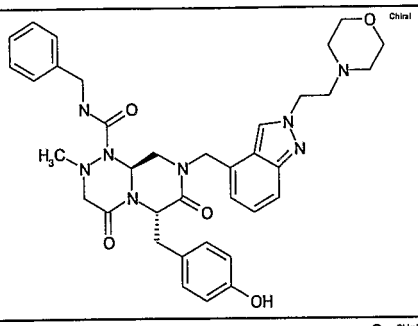
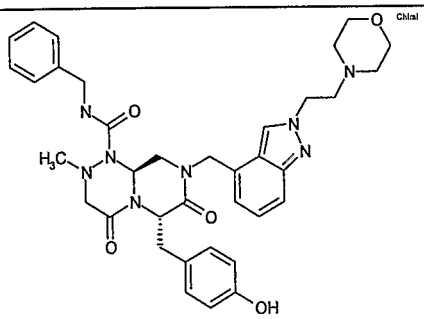
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
76		568.64	10.7 ± 2.5
77		570.67	7.2 ± 2.5
78		570.69	4.3 ± 0.9
79		632.76	16.5 ± 4.8
80		605.14	7.9 ± 2.0

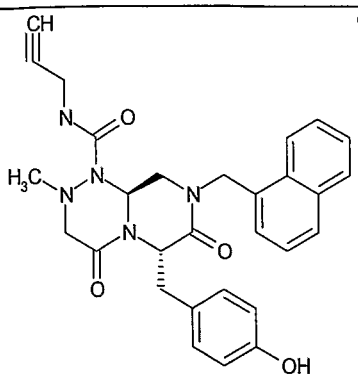
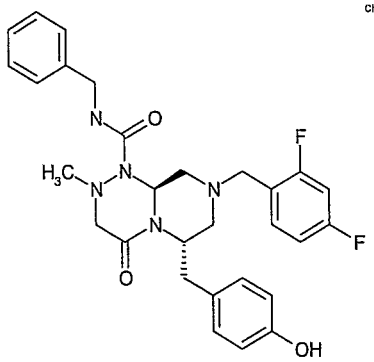
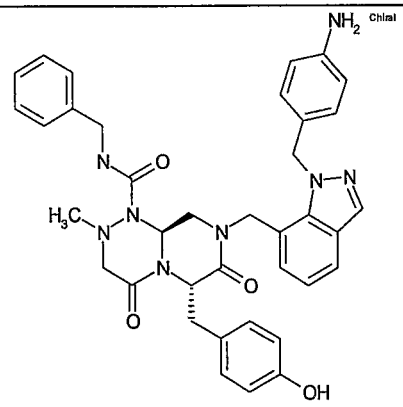
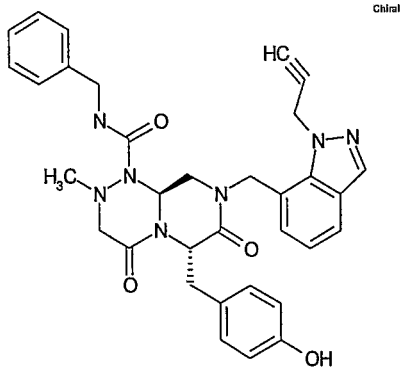
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
81		607.61	66.1 ± 6.8
82		579.60	68.1 ± 8.9
83		605.14	46.4 ± 3.7
84		740.79	46.7 ± 6.7

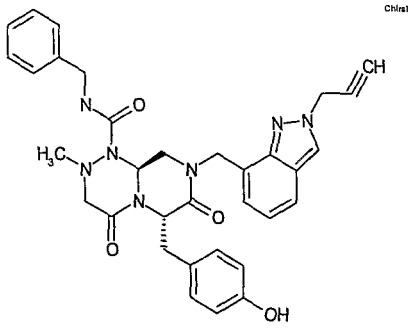
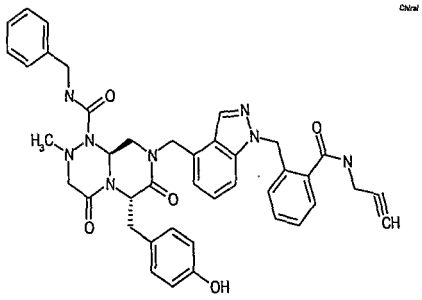
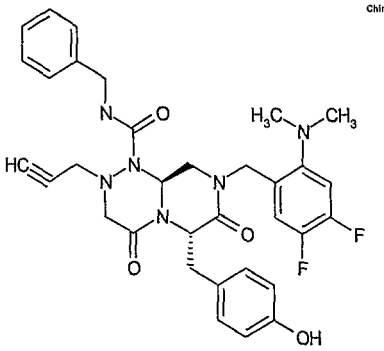
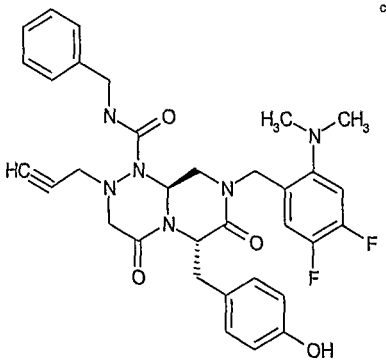
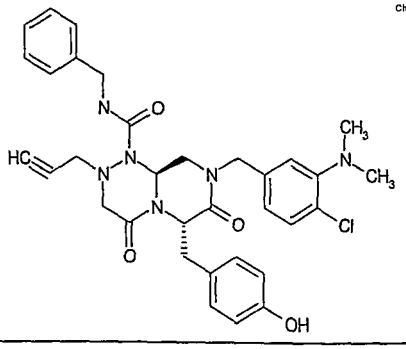
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
85		549.67	15.6 ± 2.2
86		658.76	9.9 ± 2.6
87		624.74	8.1 ± 0.8
88		658.76	2.2 ± 0.2

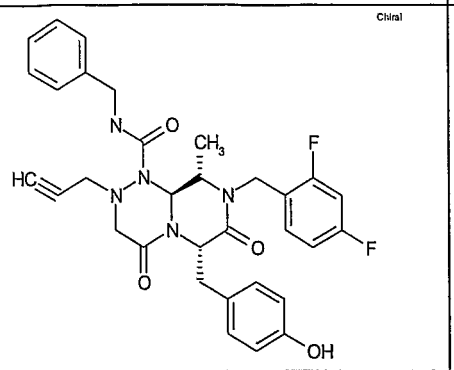
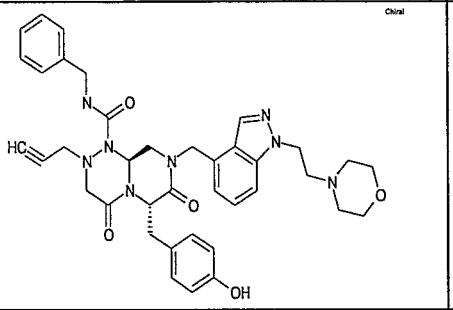
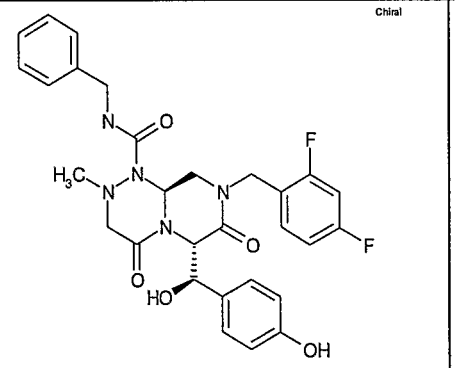
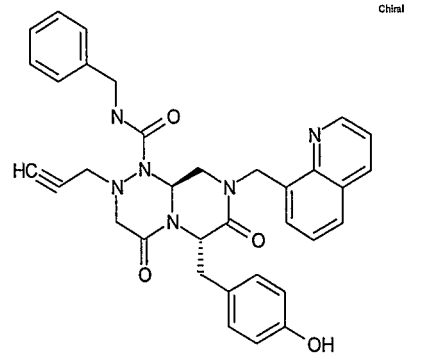
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
89		553.62	13.9 ± 0.9
90		647.78	3.9
91		658.76	2.9 ± 0.2
92		658.76	3.8 ± 1.2

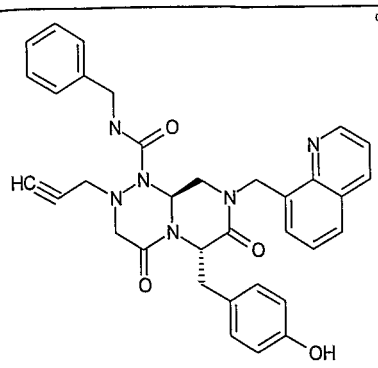
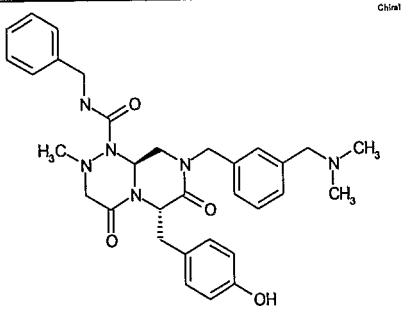
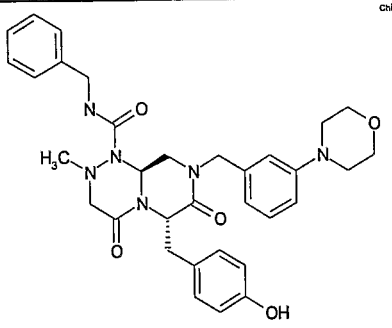
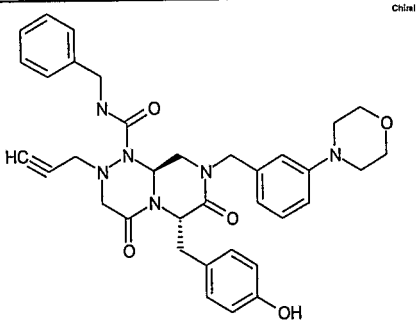
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
93		591.67	6.8 ± 1.3
94		666.78	7.6 ± 0.6
95		564.64	13.3 ± 1.4
96		591.67	8.1 ± 0.9

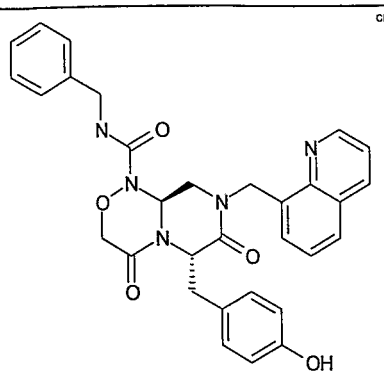
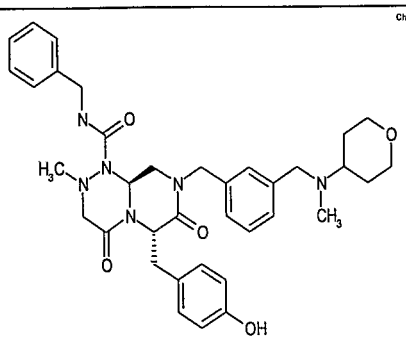
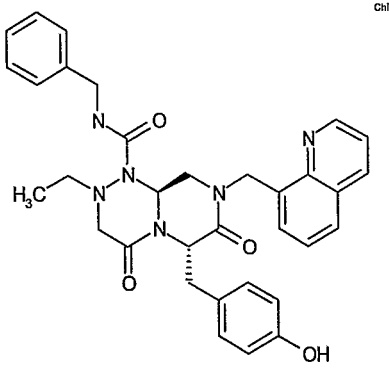
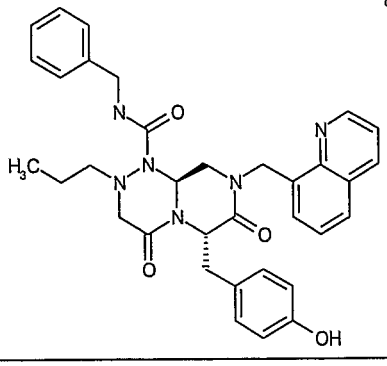
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
97		598.70	12.6 ± 1.2
98		666.78	14.4 ± 2.2
99		701.78	2.4 ± 0.3
100		666.78	2.7 ± 0.3
101		666.78	3.9

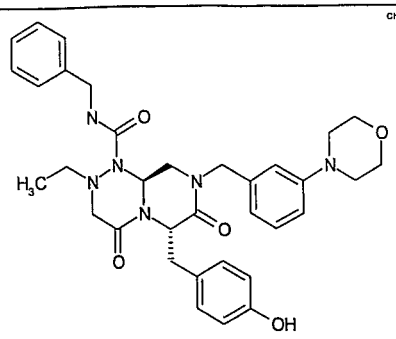
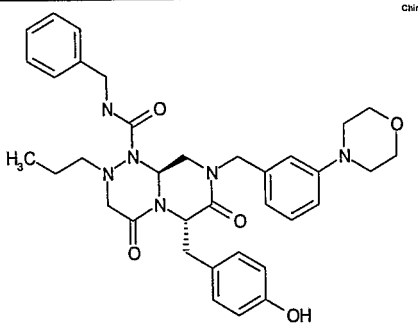
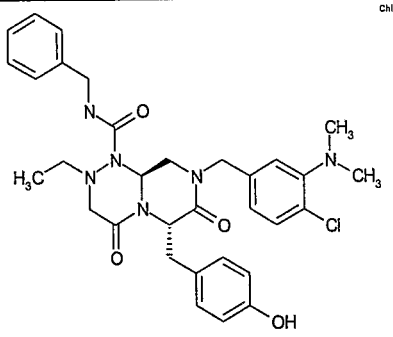
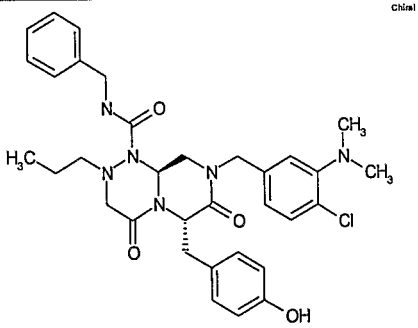
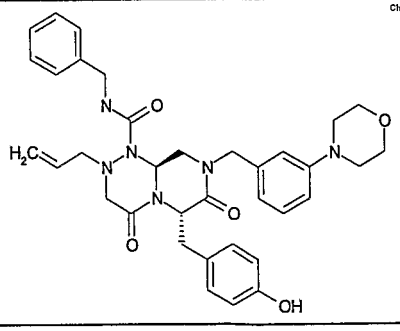
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
102		511.58	62.0 ± 17.0
103		535.59	14.5 ± 1.7
104		658.76	4.6 ± 0.4
105		591.67	16.6 ± 2.7

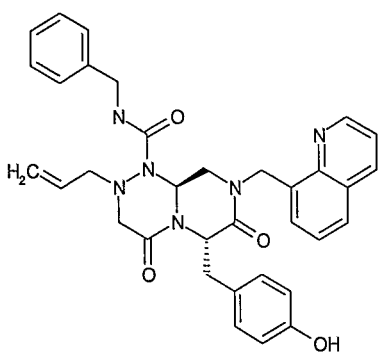
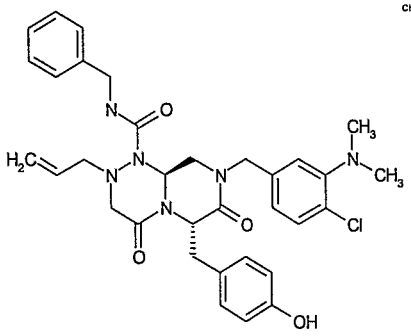
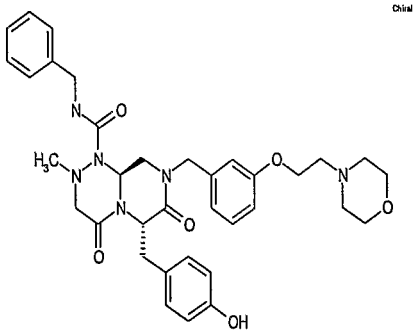
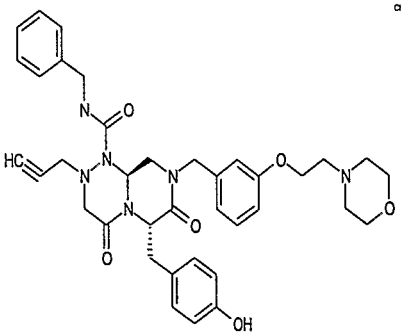
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
106		591.67	2.6 ± 0.2
107		724.82	2.7 ± 0.3
108		616.67	1.6 ± 0.1
109		616.67	2.1
110		615.13	3.8 ± 0.6

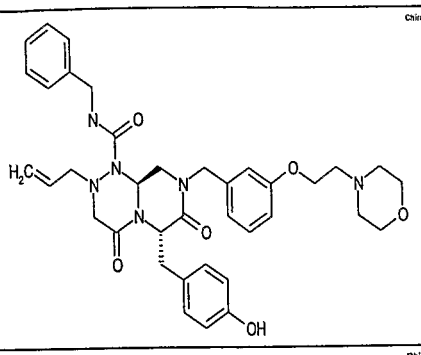
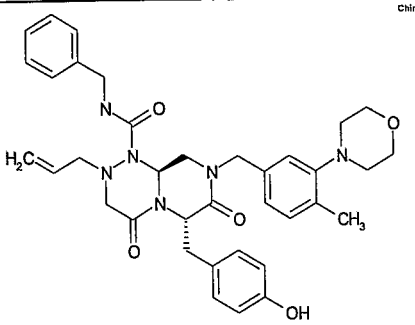
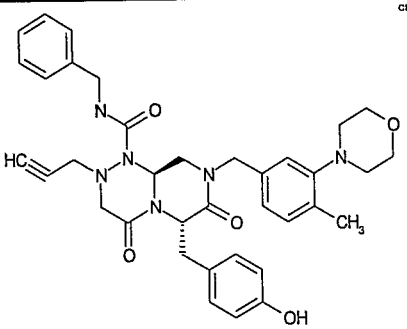
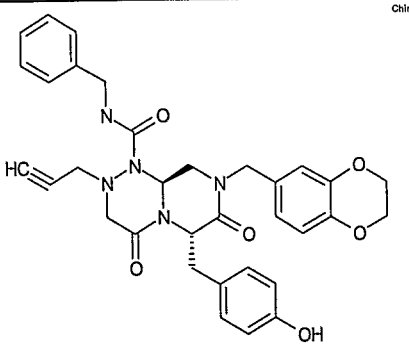
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
111		587.62	7.2 ± 0.8
112		690.80	4.1 ± 0.8
113		565.57	7.3 ± 1.1
114		588.67	0.4 ± 0.04

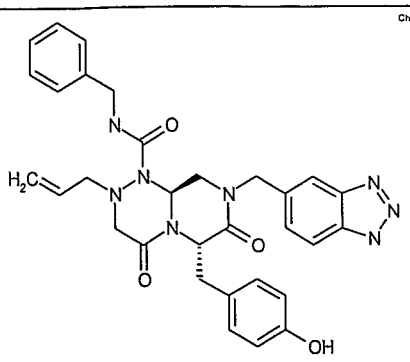
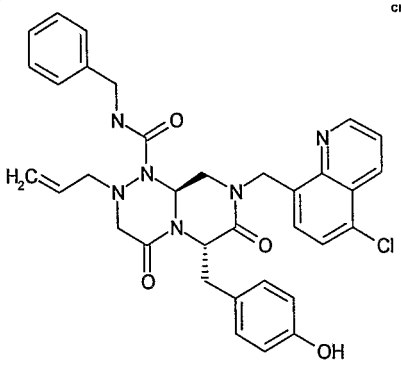
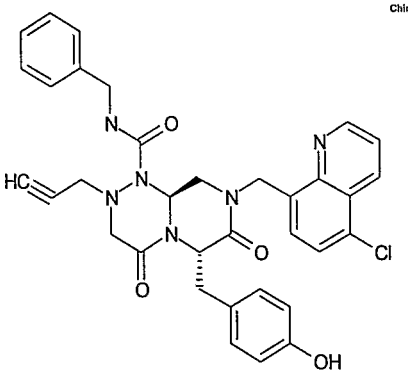
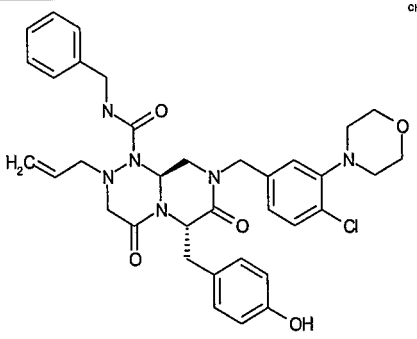
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
115		588.67	0.8
116		570.69	8.0 ± 0.7
117		598.70	6.9 ± 0.6
118		622.72	0.8 ± 0.1

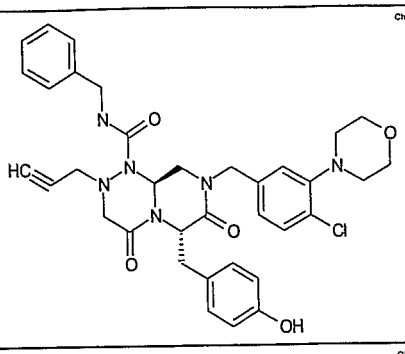
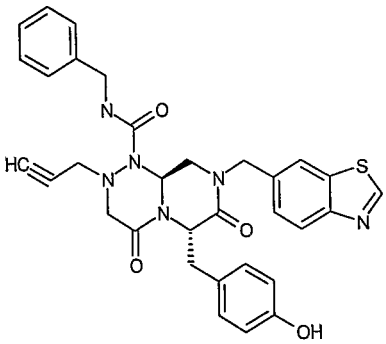
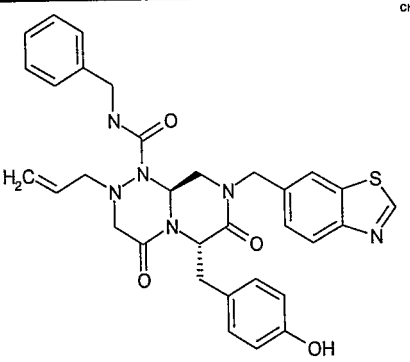
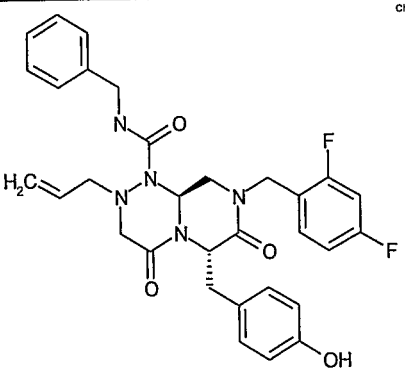
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
119		551.60	8.8 ± 1.3
120		640.78	34.4 ± 4.9
121		578.67	3.0 ± 0.4
122		592.70	2.1 ± 0.4

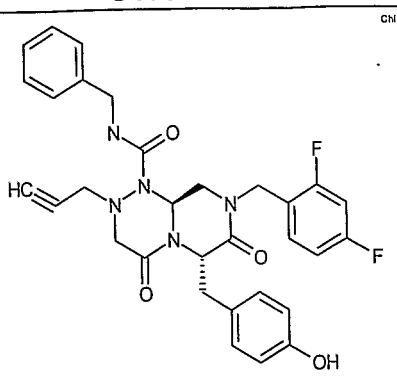
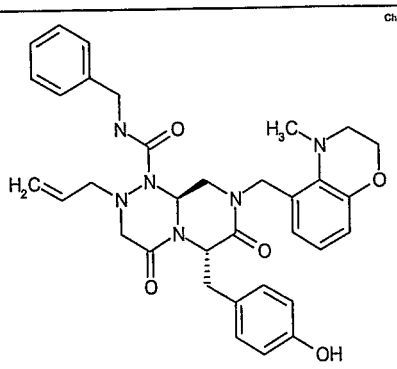
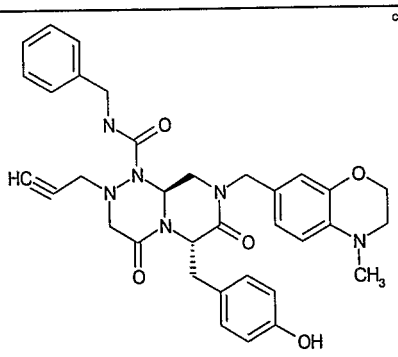
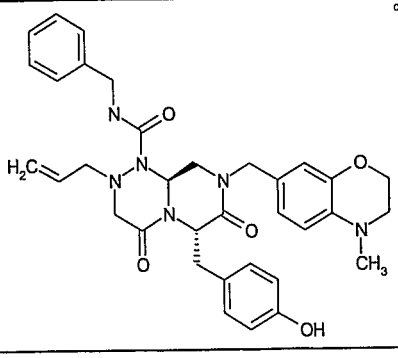
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
123		612.73	11.7 ± 1.0
124		626.75	6.4 ± 0.4
125		605.14	9.8 ± 0.7
126		619.16	10.3 ± 1.5
127		624.74	1.8 ± 0.2

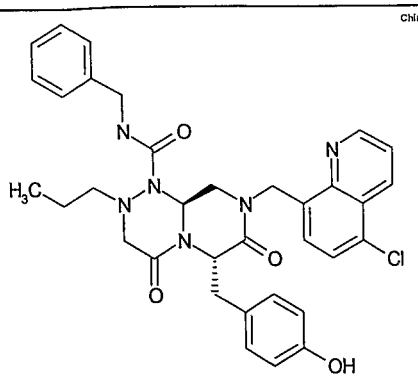
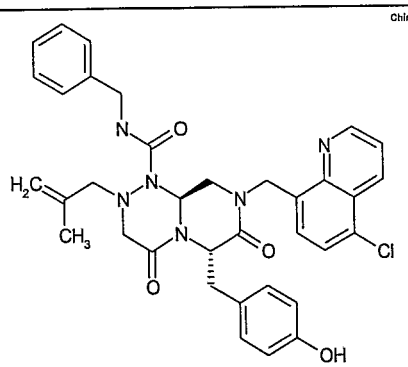
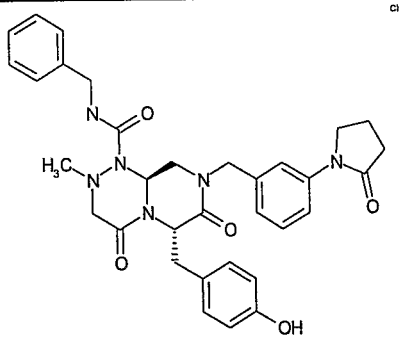
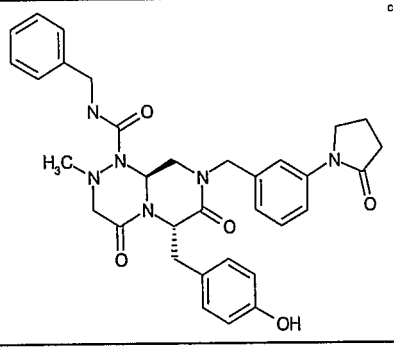
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
128		590.68	0.4 ± 0.1
129		617.15	2.4 ± 0.5
130		642.75	6.1 ± 0.4
131		666.78	2.2 ± 0.3

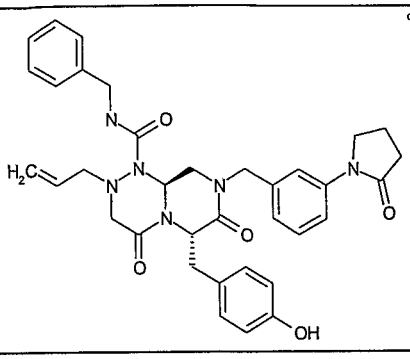
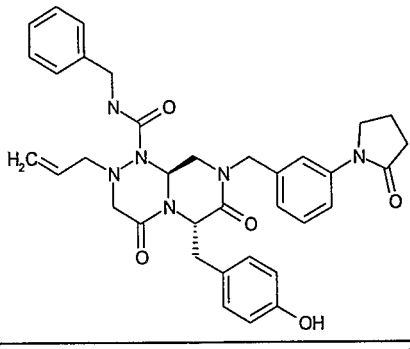
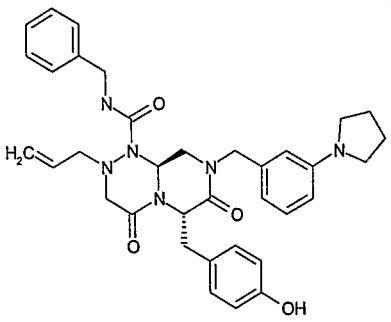
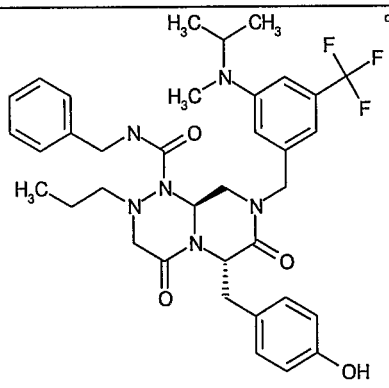
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
132		668.79	2.3 ± 0.5
133		638.77	3.5 ± 0.7
134		636.75	4.5 ± 0.9
135		595.65	2.4 ± 0.7

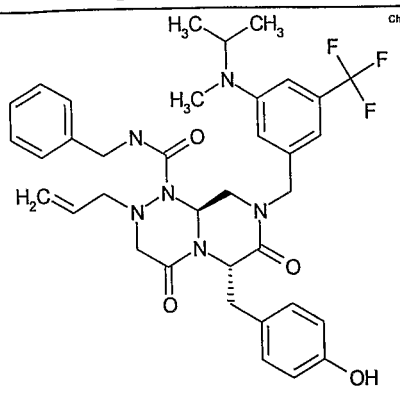
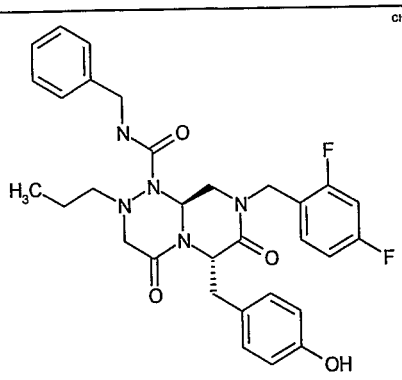
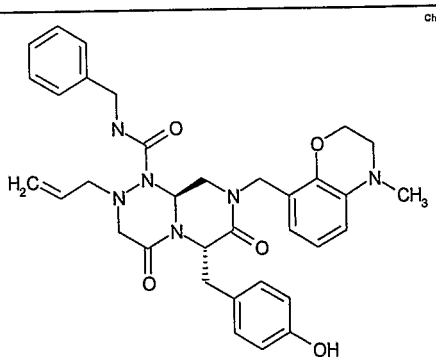
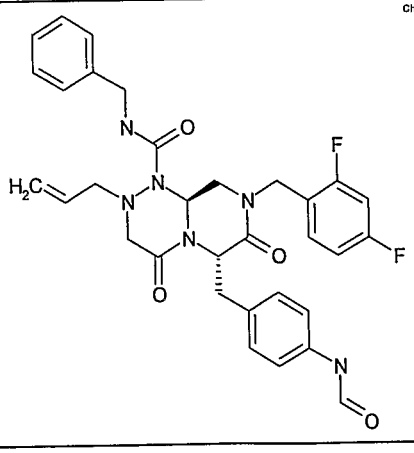
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
136		580.65	28.0 ± 2.9
137		625.13	0.6 ± 0.1
138		623.11	1.0 ± 0.2
139		659.18	1.1 ± 0.1

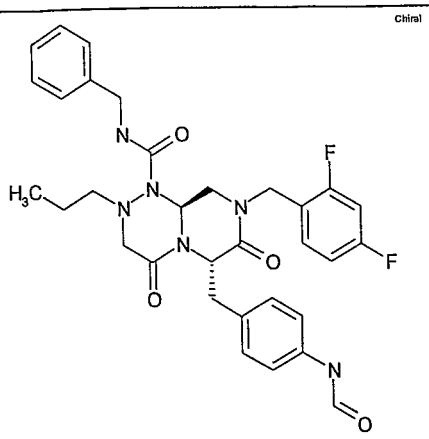
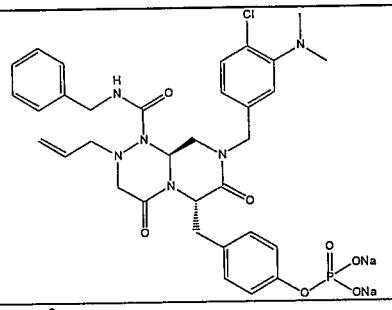
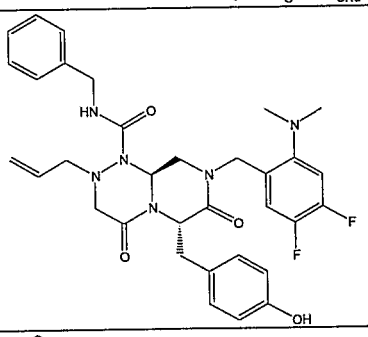
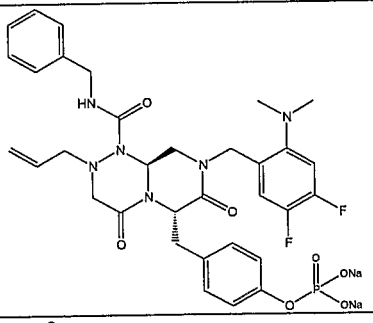
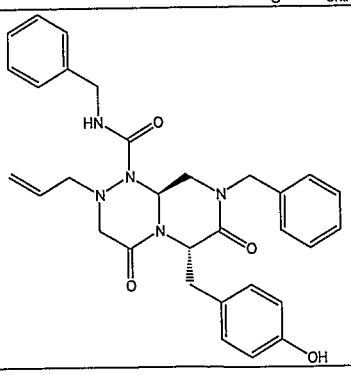
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
140		657.17	2.7 ± 0.3
141		594.69	1.8 ±0.3
142		596.71	1.6 ± 0.4
143		575.61	1.3 ± 0.2

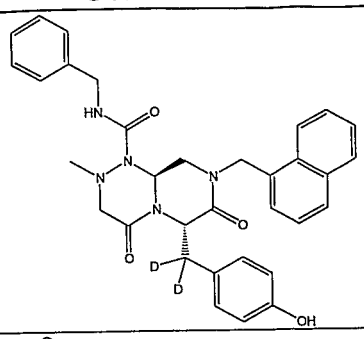
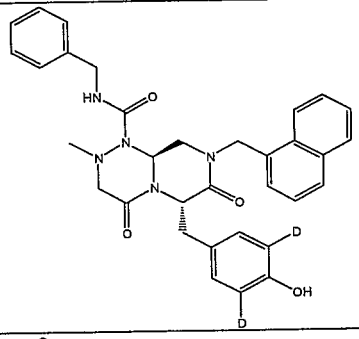
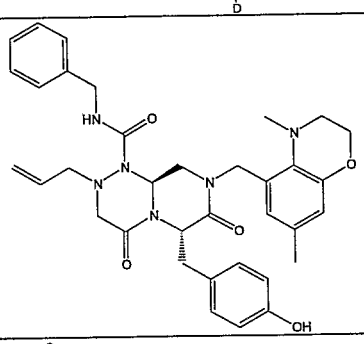
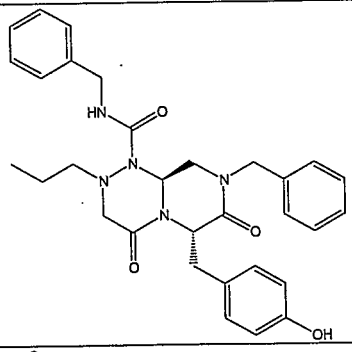
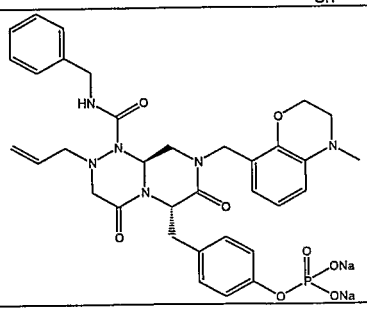
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
144		573.60	2.1 ± 0.2
145		610.71	0.3 ± 0.04
146		608.70	16.7 ± 1.4
147		610.71	9.4 ± 1.0

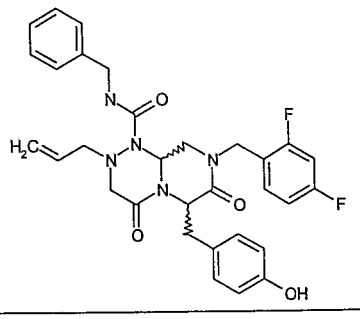
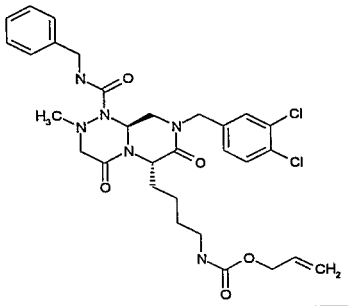
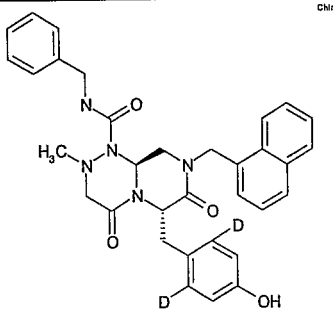
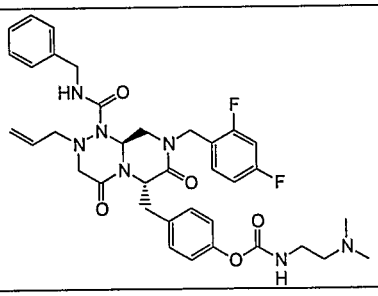
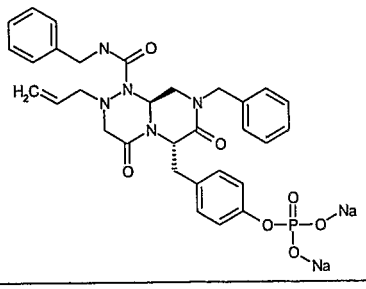
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
148		627.14	2.6 ± 0.3
149		639.15	31.0 ± 6.4
150		596.68	12.7 ± 0.7
151		596.68	9.2 ± 0.1

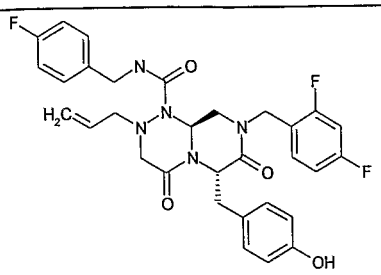
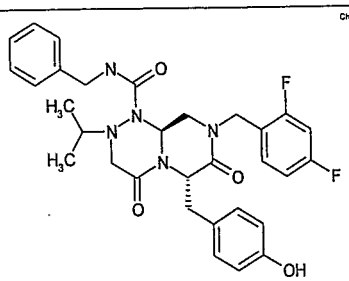
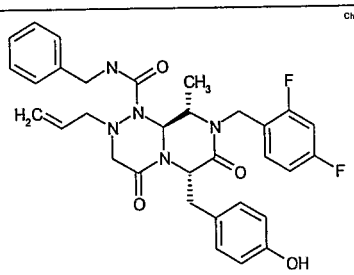
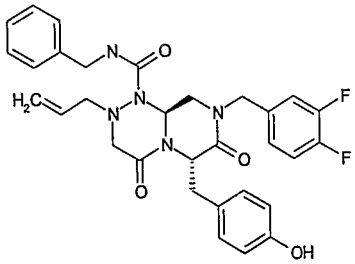
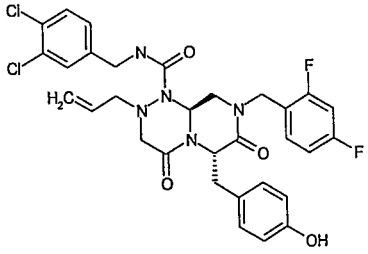
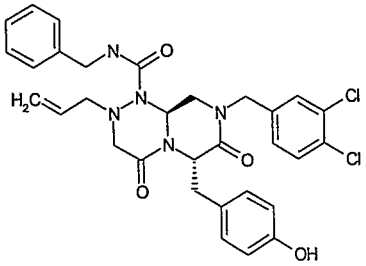
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
152		622.72	1.2 ± 0.3
153		622.72	1.9 ± 0.3
154		608.74	3.2 ± 0.4
155		680.77	30.5 ± 4.1

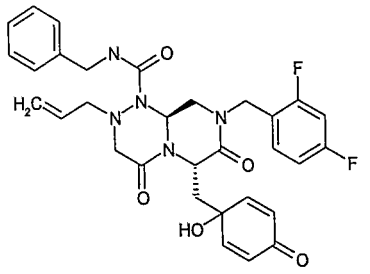
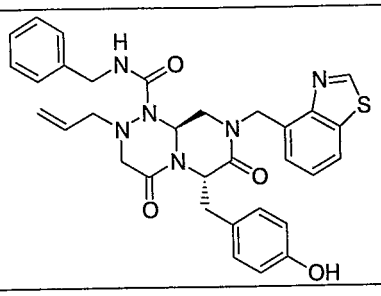
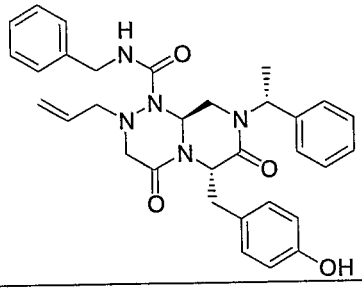
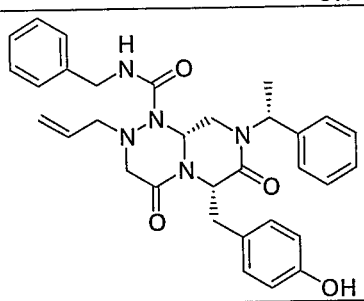
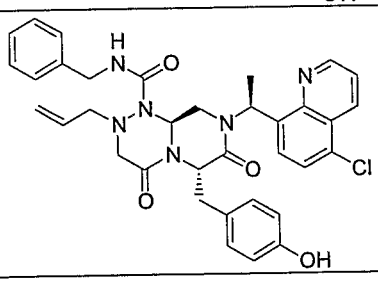
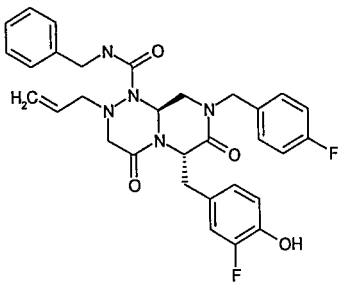
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
156		678.75	13.3 ± 1.6
157		577.63	4.2 ± 0.1
158		610.71	0.9 ± 0.02
159		602.64	2.7 ± 0.2

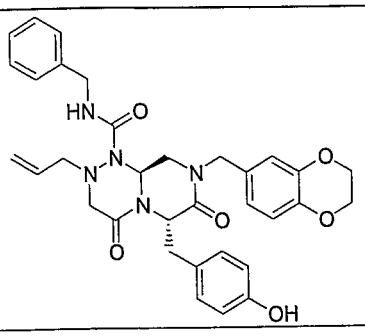
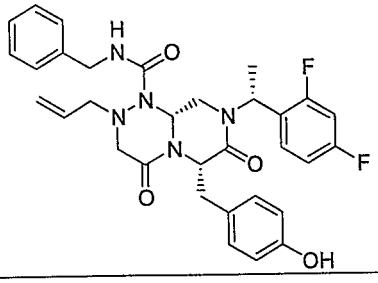
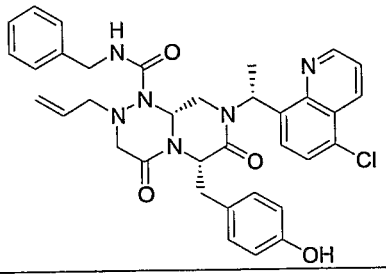
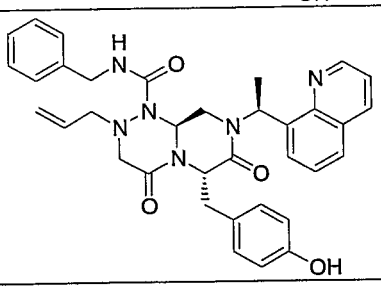
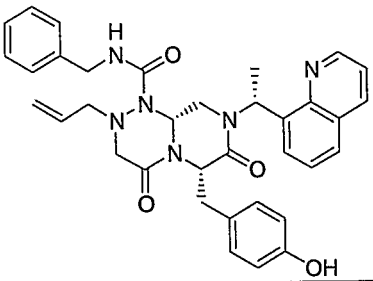
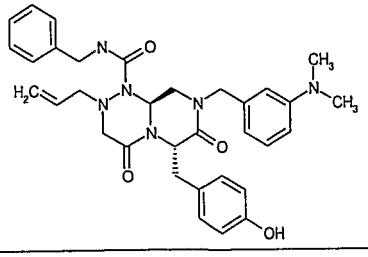
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
160		604.66	10.6 ± 0.5
161		741	1.8 ± 0.2
162		618	1.8 ± 0.6
163		742	1.7 ± 0.5
164		539	1.1 ± 0.2

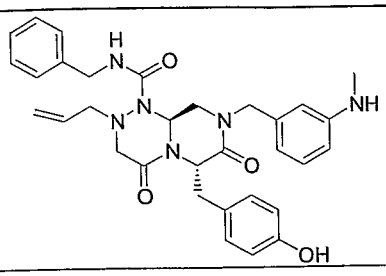
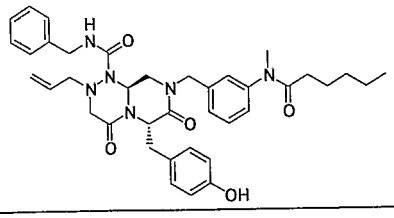
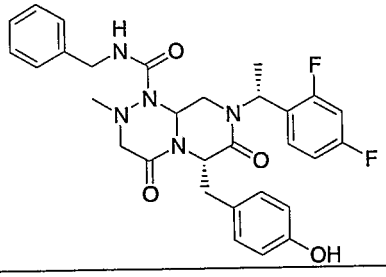
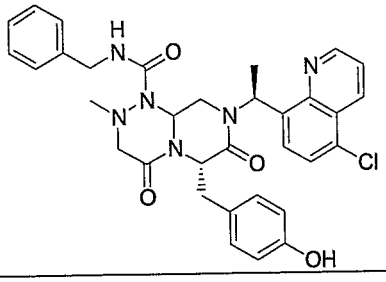
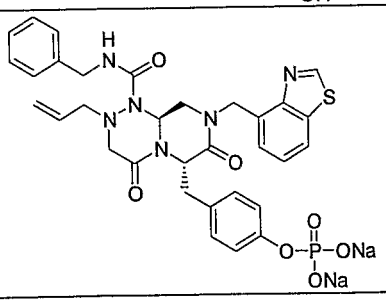
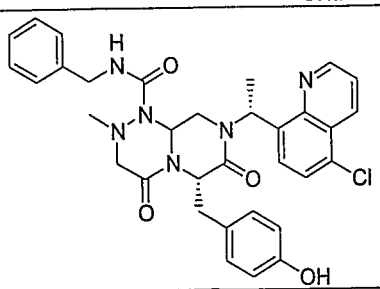
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
165		565	3.9 ± 0.3
166		565	3.3 ± 0.2
167		624	1.3 ± 0.1
168		541	3.5 ± 0.3
169		734	1.0± 0.1

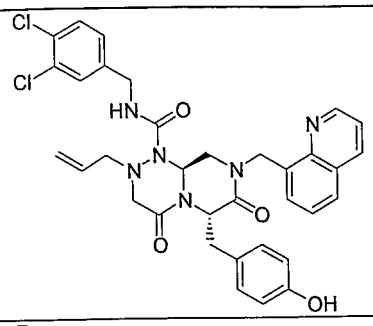
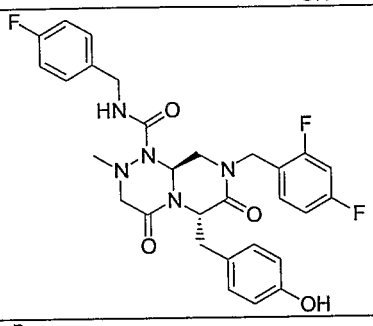
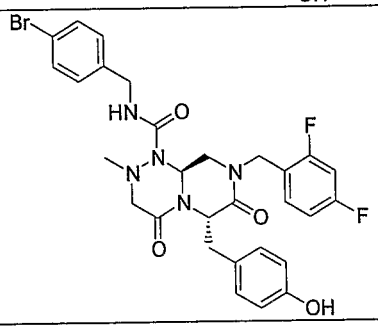
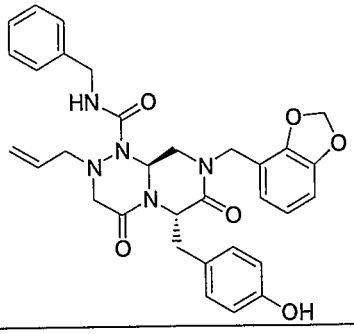
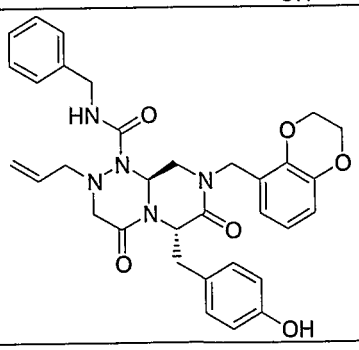
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
170		575	1.5 ± 0.5
171		617	44.7± 6.6
172		566	2.9 ± 0.4
173		690	1.8 ± 0.2
174		664	1.0 ± 0.1

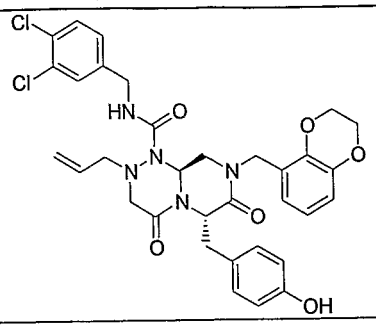
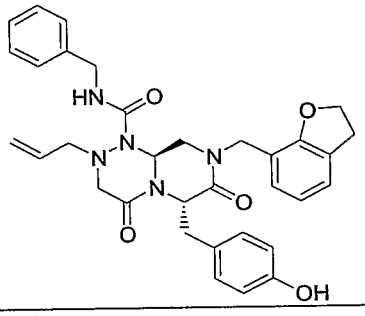
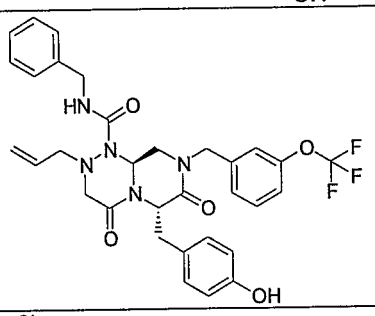
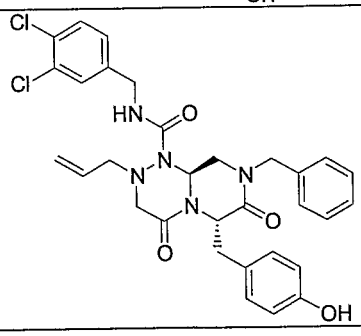
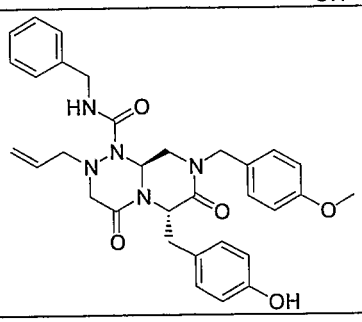
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
175		594	5.4 ± 0.5
176		578	4.0 ± 0.4
177		590	5.3 ± 0.4
178		576	1.2 ± 0.1
179		645	2.3 ± 0.2
180		609	1.3 ± 0.1

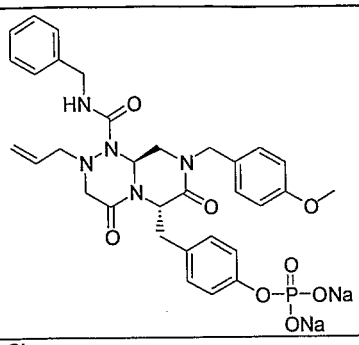
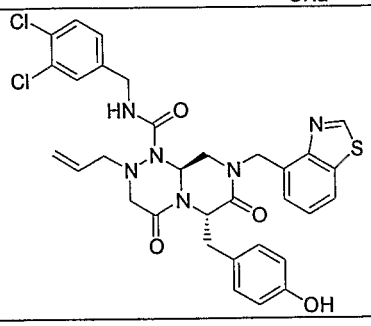
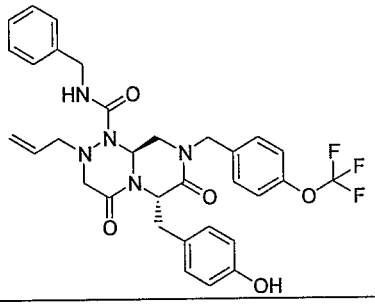
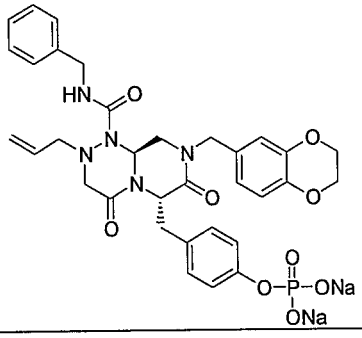
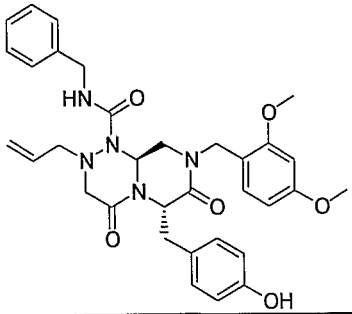
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
181		592	6.7 ± 0.6
182		597	0.6 ± 0.04
183		554	12.8 ± 0.9
184		554	1.2 ± 0.1
185		639	23.4 ± 1.9
186		576	3.6 ± 0.3

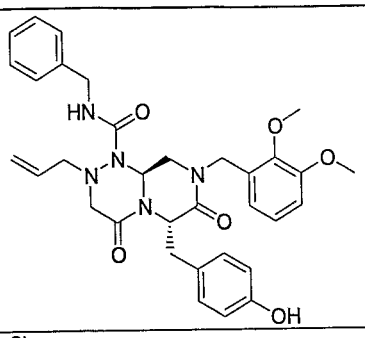
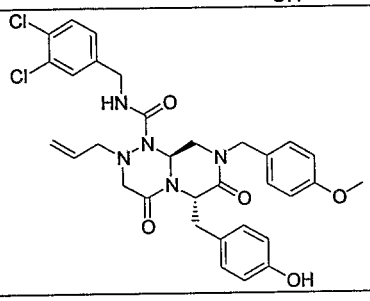
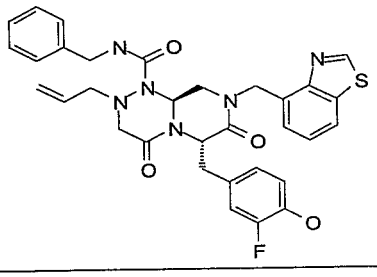
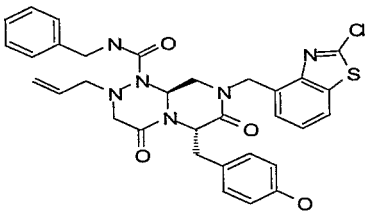
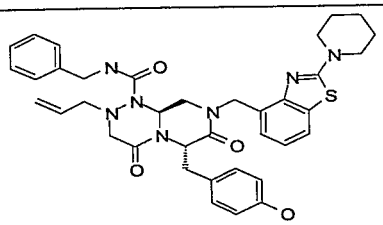
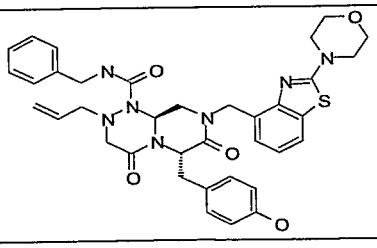
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
187		598	1.1 ± 0.2
188		590	4.4 ± 0.2
189		639	8.7 ± 0.4
190		639	13.9 ± 0.8
191		639	5.2 ± 0.4
192		583	1.3 ± 0.3

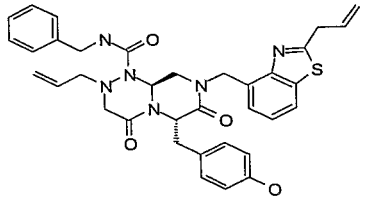
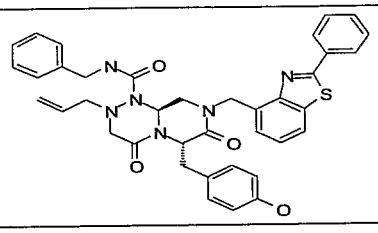
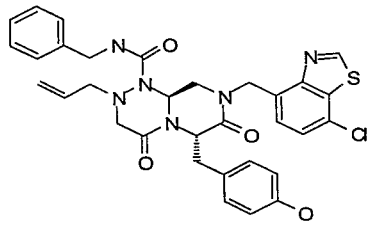
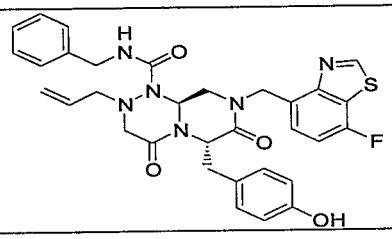
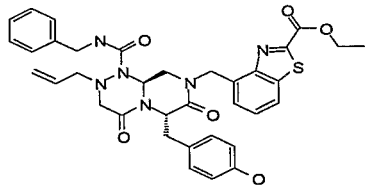
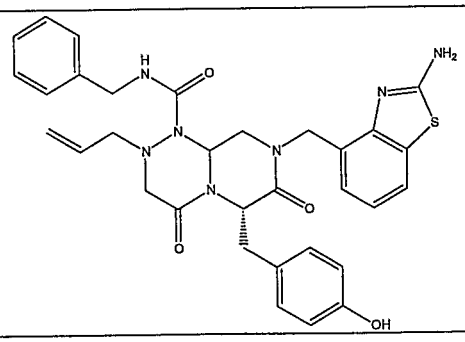
No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
193		569	2.5 ± 0.5
194		667	3.2 ± 0.4
195		564	22.3 ± 2.3
196		613	27.4 ± 2.8
197		721	0.7 ± 0.2
198		613	5.8 ± 0.3

No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
199		660	1.0 ± 0.2
200		568	8.6 ± 0.4
201		628	5.8 ± 0.4
202		584	0.7 ± 0.1
203		598	0.7 ± 0.1

No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
204		667	1.9 ± 0.1
205		582	3.5 ± 0.8
206		624	1.3 ± 0.1
207		609	1.5 ± 0.1
208		570	1.6 ± 0.4

No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
209		694	1.9 ± 0.5
210		694	0.9 ± 0.1
211		694	2.3 ± 0.2
212		694	1.3 ± 0.3
213		694	1.7 ± 0.3

No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
214		694	0.6 ± 0.2
215		639	18 ± 5.1
216		615	1.6 ± 0.2 (1.8 ± 0.3)
217		631	lower than 1.6
218		680	1.6 ± 1.2
219		682	2.2 ± 0.7

No	STRUCTURE	M.W.	$IC_{50}(\mu M)$
220		637	1.1 ± 0.3
221		673	4.7 ± 3.5
222		631	3.8 ± 2.7
223		615	0.6 ± 0.1
224		669	5.4 ± 1.0
225		611	0.1± 0.1

It has been found according to the present invention that compounds of general formula (I), and especially the compounds of general formula (VI), can inhibit CBP-mediated transcriptional activation in cancer cells due to their specific binding to CBP. This conclusion is supported by

immunoprecipitation of CBP of SW480 cells with compounds of the present invention.

The compounds of the present invention can also inhibit the survivin expression in SW480 cells, and therefore, inhibit the oncogenic activity in cancer cells. The compounds of the present invention can be used for inhibiting cancer cells, and thus, would be useful for the regulation of cell growth. Supporting such results, the compounds of the present invention further shows that it can induce the caspase-3 activation in SW480 cells, and therefore, induce the apoptotic activity in cells. The compounds of the present invention can be also advantageously used for inducing apoptosis in cells.

To confirm the oncogenic activity in cancer cell in *in vitro* MTS cytotoxicity assay was tested by following method.

(1) Cytotoxicity test

SW480 or HCT116 cells were placed into 96 well microplate (10^4cells/well) and incubated for 24 hours at 37 °C. The cells were treated with TCF4 compound at various concentrations for 24 hours. 20 μl of MTS solution (Promega) was added into each well and incubated for 2 hours at 37 °C. Cell viability was measured by reading the absorbance at 490nm using microplate reader (Molecular Device) and cytotoxicity of a compound at each concentration was calculated.

(2) Growth Inhibition assay

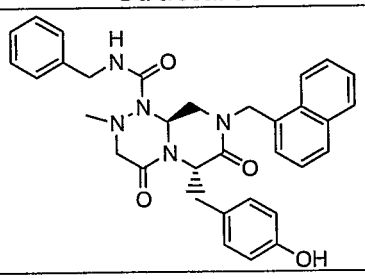
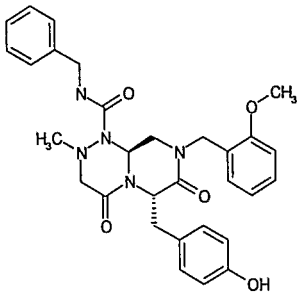
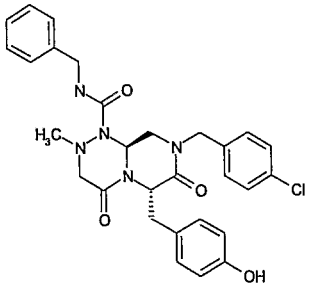
SW480 or HCT116 cells were placed into 96 well microplate (10^4cells/well) and incubated for 24 hours at 37 °C. 20 μl of [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt](MTS) solution (Promega) was added into each well and the absorbance after 2 hour incubation at 37 °C (negative control) was read. And then, the cells were treated with TCF4 compound at various concentrations for 48 hours. 20 μl of MTS solution (Promega) was added into each well and

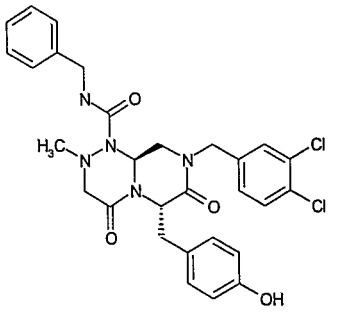
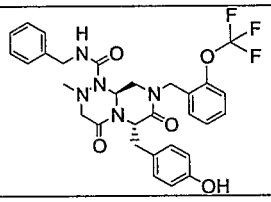
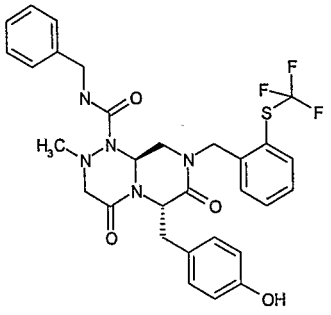
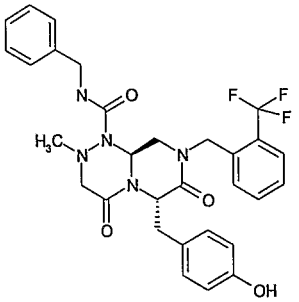
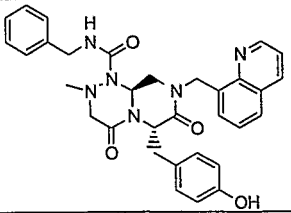
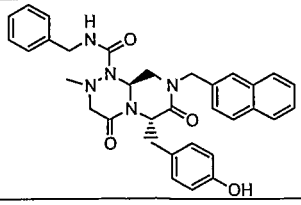
incubated for 2 hour at 37 °C. Cell viability was measured by reading the absorbance at 490nm using a microplate reader (Molecular device) and cytotoxicity of a compound at each concentration was calculated.

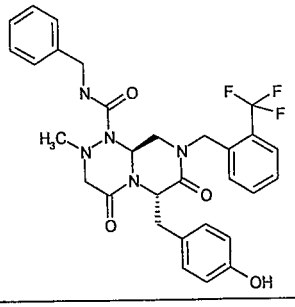
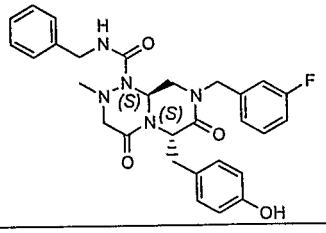
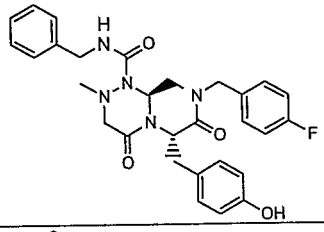
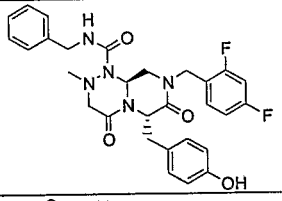
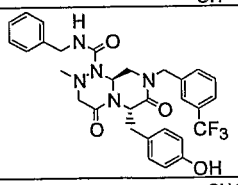
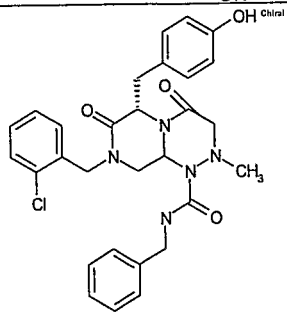
The results of oncogenic activity for selected library compounds were shown in the Table 5. The compound numbers is Table 5 are unrelated to the compound numbers in Table 4.

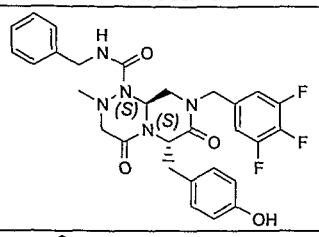
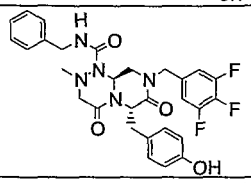
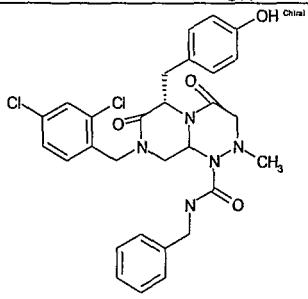
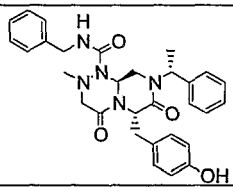
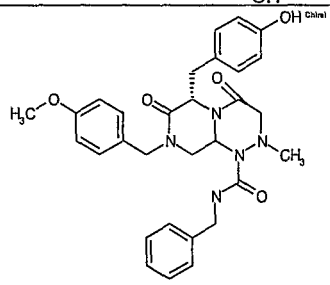
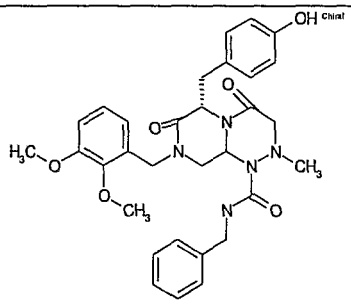
TABLE 5

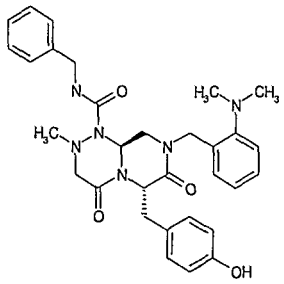
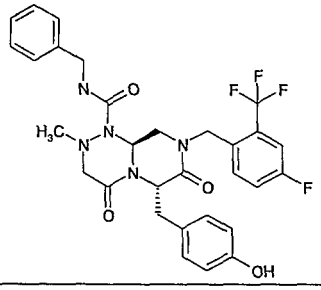
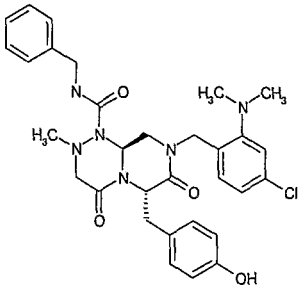
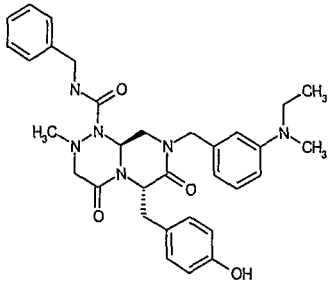
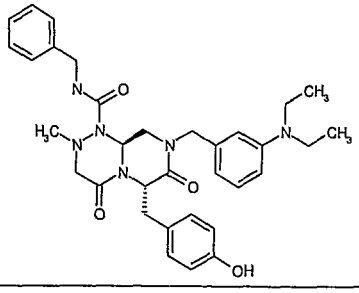
ONCOGENIC ACTIVITY BY MTS OR SULFORHODAMINE B ASSAY FOR SELECTED LIBRARY COMPOUNDS

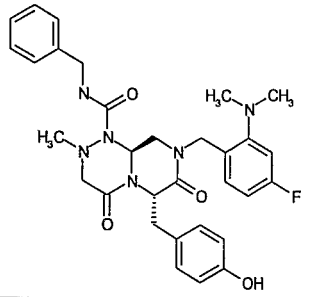
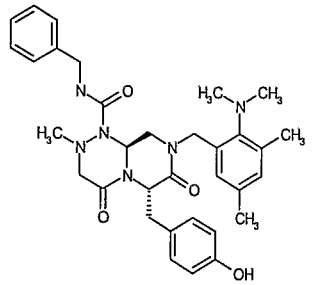
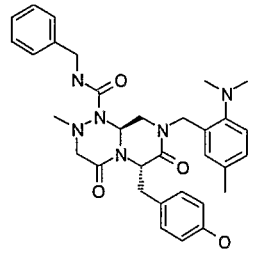
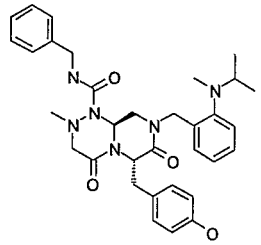
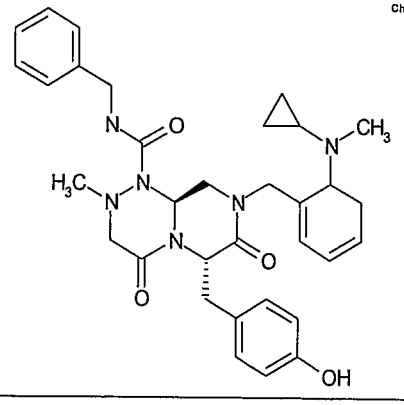
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
1		2.28	1.78
2		2.58	2.23
3		2.73	2.39

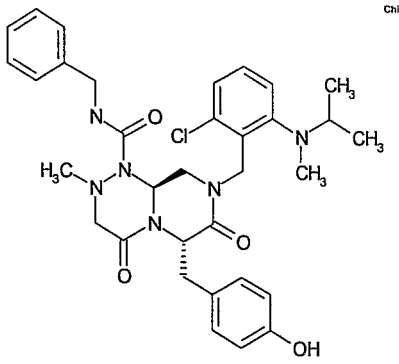
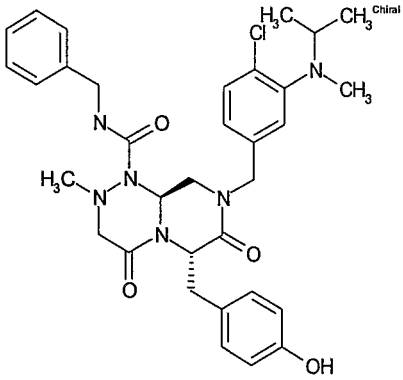
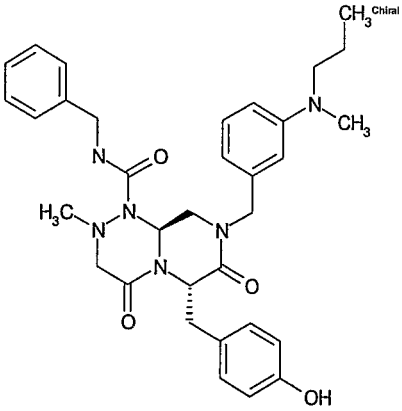
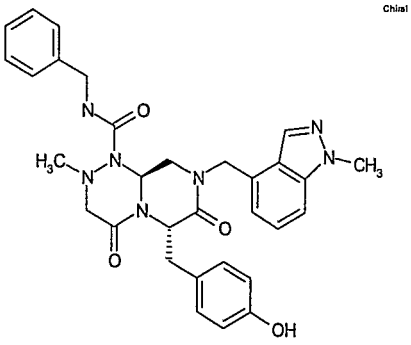
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
4		1.99	1.91
5		2.32	2.06
6		3.96	3.91
7		1.22	0.73
8		<0.3	<0.3
9		2.36	1.92

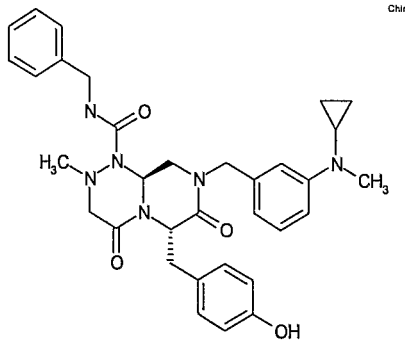
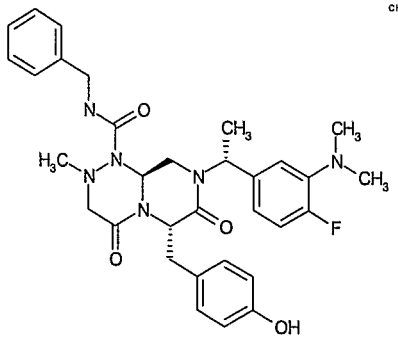
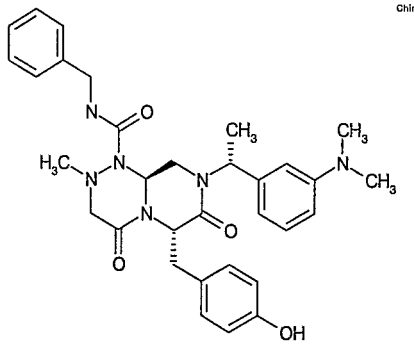
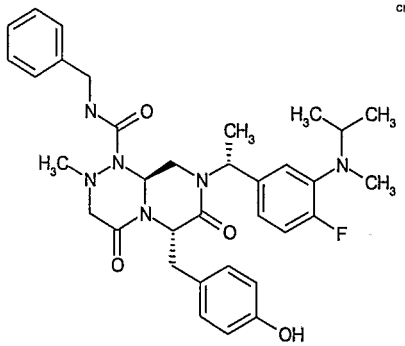
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
10		2.34	1.66
11		1.97	1.30
12		2.54	1.48
13		1.65	1.59
14		2.70	2.10
15		1.68	1.34

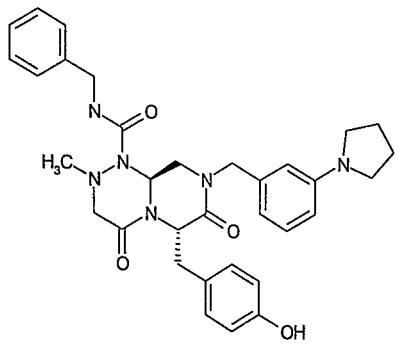
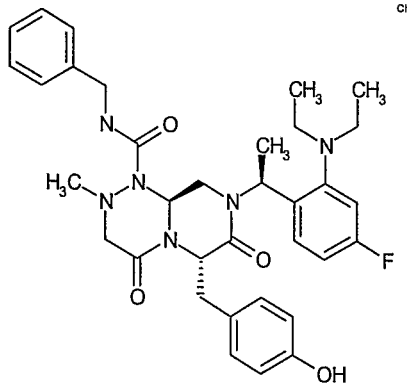
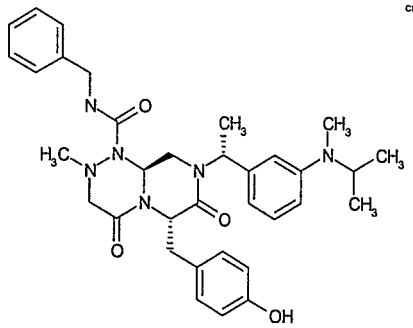
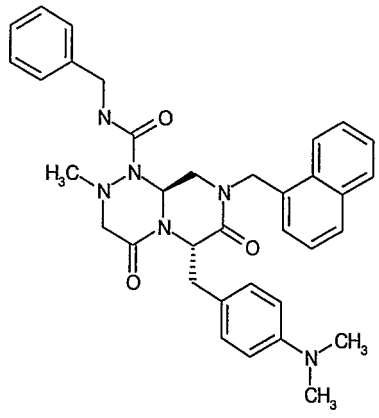
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
16		4.18	2.95
17		1.12	0.74
18		4.63	3.52
19		2.66	1.17
20		5.02	2.75
21		5.25	1.67

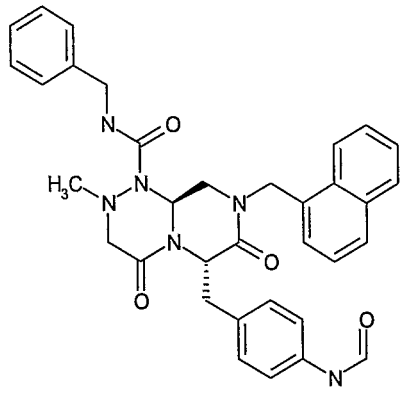
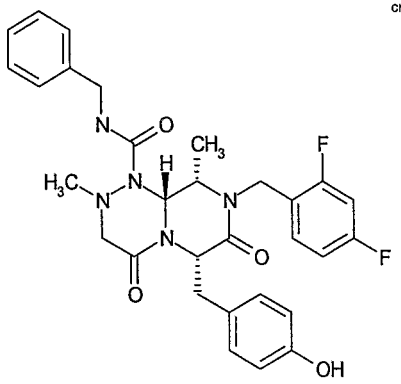
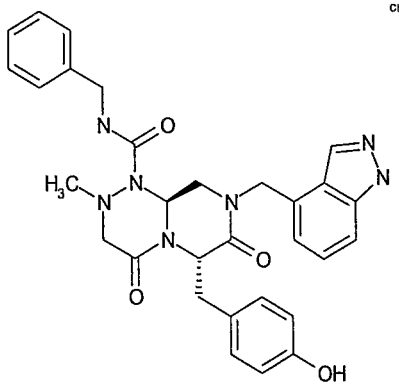
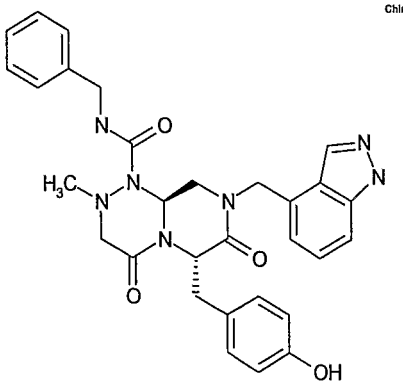
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
22		6.58	3.26
23		3.9	25.41
24		13.79	1.67
25		24.53	1.81
26		23.89	3.06

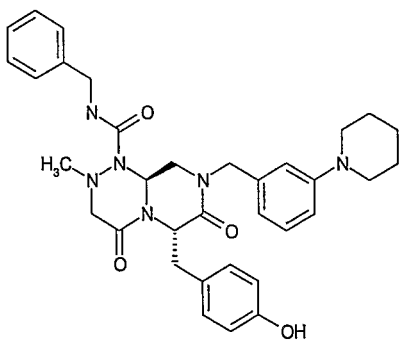
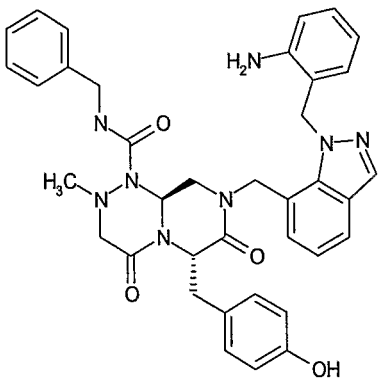
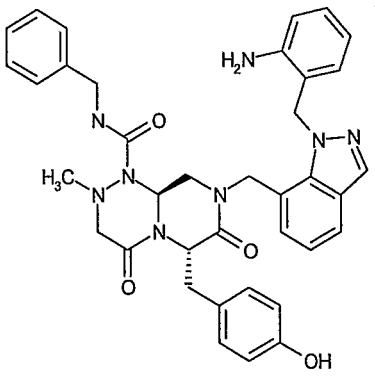
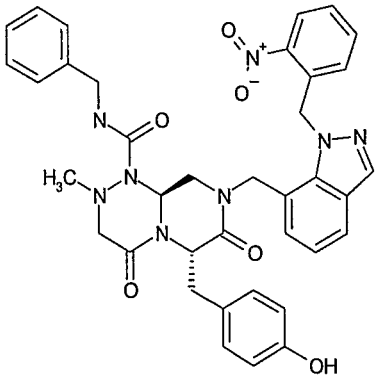
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
27		11.7	1.13
28		3.57	5.47
29		15.98	7.93
30		14.05	5.4
31		8.1 ± 0.7	5.0 ± 1.0

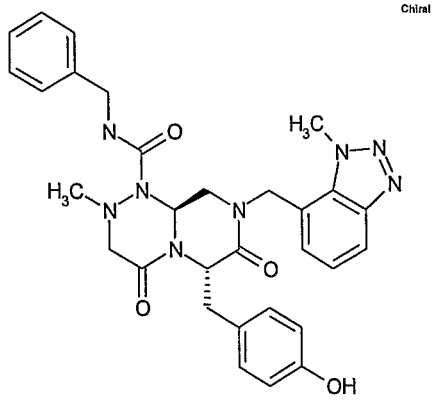
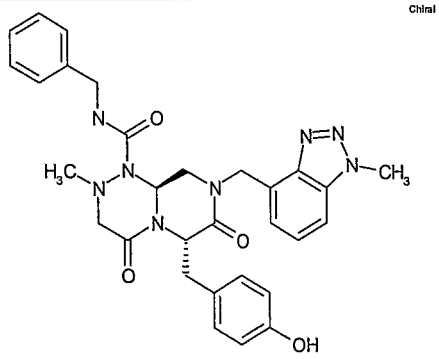
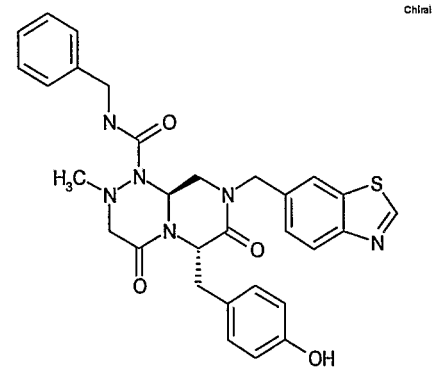
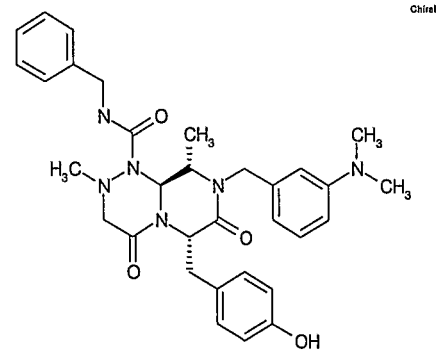
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
32		47.2 ± 12.1	16.9 ± 1.9
33		ND up to 50uM	28.6 ± 2.0
34		13.8 ± 2.4	6.4 ± 1.3
35		4.7 ± 0.5	5.0 ± 0.7

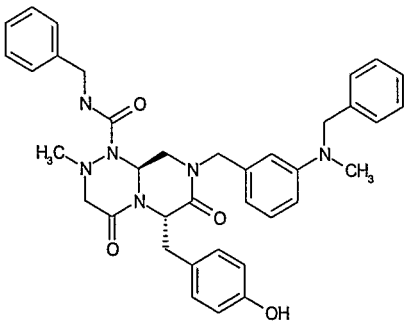
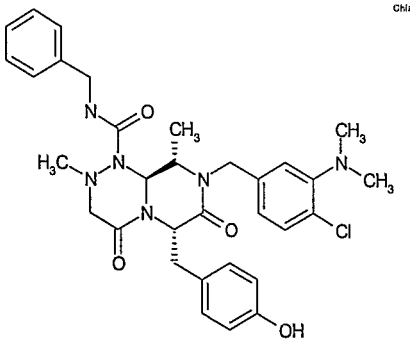
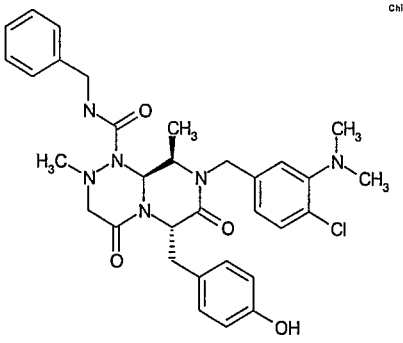
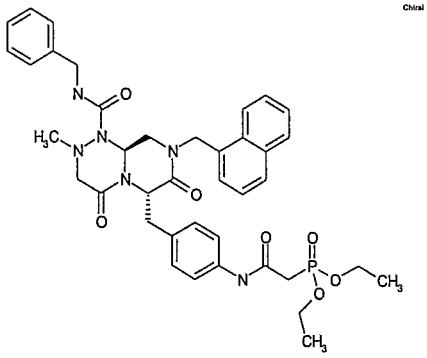
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
36		21.9 ± 2.3	12.7 ± 1.3
37		10.4 ± 0.8	9.2 ± 0.9
38		8.5	6.9
39		22.8 ± 6.5	19.7 ± 3.3

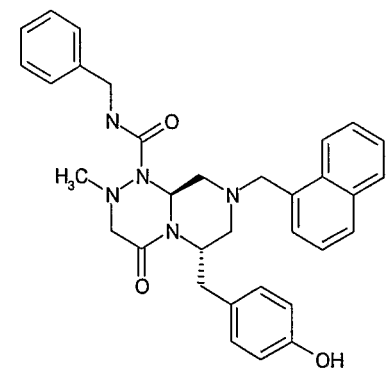
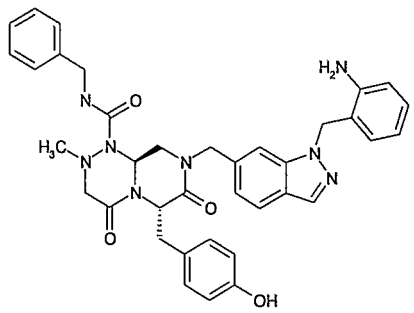
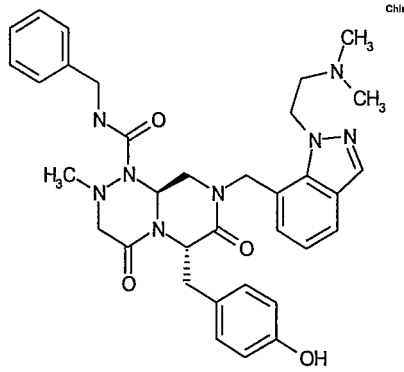
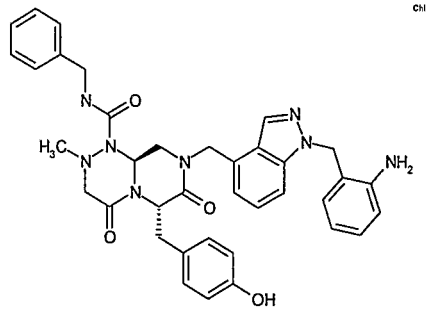
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
40		6.4 ± 0.5	5.8 ± 0.4
41		34.4 ± 9.6	14.7 ± 2.6
42		24.7	10.8
43		ND up to 50uM	39.1

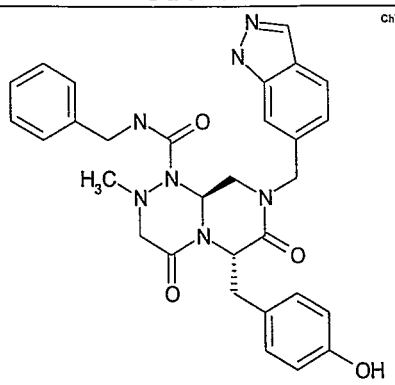
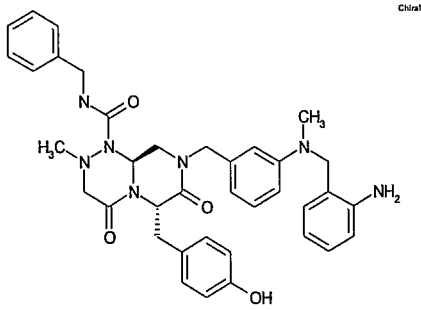
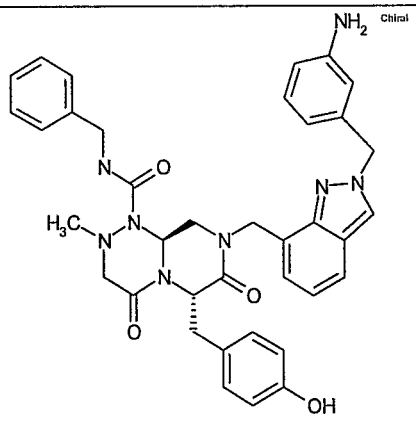
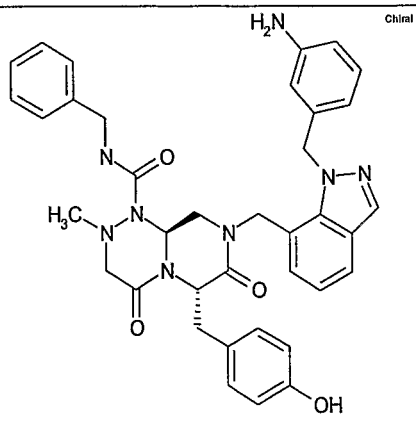
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
44		3.8 ± 0.4	4.2 ± 0.5
45		2.5 ± 0.2	2.9 ± 0.4
46		5.5 ± 0.5	9.2 ± 0.9
47		6.2	12.2

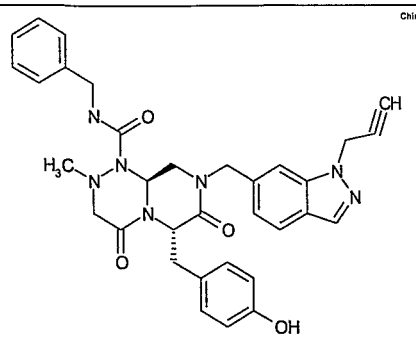
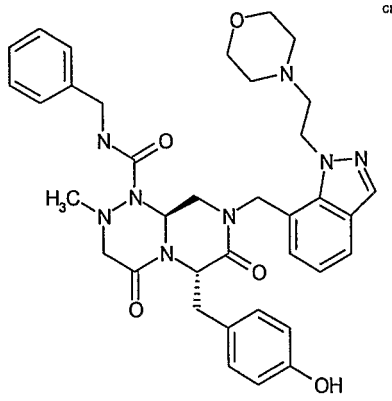
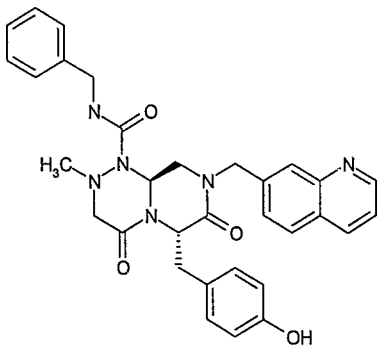
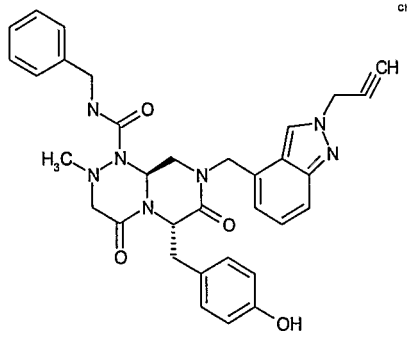
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
48		20.7 ± 2.8	15.5 ± 2.3
49		1.4 ± 0.1	1.0 ± 0.2
50		4.6	2.6
51		3.0 ± 0.1	2.8

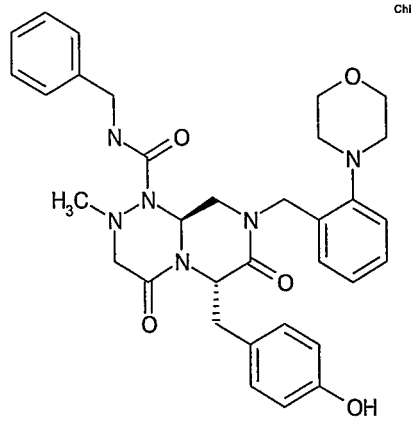
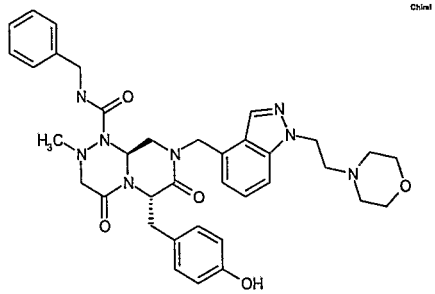
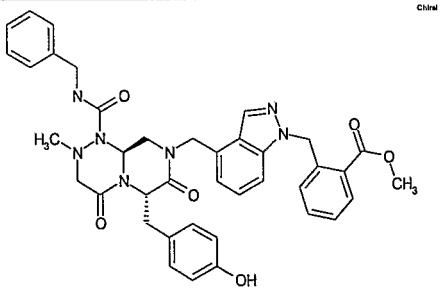
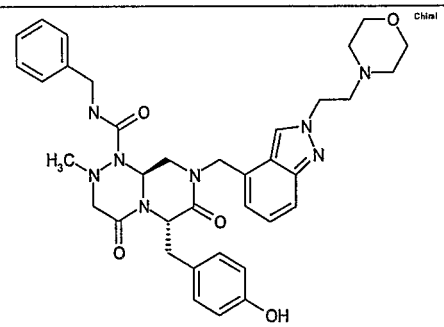
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
52		19.3 ± 2.1	9.7 ± 0.9
53		11.4 ± 0.9	4.7 ± 0.4
54		7.1 ± 0.5	4.9 ± 0.7
55		4.6 ± 0.5	4.1 ± 0.7

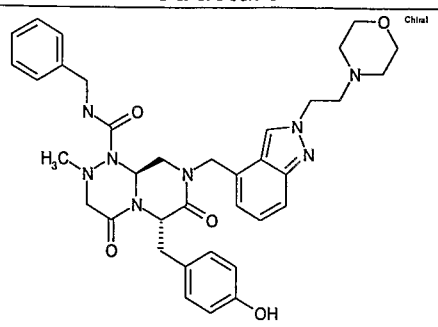
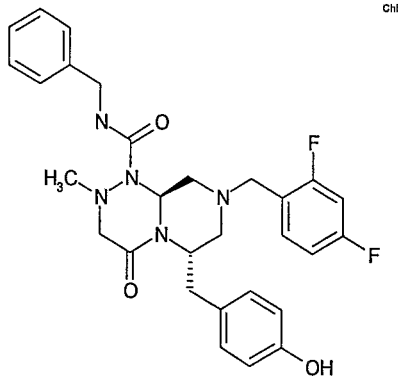
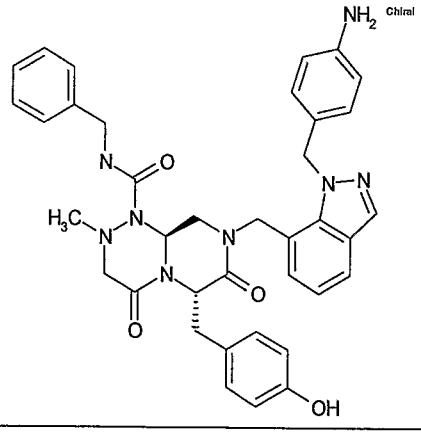
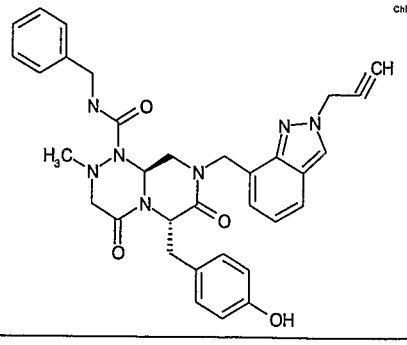
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
56		10.8	9.1
57		3.1 ± 0.3	5.1 ± 0.3
58		47.9 ± 7.2	22.3 ± 4.1
59		ND up to 50uM	55.1 ± 33.7

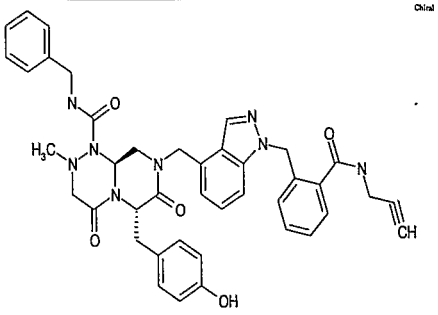
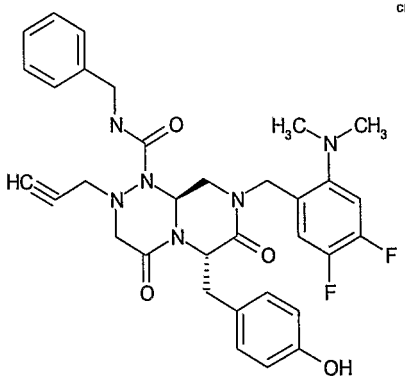
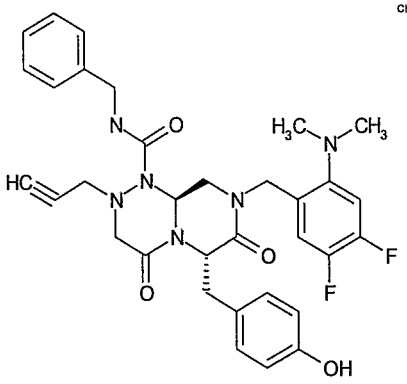
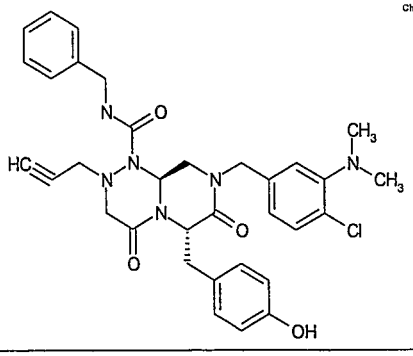
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
60		8.3 ± 1.4	6.3 ± 2.6
61		11.3 ± 6.0	3.6 ± 0.3
62		35.3 ± 4.6	23.5 ± 2.7
63		18.8 ± 4.8	1.3 ± 0.1

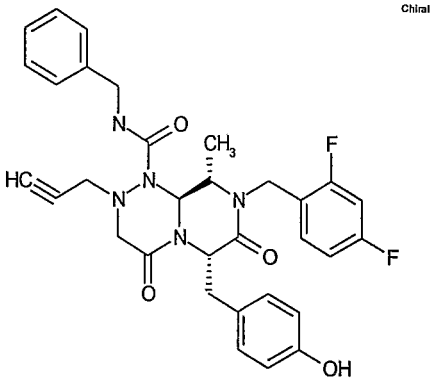
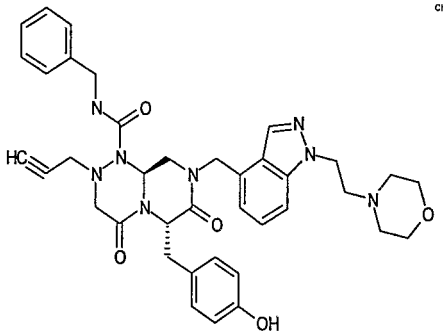
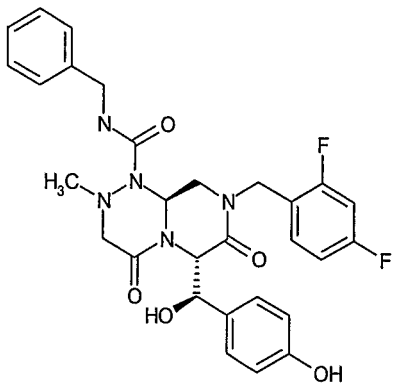
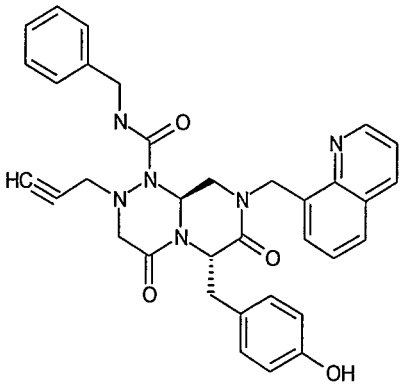
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
64		12.0 ± 0.7	19.0 ± 1.6
65		7.3	4.7
66		3.0 ± 0.3	5.8 ± 0.3
67		0.6 ± 0.2	0.3 ± 0.03

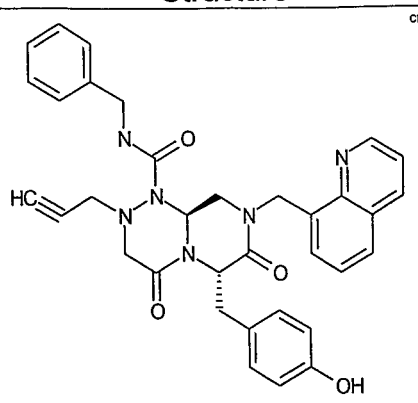
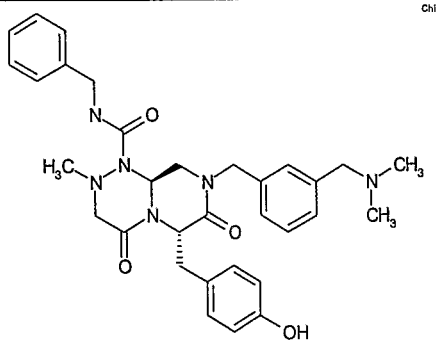
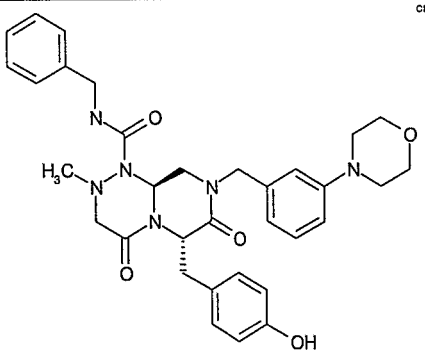
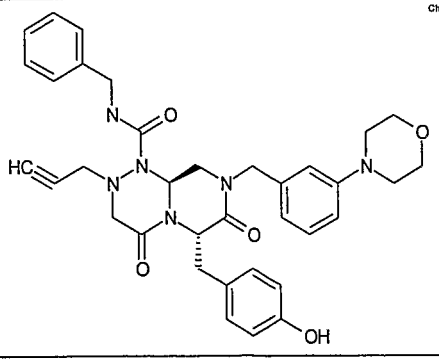
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
68		3.7 ± 0.2	3.8 ± 0.6
69		17.9 ± 3.1	9.7 ± 1.0
70		7.4 ± 0.6	7.2 ± 0.7
71		4.6 ± 0.5	3.6 ± 0.7

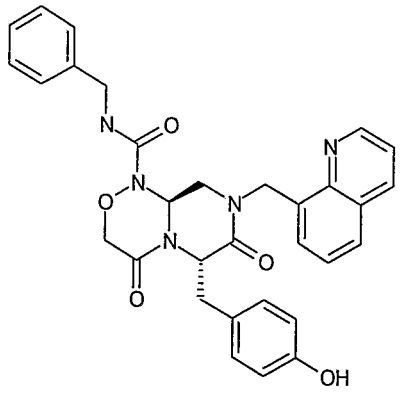
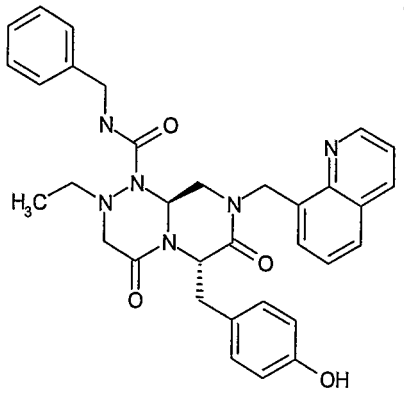
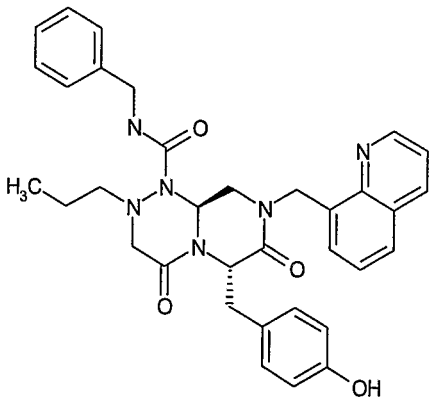
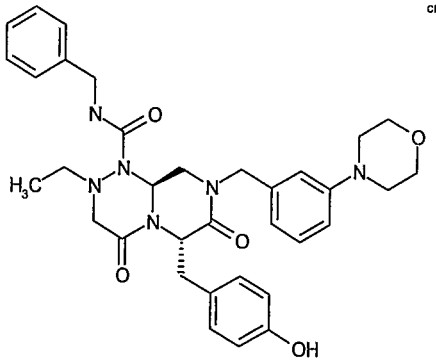
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
72		10.9 ± 0.6	10.3 ± 1.6
73		9.2 ± 0.8	15.8 ± 2.6
74		1.3 ± 0.4	2.4 ± 0.3
75		2.0 ± 0.1	4.5 ± 0.4

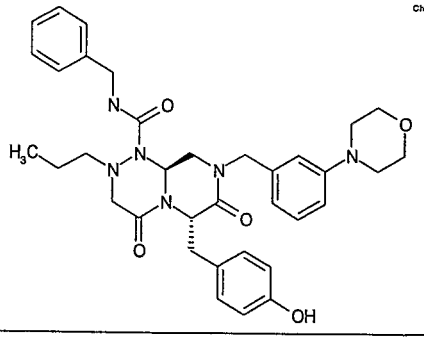
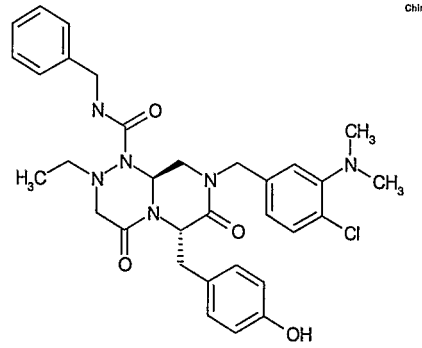
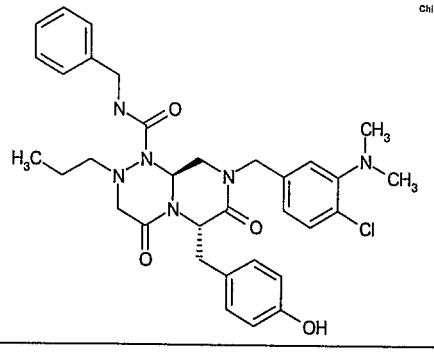
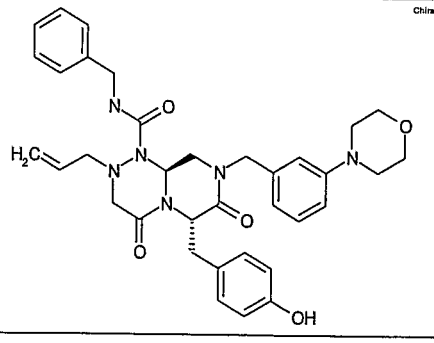
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
76		4	6.1
77		26.5 ± 6.5	10.7 ± 0.8
78		2.2 ± 0.2	3.7 ± 0.3
79		2.8 ± 0.2	5.2 ± 0.4

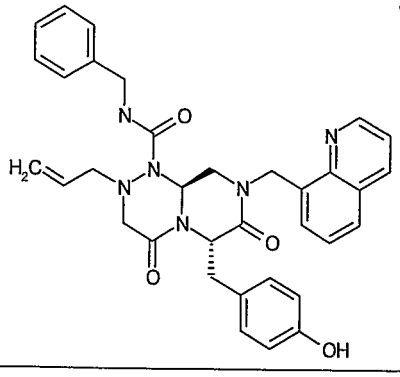
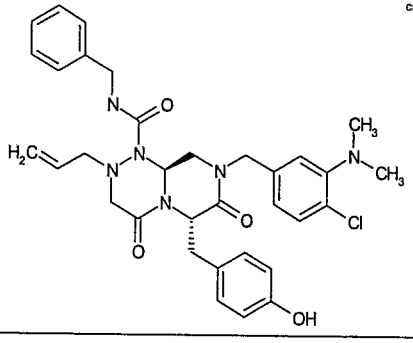
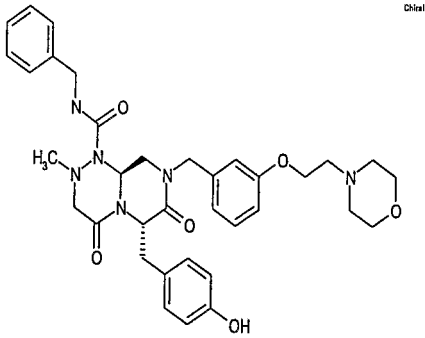
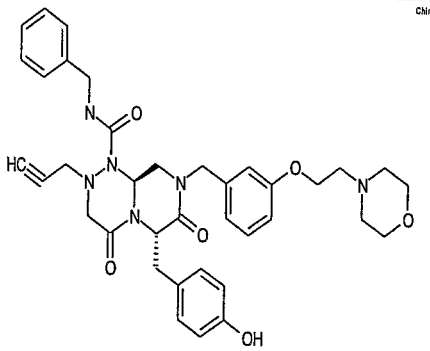
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
80		4.0 ± 0.6	3.9 ± 0.6
81		0.5 ± 0.3	1.8 ± 0.1
82		1.5	1.4
83		2.3 ± 0.3	2.5 ± 0.1

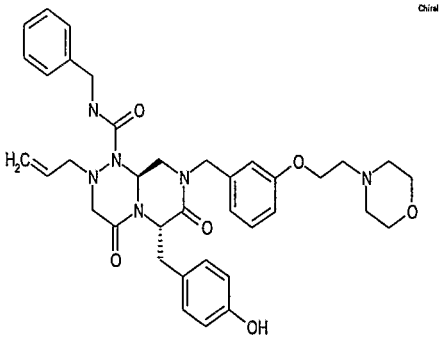
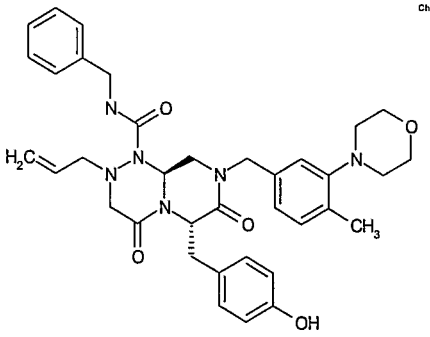
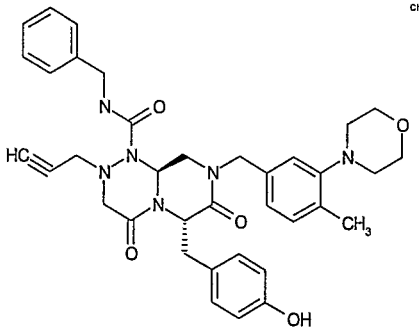
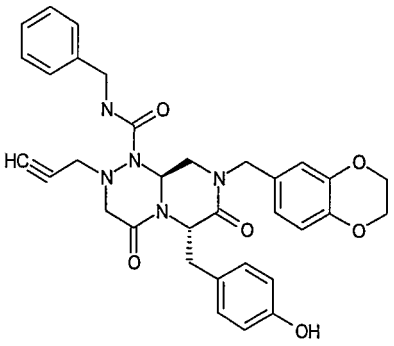
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
84		8.4 ± 1.1	9.9 ± 1.0
85		1.4 ± 0.5	2.7 ± 0.3
86		9.6 ± 1.6	6.5 ± 0.6
87		0.6 ± 0.2	0.5 ± 0.1

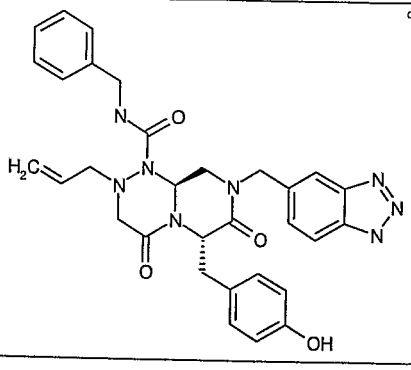
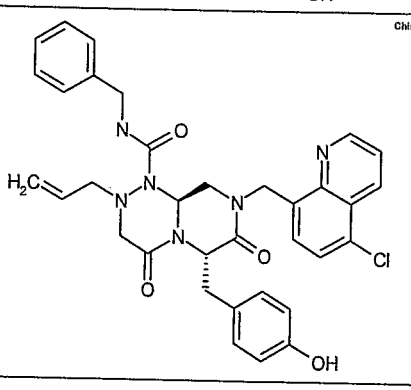
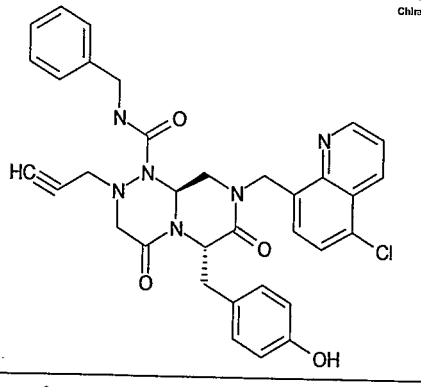
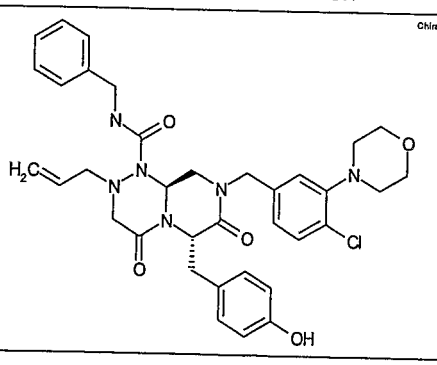
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
88		0.3	0.4
89		14.6 ± 1.4	7.5 ± 1.0
90		12.6 ± 0.9	14.7 ± 1.0
91		1.5 ± 0.1	3.2 ± 0.2

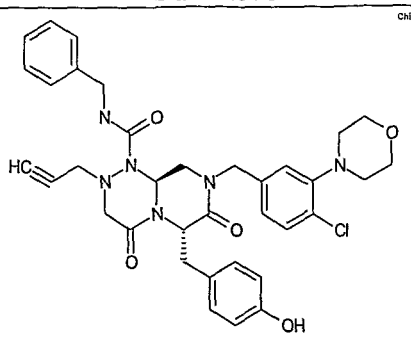
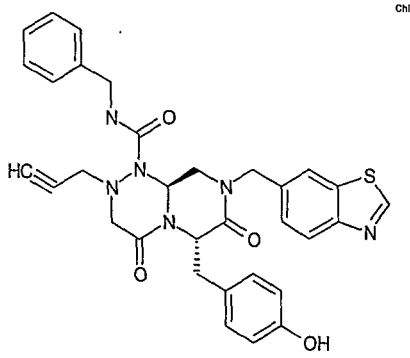
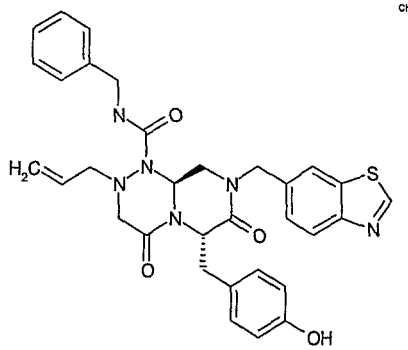
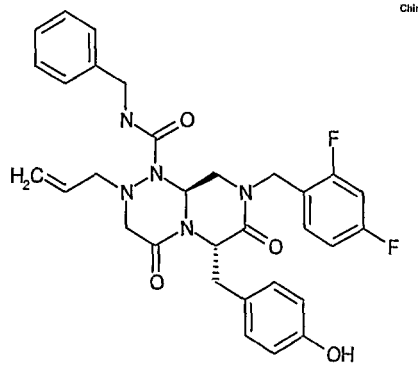
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
92		12.9 ± 1.0	14.9 ± 2.2
93		1.9 ± 0.4	1.1 ± 0.1
94		1.1 ± 0.3	0.7 ± 0.07
95		16.2 ± 2.6	7.1 ± 1.2

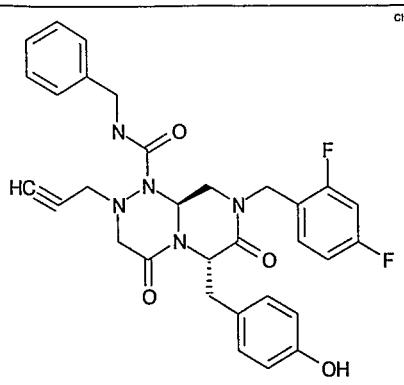
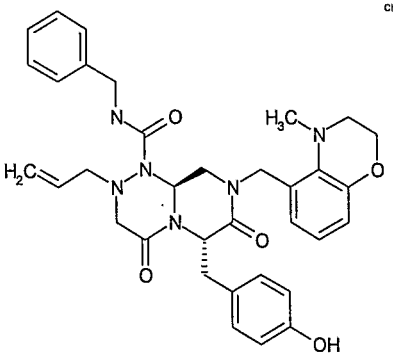
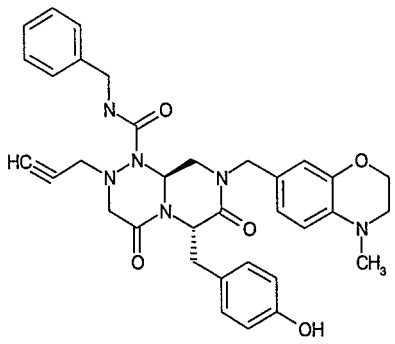
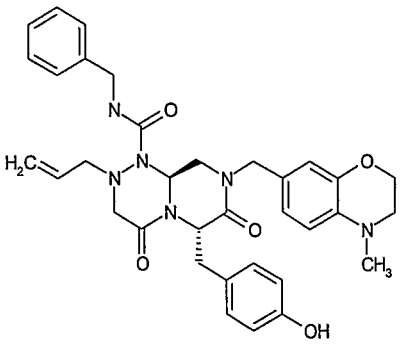
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
96		3.7 ± 0.4	3.4 ± 0.4
97		7.1 ± 1.0	5.2 ± 0.5
98		7.0 ± 1.1	4.4 ± 0.5
99		1.0 ± 0.05	0.7 ± 0.1

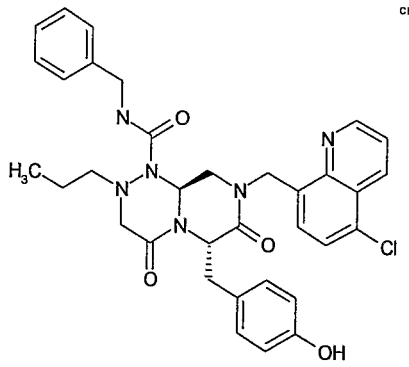
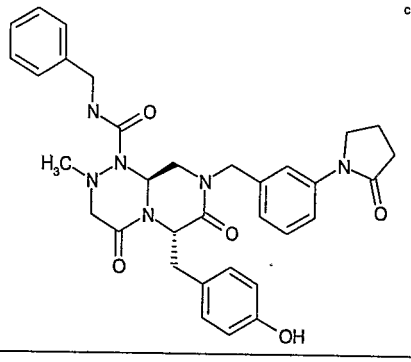
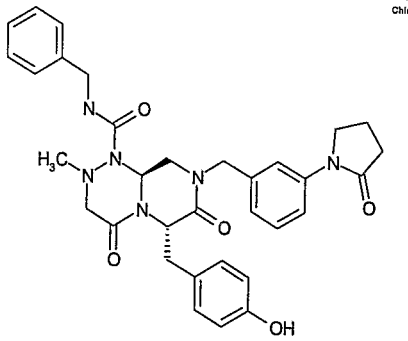
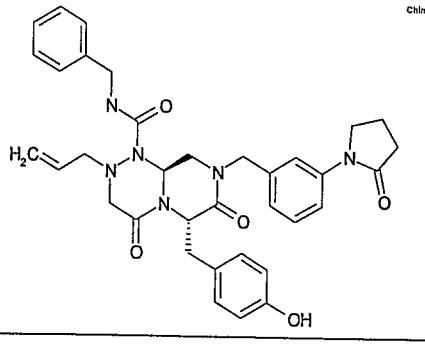
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
100		0.3 ± 0.03	0.4 ± 0.1
101		1.1 ± 0.07	0.9 ± 0.1
102		2.5 ± 0.4	4.9 ± 1.2
103		1.1 ± 0.1	1.5 ± 0.2

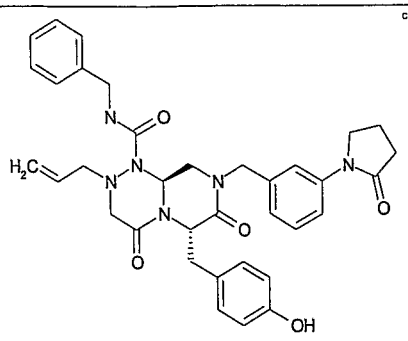
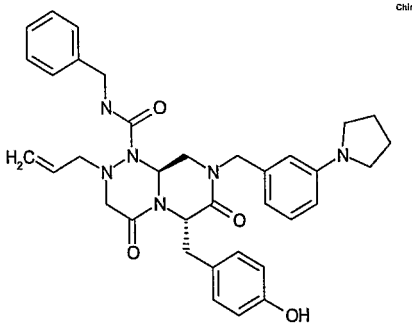
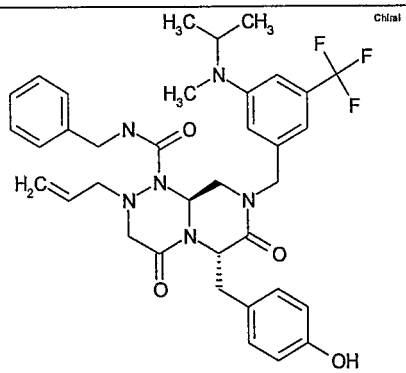
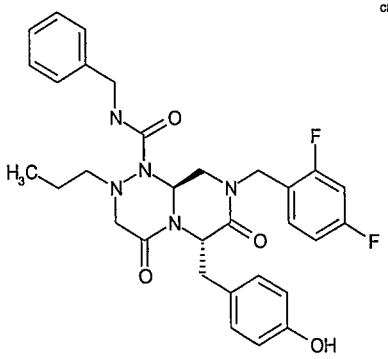
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
104		<0.4	<0.4
105		2.8 ± 0.2	2.1 ± 0.3
106		4.5 ± 0.3	2.8 ± 0.4
107		1.6 ± 0.1	1.6 ± 0.1

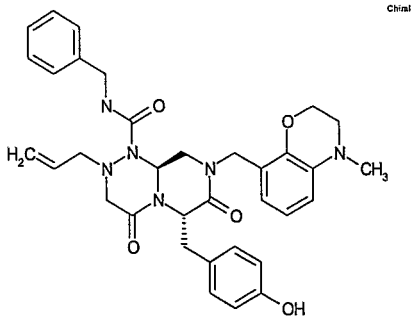
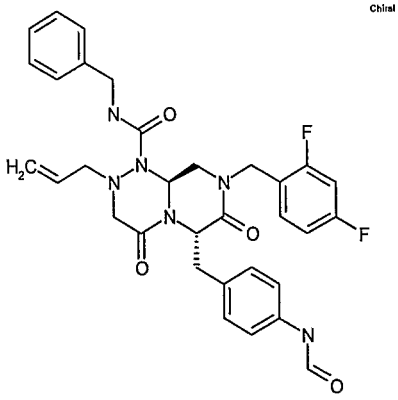
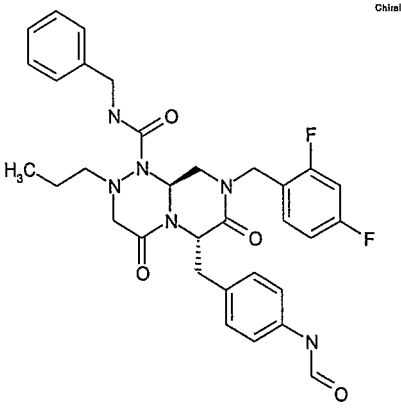
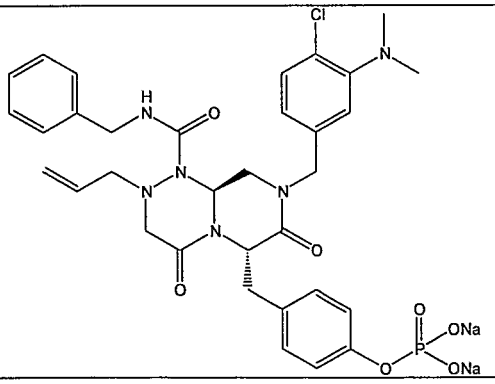
Compound	Structure	Growth Inhibition (GI50, uM)	
		SW480	HCT116
108		24.9 ± 2.2	37.9 ± 5.7
109		1.3 ± 0.3	1.1 ± 0.1
110		2.1 ± 0.3	1.9 ± 0.1
111		2.7 ± 0.8	2.1 ± 0.2

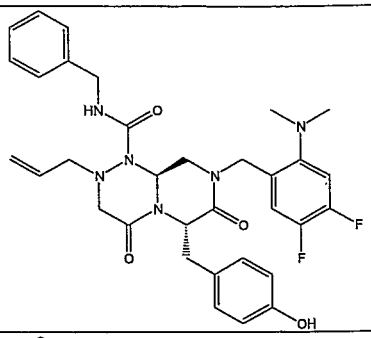
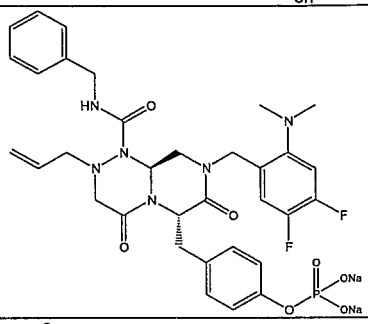
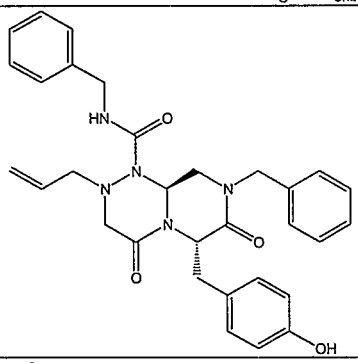
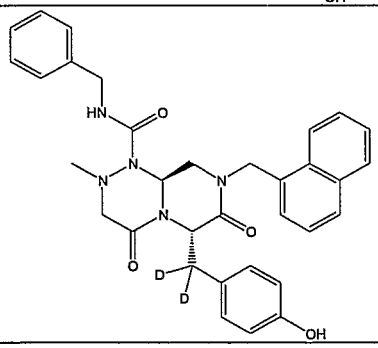
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
112		5.1 ± 0.5	4.7 ± 0.3
113		6.8 ± 1.4	3.7 ± 0.6
114		1.7 ± 0.7	1.9 ± 0.2
115		2.0 ± 0.7	1.1 ± 0.04

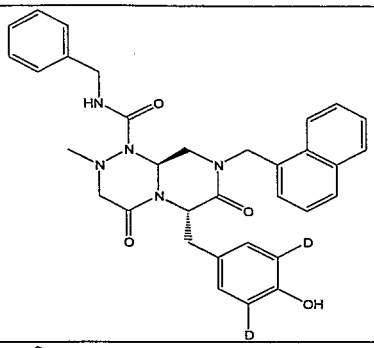
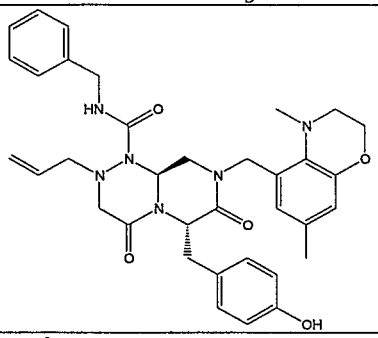
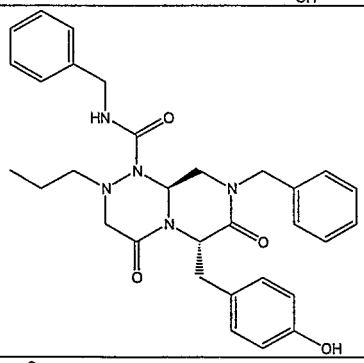
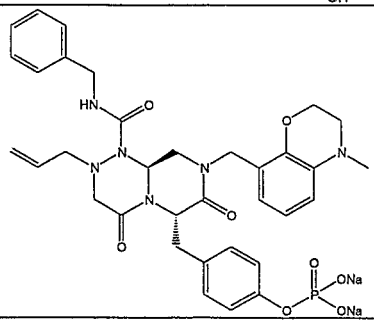
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
116		2.8 ± 0.9	1.7 ± 0.1
117		0.6 ± 0.1	0.3 ± 0.02
118		21.2 ± 1.5	23.2 ± 2.8
119		10.0 ± 1.3	9.5 ± 1.1

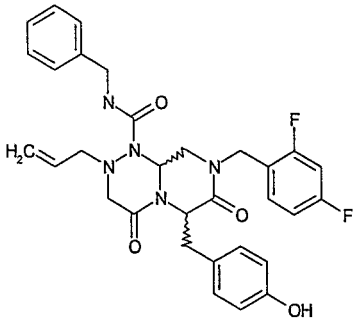
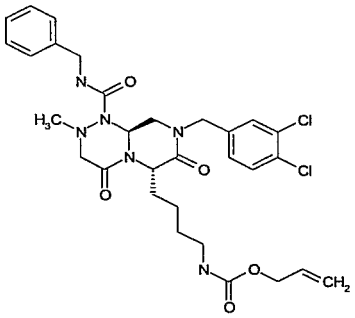
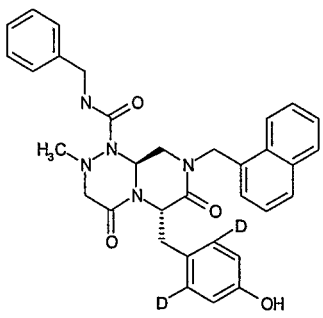
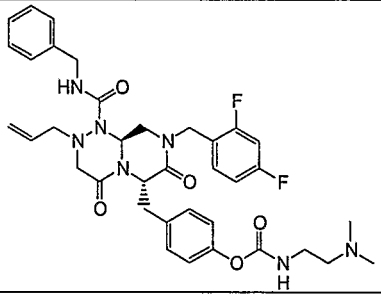
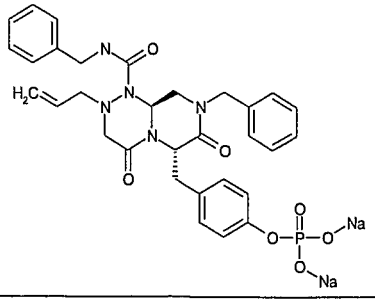
Compound	Structure	Growth Inhibition (GI50, uM)	
		SW480	HCT116
120		1.8 ± 0.2	2.6 ± 0.1
121		8.2 ± 0.5	13.1 ± 0.6
122		15.9 ± 5.2	14.8 ± 1.3
123		1.1 ± 0.3	1.7 ± 0.3

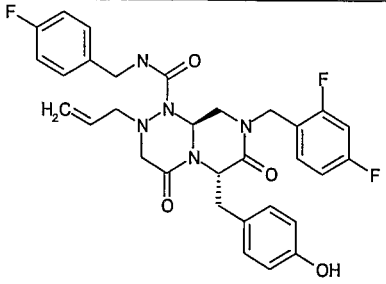
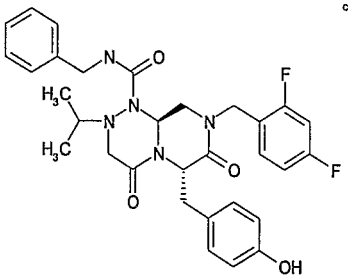
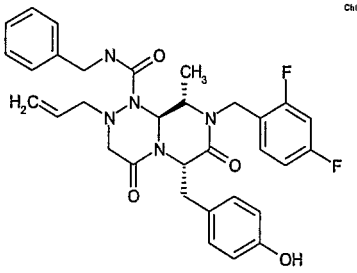
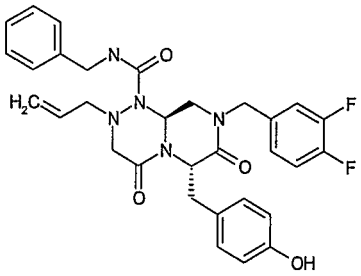
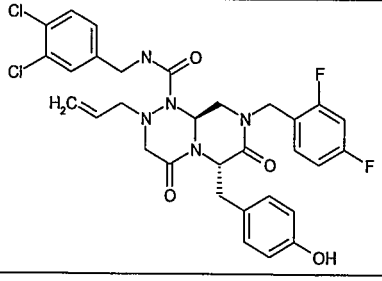
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
124		2.3 ± 0.2	1.4 ± 0.1
125		2.2 ± 0.3	1.9 ± 0.2
126		19.4 ± 3.0	11.6 ± 3.0
127		4.9 ± 0.7	4.3 ± 0.7

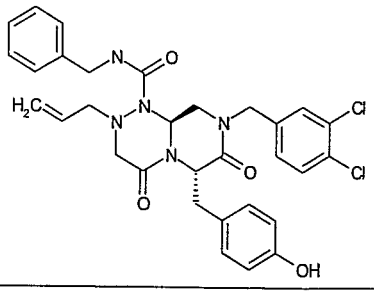
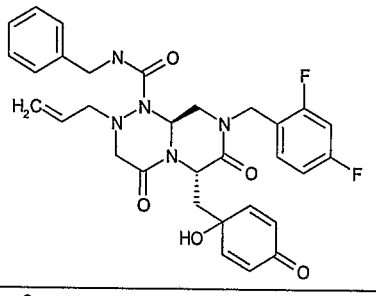
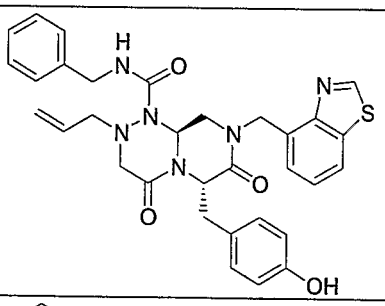
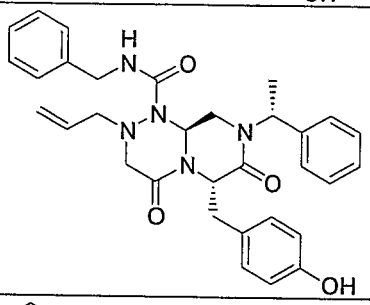
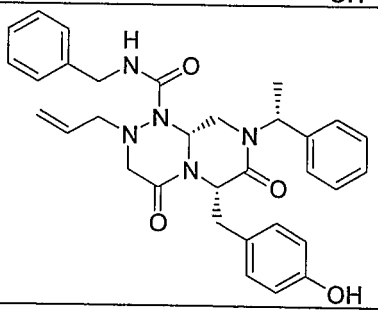
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
128		0.9 ± 0.1	1.0 ± 0.03
129		2.9 ± 0.5	3.1 ± 0.3
130		17.3 ± 1.2	10.7 ± 1.7
131		2.3 ± 0.1	1.7 ± 0.5

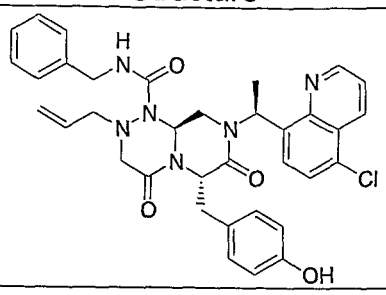
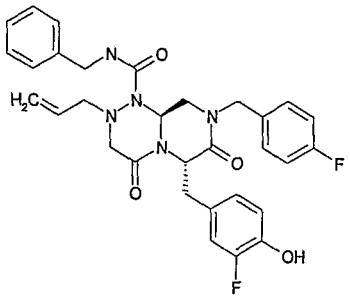
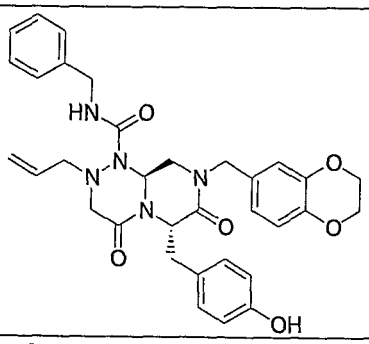
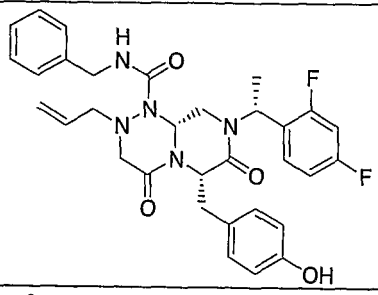
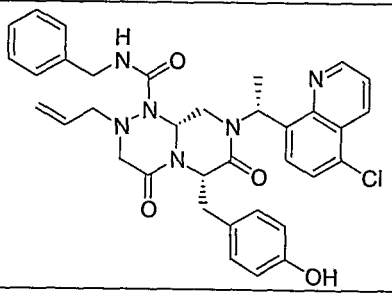
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
132		2.5 ± 0.1	2.2 ± 1.2
133		2.3 ± 0.1	2.1 ± 1.8
134		1.4 ± 0.4	0.8 ± 0.7
135		3.2 ± 0.4	3.1 ± 0.8

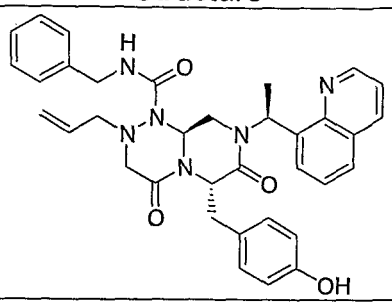
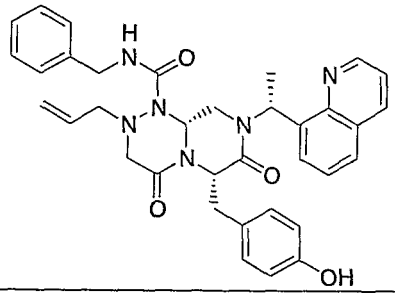
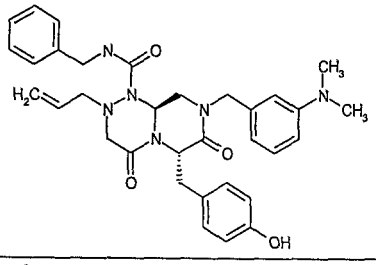
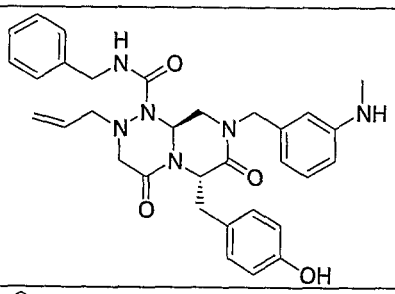
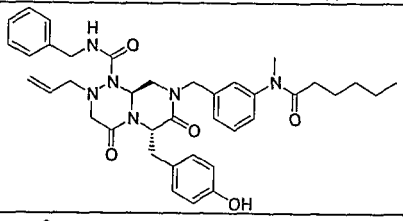
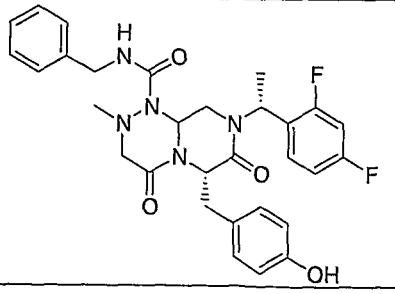
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
136		3.4 ± 0.4	3.0 ± 0.9
137		1.4 ± 0.4	1.3 ± 0.3
138		4.0 ± 0.4	3.9 ± 0.7
139		1.2 ± 0.1	1.0± 0.2

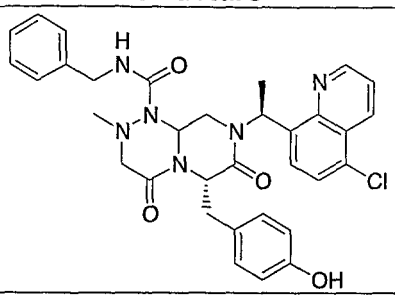
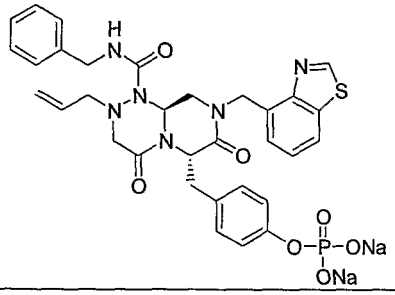
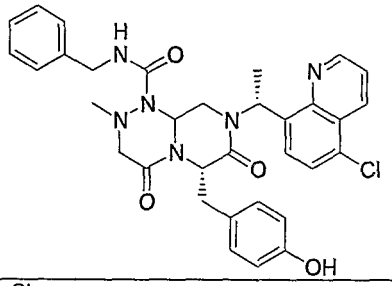
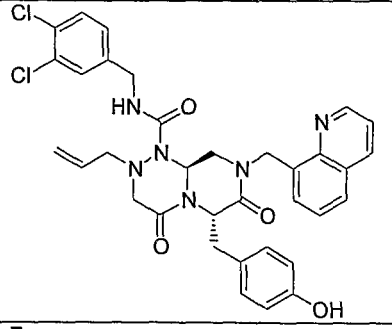
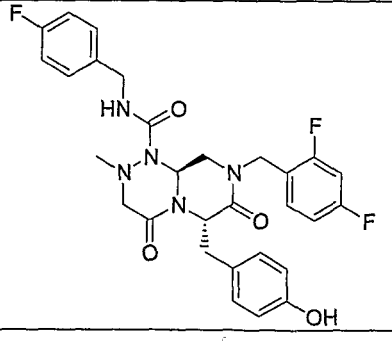
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
140		1.6 ± 0.5	1.7 ± 0.1
141		35 ± 11	21 ± 2.6
142		3.2 ± 0.3	3.3 ± 0.4
143		1.2 ± 0.1	1.2 ± 0.1
144		0.5 ± 0.03	0.6 ± 0.1

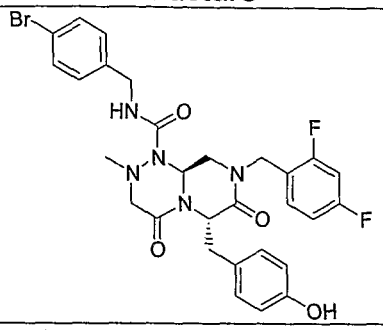
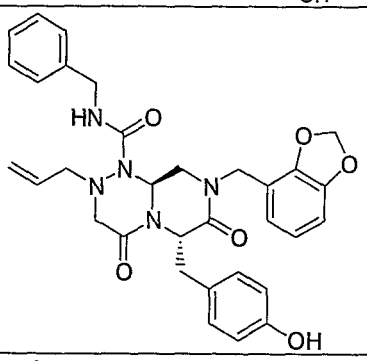
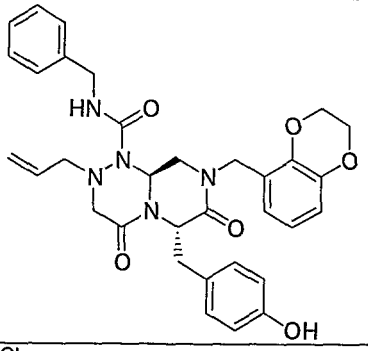
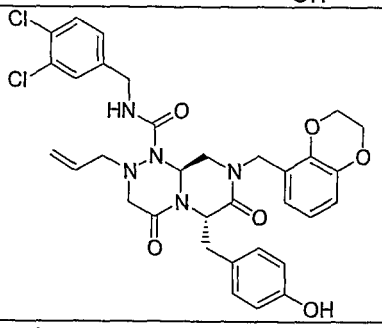
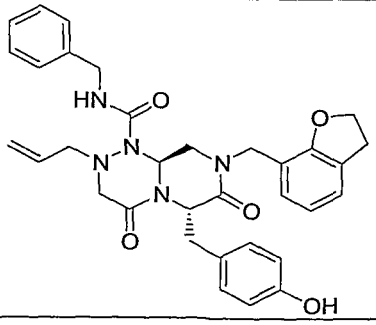
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
145		6.4 ± 0.1	5.9 ± 0.3
146		3.7 ± 0.5	4.0 ± 0.5
147		6.1 ± 0.4	5.5 ± 0.4
148		1.3 ± 0.1	1.0 ± 0.3
149		2.3 ± 0.1	2.3 ± 0.4

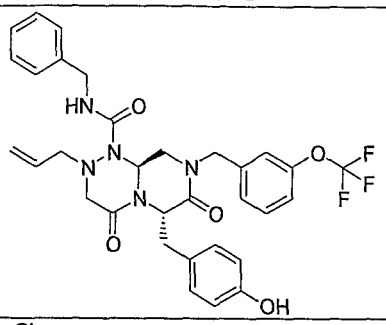
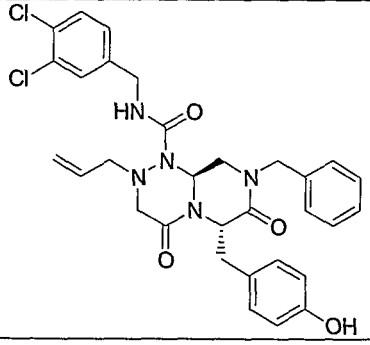
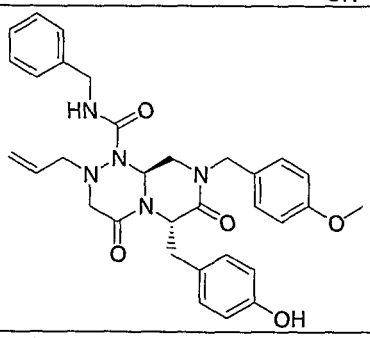
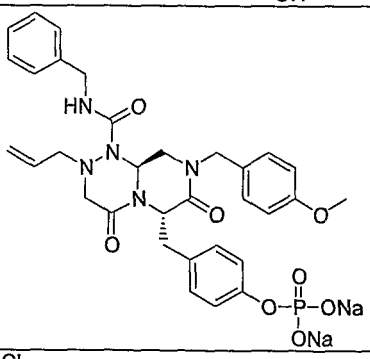
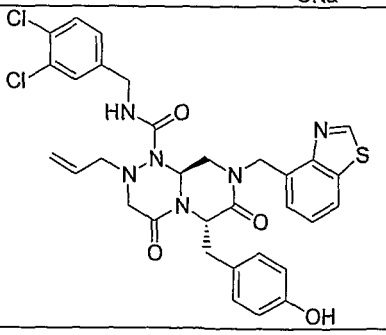
Compound	Structure	Growth Inhibition (GI50, uM)	
		SW480	HCT116
150		1.3 ± 0.1	1.4 ± 0.2
151		11.2 ± 1.3	8.6 ± 0.9
152		0.7 ± 0.1	0.6 ± 0.1
153		12.8 ± 1.6	14.3 ± 7.0
154		0.7 ± 0.2	0.7 ± 0.2

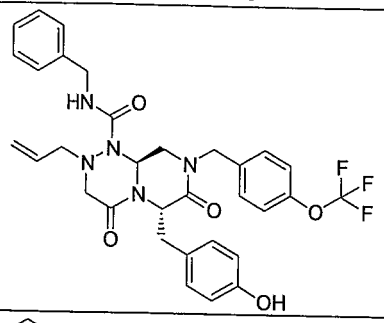
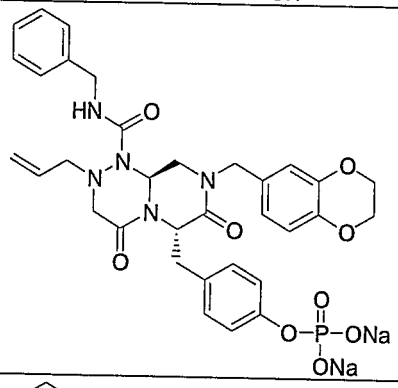
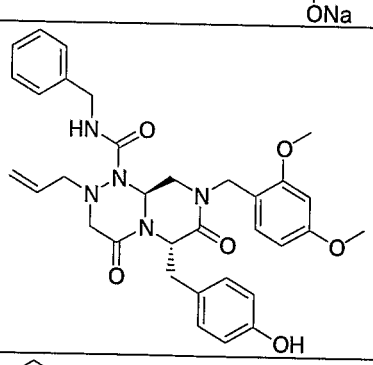
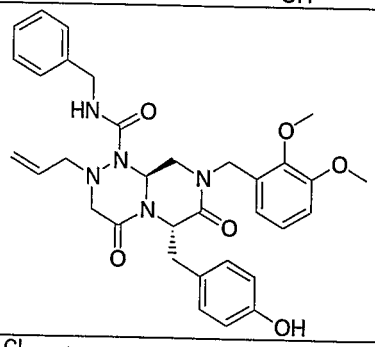
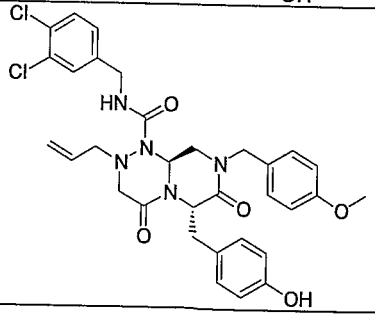
		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
155		26.3 ± 2.5	23.3 ± 1.2
156		3.7 ± 0.3	3.8 ± 0.2
157		1.0 ± 0.2	1.2 ± 0.1
58		4.4 ± 0.1	3.8 ± 0.5
159		9.1 ± 0.5	8.2 ± 0.4

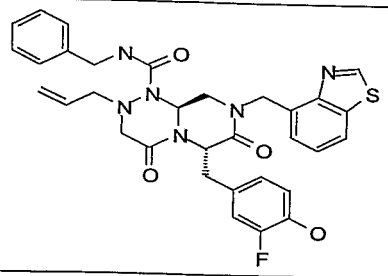
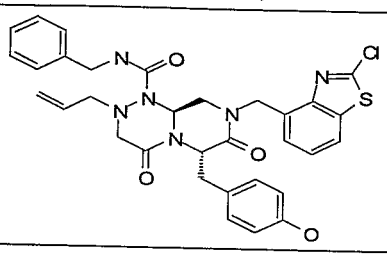
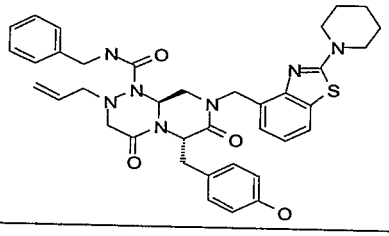
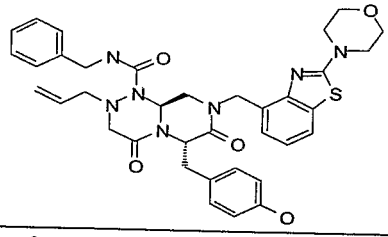
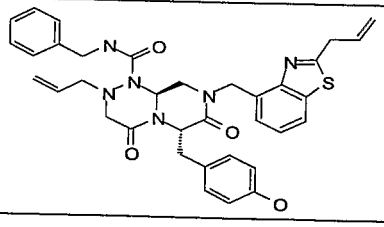
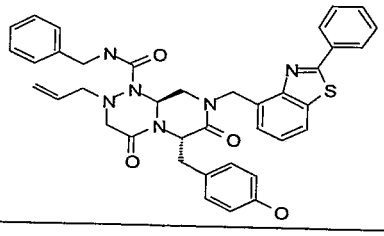
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
160		13.7 ± 0.5	10.1 ± 01.3
161		4.2 ± 0.4	4.1 ± 0.5
162		1.0 ± 0.3	1.3 ± 0.7
163		2.4 ± 0.2	2.3 ± 0.4
164		3.0 ± 0.3	2.9 ± 0.4
165		22.8 ± 0.9	24.4 ± 1.9

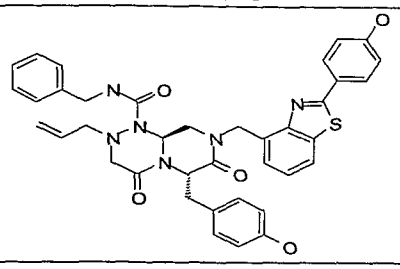
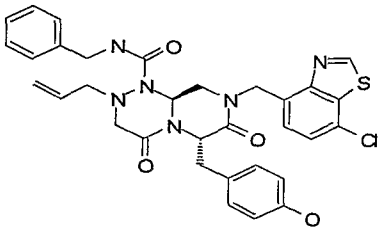
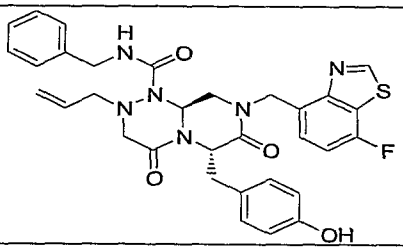
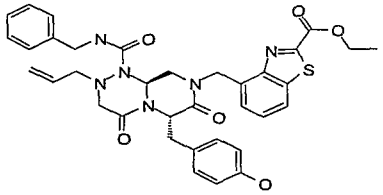
Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
166		27.9 ± 4.7	25.2 ± 3.2
167		0.3 ± 0.02	0.2 ± 0.02
168		6.2 ± 0.8	6.5 ± 0.3
169		0.8 ± 0.1	1.0 ± 0.2
170		8.9 ± 0.8	8.6 ± 0.8

		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
171		6.2 ±1.0	6.0 ± 0.4
172		0.8 ± 0.1	0.9 ± 0.1
173		0.6 ± 0.1	0.8 ± 0.1
174		1.9 ± 0.2	1.8 ± 0.1
175		3.0 ± 0.4	2.5 ± 0.1

Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
176		1.7 ± 0.2	1.7 ± 0.1
177		1.8 ± 0.1	1.6 ± 0.1
178		1.6 ± 0.2	1.5 ± 4.4
179		1.5 ± 0.1	1.6 ± 0.1
180		1.0 ± 0.1	1.1 ± 0.1

Compound	Structure	Growth Inhibition (GI50, uM) SW480	HCT116
181		2.3 ± 0.1	2.3 ± 0.1
182		1.0 ± 0.1	0.8 ± 0.1
183		1.6 ± 0.3	1.5 ± 0.1
184		0.7 ± 0.4	0.7 ± 0.1
185		4.9 ± 0.4	4.5 ± 0.2

Compound	Structure	Growth Inhibition (GI50, uM)	
		SW480	HCT116
186		1.7 ± 0.1	2.0 ± 0.2
187		1.0 ± 0.1	1.0 ± 0.1
188		1.6 ± 0.2	1.8 ± 0.2
189		1.0 ± 0.1	1.2 ± 0.1
190		1.1 ± 0.3	1.0 ± 0.1
191		1.2 ± 0.1	1.4 ± 0.1

		Growth Inhibition (GI50, uM)	
Compound	Structure	SW480	HCT116
192		1.1 ± 0.1	1.3 ± 0.1
193		0.8 ± 0.1	1.1 ± 0.1
194		0.2 ± 0.02	0.2 ± 0.02
195		3.1 ± 0.4	3.0 ± 0.3

In other aspects the present invention provides pharmaceutical compositions containing a compound having the general formula (I), or the general formula (II), or the general formula (III), or the general formula (IV), or the general formula (VI). These compositions may be used in various methods (*e.g.*, treating cancer or Alzheimer's disease) of the present invention as described in detail below.

The pharmaceutical composition of the present invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical),

transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. In addition, pH may be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for

example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, a compound having general formula (I), (II), (III), (IV), or (VI) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser that contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.,* for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds that exhibit large therapeutic indices are preferred. While compounds that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating

plasma concentration range that includes the IC50 (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

For instance, in certain embodiments, a pharmaceutical composition of the present invention is one suitable for oral administration in unit dosage form such as a tablet or capsule that contains from about 1mg to about 1g of the compound of this invention. In some other embodiments, a pharmaceutical composition of the present invention is one suitable for intravenous, subcutaneous or intramuscular injection. A patient may receive, for example, an intravenous, subcutaneous or intramuscular dose of about 1 µg/kg to about 1g/kg of the compound of the present invention. The intravenous, subcutaneous and intramuscular dose may be given by means of a bolus injection or by continuous infusion over a period of time. Alternatively a patient will receive a daily oral dose approximately equivalent to the daily parenteral dose, the composition being administered 1 to 4 times per day.

The following table illustrates representative pharmaceutical dosage forms containing the compound or pharmaceutically-acceptable salt thereof for therapeutics or prophylactic use in humans:

Tablet 1	mg/tablet
Compound	100
Lactose Ph. Eur.	179
Croscarmellose sodium	12.0
Polyvinylpyrrolidone	6
Magnesium stearate	3.0

Tablet 2	mg/tablet
Compound	50
Lactose Ph. Eur.	229
Croscarmellose sodium	12.0
Polyvinylpyrrolidone	6
Magnesium stearate	3.0

Tablet 3	mg/tablet
Compound	1.0
Lactose Ph. Eur.	92
Croscarmellose sodium	4.0
Polyvinylpyrrolidone	2.0
Magnesium stearate	1.0

Capsule	mg/capsule
Compound	10
Lactose Ph. Eur.	389
Croscarmellose sodium	100
Magnesium stearate	1.0

Injection I	(50mg/ml)
Compound	0.5% w/v
Isotonic aqueous solution	to 100%

The pharmaceutical composition containing the compound of general formulae (I) or (II) or (III) or (IV) or (VI) can be used for treatment of disorders modulated by Wnt signaling pathway, especially cancer, more especially colorectal cancer.

In one aspect, the present invention provides compounds that inhibit the binding of a radiolabeled enkephalin derivative to the δ and μ opiate receptors. Accordingly, the reverse-turn mimetics of the present invention may be used as receptor agonists and as potential analgesic agents.

In another aspect, the present invention provides methods for inhibiting tumor growth. Such methods comprise the step of administering to a subject (*e.g.*, a mammalian subject) having a tumor a compound with general formula (I), especially general formula (VI) in an amount effective to inhibit tumor growth. A compound or composition inhibits tumor growth if the tumor sizes are statistically significantly smaller in subjects with the treatment of the compound or composition than those without the treatment.

The inhibitory effect of a particular compound or composition of the present invention on tumor growth may be characterized by any appropriate methods known in the art. For instance, the effect of the compound or

composition on survivin expression may be measured. Compounds or compositions down-regulate survivin expression are likely to have inhibitory effects on tumor growth. In addition, assays using tumor cell lines (*e.g.*, soft agar assays using SW480 cells) and animal models for tumor growth (*e.g.*, nude mice grafted with tumor cells and Min mouse model) may also be used to evaluate the inhibitory effect on tumor growth of a given compound or composition as described in detail in the examples. Other exemplary animal models or xenografts for tumor growth include those for breast cancer (Guo *et al.*, *Cancer Res. 62*: 4678-84, 2002; Lu *et al.*, *Breast Cancer Res. Treat. 57*: 183-92, 1999), pancreatic cancer (Bouvet *et al., Cancer Res. 62*: 1534-40, 2002), ovarian tumor (Nilsson *et al.*, *Cancer Chemother. Pharmacol. 49*: 93-100, 2002; Bao *et al.*, *Gynecol. Oncol. 78*: 373-9, 2000), melanoma (Demidem *et al.*, *Cancer Res. 61*: 2294-300, 2001), colorectal cancer (Brown *et al.*, *Dig. Dis. Sci. 45*: 1578-84, 2000; Tsunoda *et al.*, *Anticancer Res. 19*: 1149-52, 1999; Cao *et al.*, *Clin. Cancer Res. 5*: 267-74, 1999; Shawler *et al., J. Immunother. Emphasis Tumor Immunol. 17*: 201-8, 1995; McGregor *et al.*, *Dis. Colon. Rectum. 36*: 834-9, 1993; Verstijnen *et al.*, *Anticancer Res. 8*: 1193-200, 1988), hepatocellular cancer (Labonte *et al.*, *Hepatol. Res. 18*: 72-85, 2000), and gastric cancer (Takahashi *et al.*, *Int. J. Cancer 85*: 243-7, 2000).

The compound or composition that inhibits tumor growth may be administrated into a subject with a tumor via an appropriate route depending on, for example, the tissue in which the tumor resides. The appropriate dosage may be determined using knowledge and techniques known in the art as described above. The effect of the treatment of the compound or composition on tumor growth may also be monitored using methods known in the art. For instance, various methods may be used for monitoring the progression and/or growth of colorectal cancer, including colonoscopy, sigmoidoscopy, biopsy, computed tomograph, ultrasound, magnetic resonance imaging, and positron emission tomography. Methods for monitoring the progression and/or growth

of ovarian cancer include, for example, ultrasound, computed tomography, magnetic resonance imaging, chest X-ray, laparoscopy, and tissue sampling.

In a related aspect, the present invention provides a method for treating or preventing cancer. Such methods comprise the step of administering to a subject in need thereof a compound or composition having general formula (I), especially the compound of general formular (VI), in an amount effective to treat or prevent cancer in the subject. Treating cancer is understood to encompass reducing or eliminating cancer progression (*e.g.*, cancer growth and metastasis). Preventing cancer is understood to encompass preventing or delaying the onset of cancer. Various types of cancer may be treated or prevented by the present invention. They include, but are not limited to, lung cancer, breast cancer, colorectal cancer, stomach cancer, pancreatic cancer, liver cancer, uterus cancer, ovarian cancer, gliomas, melanoma, lymphoma, and leukemia.

A subject in need of treatment may be a human or non-human primate or other animal with various types of cancer. A subject in need of prevention may be a human or non-human primate or other animal that is at risk for developing cancer. Methods for diagnosing cancer and screening for individuals with high risk of cancer are known in the art and may be used in the present invention. For instance, colorectal cancer may be diagnosized by fecal occult blood test, sigmoidoscopy, colonoscopy, barium enema with air contrast, and virtual colonoscopy. An individal with high risk of colorectal cancer may have one or more colorectal cancer risk factors such as a strong family history of colorectal cancer or polyps, a known family history of hereditary colorectal cancer syndromes, a personal history of adenomatous polyps, and a personal history of chronic inflammatory bowel disease.

A compound with general formula (I) useful in cancer treatment or prevention may be identified by appropriate methods known in the art. Methods that may be used to select compounds for inhibitory effect on tumor growth as described above may also be used. The route of administration, the

dosage of a given compound, the effectiveness of the treatment may be determined using knowledge and techniques known in the art. Factors that may be considered in making such a determination include, for example, type and stage of the cancer to be treated.

The compound with general formula (I) useful in cancer treatment and prevention may be administered in combination with an anti-neoplastic agent. An anti-neoplastic agent refers to a compound that inhibits tumor growth. Exemplary anti-neoplastic agents include Fluorouracil; 5-fluoro-2,4(1H, 3H)-pyrimidinedione (5-FU), taxol, cisplatin, mitomycin C, tegafur, raltitrexed, capecitabine, and irinotecan (Arango et al., *Cancer Research* 61, 2001 4910-4915). A compound with general formula (I) administered in combination with an anti-neoplastic agent does not necessarily require that the compound and the anti-neoplastic agent be administered concurrently. The compound and the agent may be administered separately as long as at a time point, they both have effects on same cancer cells.

In a further related aspect, the present invention provides methods for promoting apoptosis in cancer cells. Such methods comprise the step of contacting cancer cells with a compound having general formula (I), especially a compound having general formula (VI), in an amount effective to promote apoptosis in these cells. A compound promotes apoptosis if the number of cancer cells undergoing apoptosis is statistically significantly larger in the presence of the compound than that in the absence of the compound. Such compounds may be identified by methods known in the art (*e.g.*, measuring caspase activities and/or cell death) using cultured cancer cell lines, xenografts, or animal cancer models. Preferably, the compound is more active in promoting apoptosis in cancer cells than in normal cells. Cancer cells treatable by the present method may be from various tissue origins.

In another aspect of the present invention, a method for treating a disorder modulated by Wnt signaling pathway in which the method comprises administering to a patient a safe and effective amount of the compounds having

general formula (I), especially the compound of general formula (VI) is disclosed. Pharmaceutical composition containing the compound of the present invention can be also used for this purpose. In this connection, it is found in the present invention that the compounds having general formula (I), especially the compound of general formula (VI) or the pharmaceutical composition containing thereof can be useful for the treatment of disorder modulated by TCF4 - β catenin – CBP complex, which is believed to be responsible for initiating the overexpression of cancer cells related to Wnt signaling pathway. Thus, it is another aspect of the present invention to provide a method for the treatment of disorder modulated by TCF4 - β catenin – CBP complex, using the compounds having the general formula (I), especially the compound of general formula (VI).

The present invention also provides compounds and methods for inhibiting survivin expression. Survivin is a target gene of the TCF/beta-catenin pathway, and more specifically is a target gene of the TCF/beta-catenin/CBP pathway. It is a member of the IAP (Inhibitor of Apoptosis Protein) family of proteins. Biological activity associated with survivin includes: highly expressed at G_2/M, regulating cell cycle entry and exit; associated with microtubule, centrosomes, centromeres and midbody depending upon the phases of the cell cycle; and anti-apoptosis via interacting directly or indirectly with caspases (*e.g.,* caspase 3, 7 and 9). In connection with cancer, survivin is widely and highly expressed in tumor cells, but expressed to little or no extent in normal tissue cells. Also, it has been observed that cancer patients whose tumors expressed survivin had a decreased overall survival. Furthermore, the degree of surviving expression has been correlated with other cancer markers, *e.g.,* Ki67, PNCA, p53, APC, *etc.*

The effect of a particular compound of the present invention on survivin expression may be characterized by methods known in the art. Such methods include methods for characterizing survivin expression at the transcriptional or translational level. Exemplary methods for characterizing

survivin expression at the transcriptional level are: cDNA microarry, reverse transcription-polymerase chain reaction (RT-PCR), chromatin immunoprecipitation (ChIP), and assays for reporter activities driven by survivin promoter. Exemplary methods for characterizing survivin expression at the translational level are: Western blot analysis, immunochemistry and caspase activities. Detailed descriptions of the above exemplary methods may be found in the examples below.

As described above, the present invention provides methods for inhibiting survivin expression. Such methods comprise the step of contacting a survivin-expressing cell with a compound of the present invention in an amount effective to inhibit survivin expression. A compound inhibits survivin expression if survivin expression in a cell is decreased in the presence of the compound compared to survivin expression in the absence of the compound. Survivin-expressing cells include tumor cells that express, such as cells in or from lung cancer, breast cancer, stomach cancer, pancreatic cancer, liver cancer, uterus cancer, ovarian cancer, gliomas, melanoma, colorectal cancer, lymphoma and leukemia. The step of contacting the survivin-expressing cells with the compound may be performed *in vitro*, *ex vivo*, or *in vivo*. A compound useful in inhibiting survivin expression may be identified, and the effects of a particular compound of the present invention may be characterized, by appropriate methods known in the art, as described in detail above.

Compounds of the present invention have been shown to inhibit the expression of survivin. Blanc-Brude *et al.*, *Nat. Medicine* 8:987 (2002), have shown that survivin is a critical regulator of smooth muscle cell apoptosis which is important in pathological vessel-wall remodeling. Accordingly, another aspect of the present invention provides a method of treating or preventing restenosis associated with angioplasty comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic of the present invention. In one embodiment the invention treats the restenosis, *i.e.,* administration of a reverse-turn mimetic of the present invention to a

subject having restenosis achieves a reduction in the severity, extent, or degree, etc. of the restenosis. In another embodiment the invention prevents the restenosis, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional restenosis achieves a reduction in the anticipated severity, extent, or degree, etc. of the restenosis. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit TCF/B-catenin transcription. Rodova *et al.*, *J. Biol. Chem.* 277:29577 (2002), have shown that PKD-1 promoter is a target of the B-catenin/TCF pathway. Accordingly, another aspect of the present invention provides a method of treating or preventing polycystic kidney disease comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic of the present invention. In one embodiment the invention treats the polycystic kidney disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having polycystic kidney disease achieves a reduction in the severity, extent, or degree, etc. of the polycystic kidney disease. In another embodiment the invention prevents polycystic kidney disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional polycystic kidney disease achieves a reduction in the anticipated severity, extent, or degree, etc. of the polycystic kidney disease. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit the expression of Wnt signaling. Hanai *et al.*, *J. Cell Bio.* 158:529 (2002), have shown that endostatin, a known anti-angiogenic factor, inhibits Wnt signaling. Accordingly, another aspect of the present invention provides a method of treating or preventing aberrant angiogenesis disease comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic of the present invention. In one embodiment the invention treats the aberrant angiogenesis disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having aberrant angiogenesis disease

achieves a reduction in the severity, extent, or degree, etc. of the aberrant angiogenesis disease. In another embodiment the invention prevents aberrant angiogenesis disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional aberrant angiogenesis disease achieves a reduction in the anticipated severity, extent, or degree, etc. of the aberrant angiogenesis disease. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit the expression of Wnt signalling. Sen *et al.*, *P.N.A.S. (USA)* 97:2791 (2000), have shown that mammals with rheumatoid arthritis demonstrate increased expression of Wnt and Fz in RA synovial tissue. Accordingly, another aspect of the present invention provides a method of treating or preventing rheumatoid arthritis disease comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic of the present invention. In one embodiment the invention treats the rheumatoid arthritis disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having rheumatoid arthritis disease achieves a reduction in the severity, extent, or degree, etc. of the rheumatoid arthritis disease. In another embodiment the invention prevents rheumatoid arthritis disease, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional rheumatoid arthritis disease achieves a reduction in the anticipated severity, extent, or degree, etc. of the rheumatoid arthritis disease. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit the expression of Wnt signalling. Uthoff *et al.*, *Int. J. Oncol.* 19:803 (2001), have shown that differential upregulation of disheveled and fz (Wnt pathway molecules) occurs in ulcerative colitis (compared to Chron's disease patients). Accordingly, another aspect of the present invention provides a method of treating or preventing ulcerative colitis comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic the present

invention. In one embodiment the invention treats the ulcerative colitis, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having ulcerative colitis achieves a reduction in the severity, extent, or degree, etc. of the ulcerative colitis. In another embodiment the invention prevents ulcerative colitis, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional ulcerative colitis achieves a reduction in the anticipated severity, extent, or degree, etc. of the ulcerative colitis. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit Wnt TCF/catenin signalling. Accordingly, another aspect of the invention provides a method of treating or preventing tuberious sclerosis complex (TSC) comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic the present invention. Subjects having TSC typically develop multiple focal lesions in the brain, heart, kidney and other tissues (*see, e.g.,* Gomez, M.R. *Brain Dev.* 17(suppl): 55-57 (1995)). Studies in mammalian cells have shown that overexpression of TSC1 (which expresses hamartin) and TSC2 (which expresses tuberin) negatively regulates cell proliferation and induces G_1/S arrest (*see, e.g.,* Miloloza, A. et al., *Hum. Mol. Genet.* 9: 1721-1727 (2000)). Other studies have shown that hamartin and tuberin function at the level of the β -catenin degradation complex, and more specifically that these proteins negatively regulate beta-catenin stability and activity by participating in the beta-catenin degradation complex (*see, e.g.,* Mak, B.C., et al. *J. Biol. Chem.* 278(8): 5947-5951, (2003)). Beta-catenin is a 95-kDa protein that participates in cell adhesion through its association with members of the membrane-bound cadherin family, and in cell proliferation and differentiation as a key component of the Wnt/Wingless pathway (*see, e.g.,* Daniels, D.L., et al., *Trends Biochem. Sci.* 26: 672-678 (2001)). Misregulation of this pathway has been shown to be oncogenic in humans and rodents. The present invention provides compounds that modulate β-catenin activity, and particularly its interactions with other proteins, and accordingly may be used in

the treatment of TSC. Thus, in one embodiment the invention treats TSC, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having TSC achieves a reduction in the severity, extent, or degree, etc. of the TSC. In another embodiment the invention prevents TSC, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional TSC achieves a reduction in the anticipated severity, extent, or degree, etc. of the TSC. Optionally, the subject is a mammalian subject.

Compounds of the present invention have been shown to inhibit the expression of Wnt signalling. The Kaposi's sarcoma-associated herpesvirus (KSHV) latency-associated nuclear antigen (LANA) is expressed in all KSHV-associated tumors, including Kaposi's sarcoma (KS) and β-cell malignancies such as primary effusion lymphoma (PEL) and multicentric Castleman's disease. Fujimuro, M. *et al., Nature Medicine* 9(3):300-306 (2003), have shown that LANA acts to stabilize β-catenin, apparently by redistribtution of the negative regular GSK-3 β. The present invention provides compounds and methods for inhibiting β-catenin protein interactions, *e.g.,* β-catenin/TCF complex formation. Thus, the compounds of the present invention thwart the LANA-induced accumulation of β-catenin/TCF complex and, at least in part, the consequences of KSHV infection. Accordingly, another aspect of the present invention provides a method of treating or preventing conditions due to infection by Karposi's sarcoma-associated herpesvirus (KSHV). Such conditions include KSHV-associated tumors, including Kaposi's sarcoma (KS) and primary effusion lymphoma (PEL). The method comprises administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic the present invention. In one embodiment the invention treats the KSHV-associated tumor, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject having a KSHV-associated tumor achieves a reduction in the severity, extent, or degree, etc. of the tumor. In another embodiment the invention prevents a

KSHV-associated tumor, *i.e.,* administration of a reverse-turn mimetic of the present invention to a subject that is anticipated to develop new or additional KSHV-associated tumors achieves a reduction in the anticipated severity, extent, or degree, etc. of the tumor. Optionally, the subject is a mammalian subject.

LEF/TCF DNA-binding proteins act in concert with activated β-catenin (the product of Wnt signaling) to transactivate downstream target genes. DasGupta, R. and Fuchs, E. *Development* 126(20):4557-68 (1999) demonstrated the importance of activated LEF/TCF complexes at distinct times in hair development and cycling when changes in cell fate and differentiation commitments take place. Furthermore, in skin morphogenesis, β-catenin has been shown to be essential for hair follicle formation, its overexpression causing the "furry" phenotype in mice (Gat, U., et al. *Cell* 95:605-614 (1998) and Fuchs, E. *Harvey Lect.* 94:47-48 (1999). *See also* Xia, X. et al. *Proc. Natl. Aad. Sci. USA* 98:10863-10868 (2001). Compounds of the present invention have been shown to inhibit the expression of Wnt signaling, and interfere with formation of β-catenin complexes. Accordingly, the present invention provides a method for modulating hair growth comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic the present invention, where the amount is effective to modulate hair growth in the subject. Optionally, the subject is a mammalian subject.

The present invention provides compounds useful in treating or preventing Alzheimer's disease. Alzheimer's disease (AD) is a neurodegenerative disease with progressive dementia. This disease is accompanied by three main structural changes in the brain, namely, i) intracellular protein deposits (also known as neurofibrillary tangles, or NFT), ii) extracellular protein deposits termed amyloid plaques that are surrounded by dystrophic neuritis, and iii) diffuse loss of neurons.

The compounds or compositions of the present invention rescue defectes in neuronal differentiation caused by a presenilin-1 mutation and may

decrease the number, or rate at which neuronal precursor populations differentiate to neurons in Alzheimer's brains. Presenilins are transmembrane proteins whose functions are related to trafficking, turnover and cleavage of Notch and Amyloid Precursor Protein. Missense mutations in presenilin 1 (PS-1) are associated with early-onset familial Alzheimer's disease (Fraser *et al.*, *Biochem. Soc. Symp.* **67,** 89 (2001)). The compounds of the present invention may be applicable not only to individuals with PS-1 familial Alzheimer's mutations, but also to general Alzheimer's patients.

In addition, the present invention provides a method for treating or preventing Alzheimer's disease comprising administering to a subject in need thereof a safe and effective amount of a reverse-turn mimetic of the present invention, where the amount is effective to treat or prevent Alzheimer's disease in the subject. Treating Alzheimer's disease is understood to encompass reducing or eliminating the manifestation of symptoms characteistic of Alzheimer's disease, or delaying the progression of this disease. Preventing Alzheimer's disease is understood to encompass preventing or delaying the onset of this disease.

A subject in need of treatment may be a human or non-human primate or other animal that is at various stages of Alzheimer's disease. Methods for diagnosing Alzheimer's disese are known in the art (*see, e.g.*, Dinsmore, *J. Am. Osteopath. Assoc. 99(9 Suppl.)*:S1-6, 1999; Kurz *et al.*, *J. Neural Transm. Suppl. 62*: 127-33, 2002; Storey *et al.*, *Front Viosci. 7*: e155-84, 2002; Marin *et al.*, *Geriatrics 57*: 36-40, 2002; Kril and Halliday, *Int. Rev. Neurobiol. 48*: 167-217, 2001; Gurwitz, *Trends Neurosci. 23*: 386, 2000; Muller-Spahn and Hock, *Eur. Arch. Psychiatry Clin. Neurosci. 249 Suppl. 3*: 37-42; Fox and Rossor, *Rev. Neuro. (Paris) 155 Suppl. 4*: S33-7, 1999), including the use of neuropsychological measures, functional imaging measures, biological markers, and autopsy of brain tissue. A subject in need of prevention may be a human or non-human primate or other animal that is at risk for developing Alzheimer's disease, such as an individual having a mutation of certain genes

responsible for this disease (*e.g.*, genes encoding amyloid precursor protein, presenilin 1, and presenilin 2), and/or a gene involved in the pathogenesis of this disease (*e.g.*, apolipoprotein E gene) (Rocchi *et al.*, *Brain Res. Bull. 61*: 1-24, 2003).

Compounds with structures as set forth in formula (I) may be screened for their activities in treating or preventing Alzheimer's disease by any appropriate methods known in the art. Such screening may be initially performed using *in vitro* cultured cells (*e.g*, PC-12 cells as described in Example 8). Compounds capable of rescuing defects in neuronal differentiation caused by a presenilin 1 mutation may be further screened using various animal models for Alzheimer's disease. Alternatively, compounds with structures as set forth in formula (I) may be directedly tested in animal models for Alzheimer's disease. Many model systems are known in the art and may be used in the present invention (*see, e.g.*, Rowan *et al.*, *Philos. Trans. R. Soc. Lond. B. Biol. Sci. 358*: 821-8, 2003; Lemere *et al.*, *Neurochem. Res. 28*: 1017-27, 2003; Sant'Angelo *et al.*, *Neurochem. Res. 28*: 1009-15, 2003; Weiner *Harv. Rev. Psychiatry 4*: 306-16, 1997). The effects of the selected compounds on treating or preventing Alzheimer's disease may be characterized or monitored by methods known in the art for evaluating the progress of Alzheimer's disease, including those described above for diagnosing this disease.

The present invention also provides methods for promoting neurite outgrowth. Such methods comprise the step of contacting a neuron with a compound according to formula (I) in an amount effective to promote neurite outgrowth. These methods are useful in treating neurodegenerative diseases (*e.g.*, glaucoma, macular degeneration, Parkinson's Disease, and Alzheimer's disease) and injuries to nervous system. A compound promotes neurite outgrowth if the neurite lengths of neurons are statistically significantly longer in the presence of the compound than those in the absence of the compound. Such a compound may be identified using *in vitro* cultured cells

(*e.g*, PC-12 cells, neuroblastoma B104 cell) (Bitar *et al.*, *Cell Tissue Res.* 298: 233-42, 1999; Pellitteri *et al.*, *Eur. J. Histochem. 45*: 367-76, 2001; Satoh *et al.*, *Biochem. Biophys. Res. Commun. 258*: 50-3, 1999; Hirata and Fujisawa, *J. Neurobiol. 32*:415-25, 1997; Chauvet *et al.*, *Glia 18*: 211-23, 1996; Vetter and Bishop, *Curr. Biol. 5*: 168-78, 1994; Koo *et al.*, *Proc. Natl. Acad. Sci. USA 90*: 4748-52, 1993; Skubitz *et al.*, *J. Cell Biol. 115*: 1137-48, 1991; O'Shea *et al.*, *Neuron 7*: 231-7, 1991; Rydel and Greene, *Proc. Natl. Acad. Sci. USA 85*: 1257-61, 1988) or using explants (Kato *et al.*, *Brain Res. 31*: 143-7, 1983; Vanhems *et al.*, *Eur. J. Neurosci. 2*: 776-82, 1990; Carri *et al.*, *Int. J. Dev. Neurosci. 12*: 567-78, 1994). Contacting a neuron with a compound according to the present invention may be carried out *in vitro* or *in vivo*. The resulting treated neuron, if generated *in vitro*, may be transplanted into a tissue in need thereof (Lacza *et al.*, *Brain Res. Brain Res. Protoc. 11*: 145-54, 2003; Chu *et al.*, *Neurosci. Lett 343*: 129-33, 2003; Fukunaga *et al.*, *Cell Transplant 8*: 435-41, 1999).

The present invention also provides methods for promoting differentiation of a neural stem cell comprising contacting a neural stem cell with a compound according to formula (I) in an amount effective to promote differentiation of a neural stem cell. Such methods are also useful in treating neurodegenerative diseases (*e.g.*, glaucoma, macular degeneration, Parkinson's Disease, and Alzheimer's disease) and injuries to nervous system. "Neural stem cell" refers to a clonogenic, undifferentiated, multipotent cell capable of differentiating into a neuron, an astrocyte or an oligodendrocyte under appropriate conditions. A compound promotes differentiation of neural stem cells if neural stem cells exhibit a statistically significantly higher degree of differentiation in the presence of the compound than in the absence of the compound. Such a compound may be identified using assays involving *in vitro* cultured stem cells or animal models (Albranches *et al.*, *Biotechnol. Lett. 25*: 725-30, 2003; Deng *et al.*, *Exp. Neurol. 182*: 373-82, 2003; Munoz-Elias *et al.*, *Stem Cells 21*: 437-48, 2003; Kudo *et al.*, *Biochem. Pharmacol. 66*: 289-95,

2003; Wan *et al.*, *Chin. Med. J. 116*: 428-31, 2003; Kawamorita *et al.*, *Hum. Cell 15*: 178-82, 2002; Stavridis and Smith, *Biochem. Soc. Trans. 31*: 45-9, 2003; Pachernik *et al.*, *Reprod. Nutr. Dev. 42*: 317-26, 2002; Fukunaga *et al.*, *supra*). The neural stem cell may be a cultured stem cell, a stem cell freshly isolated from its source tissue, or a stem cell within its source organism. Thus, contacting the neural stem cell with a compound according to the present invention may be carried out either *in vitro* (for a cultured or freshly isolated stem cell) or *in vivo* (for a stem cell within its source organism). The resulting differentiated neural cell, if generated *in vitro*, may be transplanted into a tissue in need thereof (Lacza *et al.*, *supra*; Chu *et al.*, *supra*; Fukunaga *et al.*, *supra*). Such a tissue includes a brain tissue or other nervous tissue that suffers from a trauma or a neurodegenerative disease.

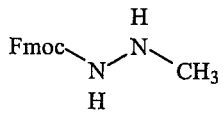
The following non-limiting examples illustrate the compounds, compositions, and methods of use of this invention.

EXAMPLES

PREPARATION EXAMPLE 1

PREPARATION OF (*N*-FMOC-*N'*-R_3-HYDRAZINO)-ACETIC ACID

(1) Preparation of *N*-Fmoc-*N'*-Methyl Hydrazine

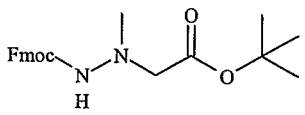


2 L, two-neck, round-bottomed-flask was fitted with a glass stopper and a calcium tube. A solution of methylhydrazine sulfate (20 g, 139 mmol, where R_3 is methyl) in THF (300 mL) was added and a solution of DiBoc (33 g, 153 mmol) in THF was added. Saturated sodium bicarbonate aqueous solution (500mL) was added dropwise via addition funnel over 2 hours with vigorous stirring. After 6 hours, a solution of Fmoc-Cl (39 g, 153 mmol) in THF

was added slowly. The resulting suspension was stirred for 6 hours at 0°C. The mixture was extracted with ethyl acetate (EA, 500 mL) and the organic layer was retained. The solution was dried with sodium sulfate and evaporated *in vacuo*. The next step proceeded without purification.

A 1 L, two-necked, round-bottom-flask was fitted with a glass stopper and a calcium tube. A solution of the product from the previous step in MeOH (300mL) was added and conc. HCl (30 mL, 12 N) was added slowly via addition funnel with magnetic stirring in ice water bath and stirred overnight. The mixture was extracted with EA (1000 mL) and the organic layer was retained. The solution was dried with sodium sulfate and evaporated *in vacuo*. The residue was purified by recrystallization with n-hexane and EA to give *N*-Fmoc-*N'*-methyl hydrazine (32.2 g, 83 %). ^{1}HNMR (DMSO-D6) δ 7.90~7.88 (d, *J*=6 Hz, 2H,), δ 7.73~7.70 (d, *J*=9 Hz, 2H,), 7.44~7.31 (m, 4H), 4.52~4.50 (d, *J*=6 Hz, 2H), 4.31~4.26 (t, *J*=6 Hz, 1H), 2.69 (s, 1H).

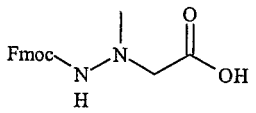
(2) Preparation of (*N*-Fmoc-*N'*-methyl-hydrazino)-acetic acid t-butyl ester



1 L, two-necked, round-bottom-flask was fitted with a glass stopper and reflux condenser connected to a calcium tube. A solution of *N*-Fmoc-*N'*-methyl hydrazine (20 g, 75 mmol) in toluene (300 mL) was added. A solution of t-butylbromo acetate (22 g, 111 mmol) in toluene (50 mL) was added slowly. Cs_2CO_3 (49 g, 149 mmol) was added slowly. NaI (11 g, 74 mmol) was added slowly with vigorous stirring. The reaction mixture was stirred at reflux temperature over 1 day. The product mixture was filtered and extracted with EA (500 mL). The solution was dried over sodium sulfate and evaporated *in vacuo*. The product was purified by chromatography with hexane:EA = 2 : 1 solution to give (*N*-Fmoc-*N'*-methyl-hydrazino)-acetic acid t-butyl ester (19.8 g, 70 %).

^{1}H-NMR ($CDCl_3$-d) δ 7.78~7.75 (d, *J*=9 Hz, 2H,), δ 7.61~7.59 (d, *J*=6 Hz, 2H,), 7.43~7.26 (m, 4H), 4.42~4.40 (d, *J*=6 Hz, 2H), 4.23 (b, 1H), 3.57 (s, 2H), 2.78 (s, 3H), 1.50 (s, 9H).

(3) Preparation of (*N*-Fmoc-*N'*-methyl-hydrazino)-acetic acid

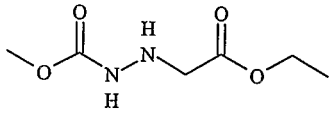


1 L, two-neck, round-bottomed-flask was fitted with a glass stopper and reflux condenser connected to a calcium tube. (*N*-Fmoc-*N'*-methyl-hydrazino)-acetic acid t-butyl ester (20 g, 52 mmol) was added. A solution of HCl (150 mL, 4 M solution in dioxane) was added slowly with vigorous stirring in an ice water bath. The reaction mixture was stirred at RT over 1 day. The solution was concentrated completely under reduced pressure at 40°C. A saturated aq. $NaHCO_3$ solution (100 mL) was added and the aqueous layer was washed with diethyl ether (100 mL). Conc. HCl was added dropwise slowly at 0°C (pH 2-3). The mixture was extracted and the organic layer was retained (500 mL, MC). The solution was dried with sodium sulfate and evaporated *in vacuo*. The residue was purified by recrystallization with n-hexane and ethyl acetate to give (*N*-Fmoc-*N'*-methyl-hydrazino)-acetic acid (12 g, 72 %). ^{1}H-NMR (DMSO-d_6) δ 12.38 (s, 1H), 8.56 (b, 1H), 7.89~7.86 (d, *J*=9 Hz, 2H,), 7.70~7.67 (d, *J*=9 Hz, 2H,), 7.43~7.29 (m, 4H), 4.29~4.27 (d, *J*=6 Hz, 2H), 4.25~4.20 (t, *J*=6 Hz, 1H), 3.47 (s, 2H), 2.56 (s, 3H).

PREPARATION EXAMPLE 2

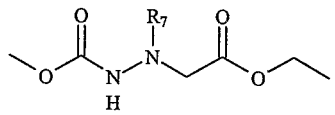
PREPARATION OF (*N*-MOC-*N'*-R_7-HYDRAZINO)-ACETIC ACID

(1) Preparation of (*N'*-Methoxycarbonyl-hydrazino)-acetic acid ethyl ester



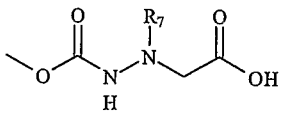
MOC-NH-NH_2 (50g, 0.55 mol) was dissolved in DMF (300ml), and then ethyl bromoacetate (68ml, 0.555 mol) and potassium carbonate (77g, 0.555mol) were added to the reaction vessel. The mixture was warmed to 50°C for 5 hours. After the reaction was completed, the mixture was filtered, and diluted with EtOAc, and washed with brine (3 times). The crude product was purified by column (eluent : Hex/EtOAc = 4/1) to provide 72 of colorless oil.

(2) [*N*-R_7-*N'*-methoxycarbonyl-hydrazino]-acetic acid ethyl ester



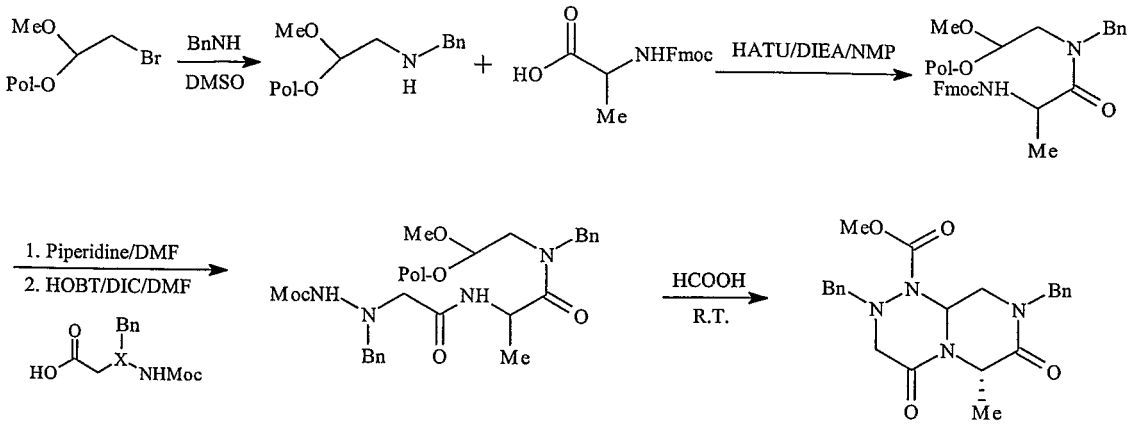
The ethyl ester (10g, 0.05 mol), potassium carbonate (6.9g, 0.05mol), and R_7-bromide (14.1g, 0.06mol) were dissolved in DMF (200ml), and The mixture was warmed to 50°C for 5hours. After the reaction was completed, the mixture was filtered, and diluted with EA, and washed with brine (3 times). The crude product was purified by Chromatography (eluent : Hex/EtOAc = 4/1).

(3) [*N*-R_7-*N'*-methoxycarbonyl-hydrazino]-acetic acid

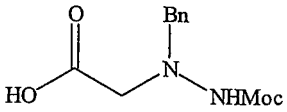


The alkylated ethyl ester (9.5g, 0.03mol) was dissolved in THF/water (1/1, ml), and added 2N NaOH (28.3ml) solution at 0 °C. The mixture was stirred at RT for 2 hours. After the starting ester was not detected on UV, the solution was diluted with EA, then separated. The aqueous layer was acidified to pH 3~4 by 1N HCl, and the compound was extracted by DCM (3 times). The combined organic layer was dried over MgSO4, and evaporated to give a yellow solid.

EXAMPLE 1



(1) Preparation of N^{β}-Moc-N^{α}-benzyl-hydrazinoglycine



This compound was prepared according to literature procedure. (Cheguillaume et. al., *Synlett* 2000, 3, 331)

(2) Preparation of 1-Methoxycarbonyl-2,8-dibenzyl-6-methyl-4,7-dioxo-hexahydro-pyrazino[2,1-c][1,2,4]triazine

Bromoacetal resin (60 mg, 0.98 mmol/g) and a solution of benzyl amine in DMSO (2.5 ml, 2 M) were placed in vial with screw cap. The reaction mixture was shaken at 60 °C using rotating oven [Robbins Scientific] for 12 hours. The resin was collected by filtration, and washed with DMF, then DCM, to provide a first component piece.

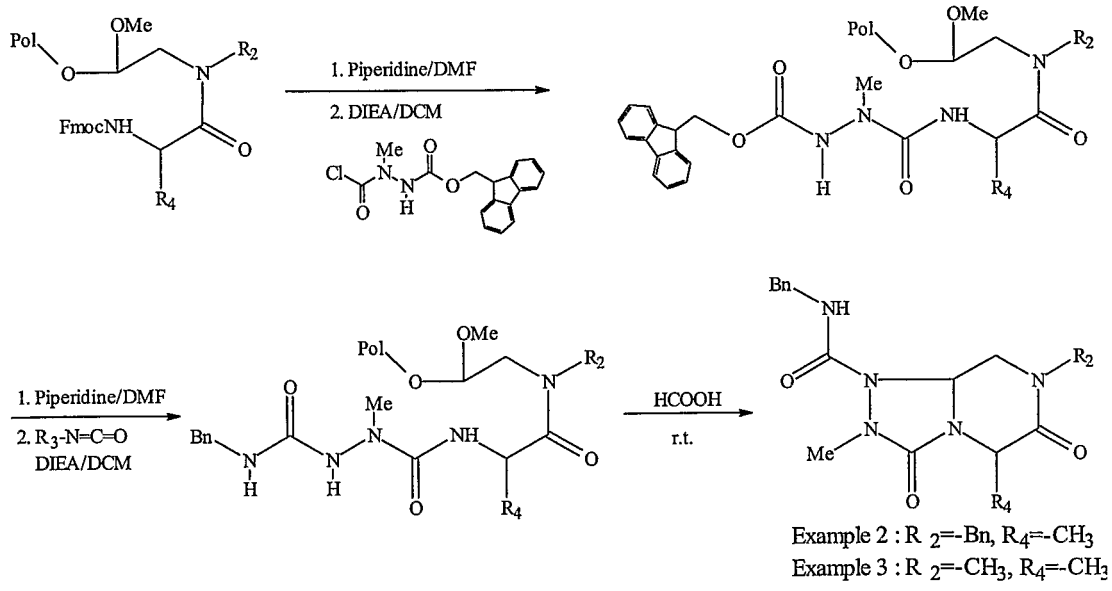
A solution of Fmoc-alanine (4 equiv., commercially available, the second component piece), HATU (PerSeptive Biosystems, 4 equiv.), and DIEA (4 equiv.) in NMP (Advanced ChemTech) was added to the resin. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

To the resin was added 20% piperidine in DMF. After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

A solution of N^{β}-Moc-N^{α}-benzyl-hydrazinoglycine (4 equiv., compound (3) in preparative example 2, where R_7 is benzyl, 3rd component piece), HOBT [Advanced ChemTech] (4 equiv.), and DIC (4 equiv.) in DMF was added to the resin prepared above. After the reaction mixture was shaken for 3 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then MeOH. The resin was dried *in vacuo* at room temperature.

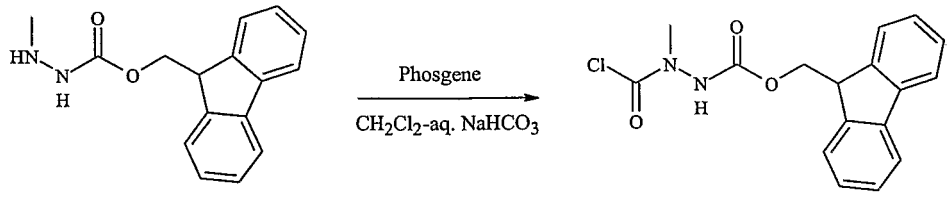
The resin was treated with formic acid (2.5 ml) for 18 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under reduced pressure to give the product as an oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ ppm; 1.51 (d, 3H), 2.99 (m, 1H), 3.39 (d, 1H), 3.69 (m, 1H), 3.75 (m, 1H), 3.82 (s, 3H), 4.02 (d, 1H), 4.24 (d, 1H), 4.39 (d, 1H), 4.75 (d, 1H), 5.14 (q, 1H), 5.58 (dd, 1H), 7.10-7.38 (m, 10H).

EXAMPLE 2



Example 2 : R_2=-Bn, R_4=-CH_3
Example 3 : R_2=-CH_3, R_4=-CH_3

(1) Preparation of *N'*-Fmoc-*N*-methyl-hydrazinocarbonyl chloride



An ice-cooled biphasic mixture of N-methyl hydrazine carboxylic acid 9H-fluoren-9-ylmethyl ester (107 mg, 0.4 mmol) in 15 ml of CH_2Cl_2 and 15 ml of saturated aq. $NaHCO_3$ was rapidly stirred while 1.93 M phosgene in toluene (1.03 ml, 2 mmol) was added as a single portion. The reaction mixture was stirred for 30 min, the organic phase was collected, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford 128 mg (97 %) of carbamoyl chloride as a foamy solid. [Caution: Phosgene vapor is highly toxic. Use it in a hood]. This product was used for the following solid phase synthesis without further purification.

(2) Preparation of 2,5-Dimethyl-7-benzyl-3,6-dioxo-hexahydro-[1,2,4]triazolo[4,5-a]pyrazine-1-carboxylic acid benzylamide

Bromoacetal resin (30 mg, 0.98 mmol/g) and a solution of benzyl amine in DMSO (1.5 ml, 2 M) were placed in vial with screw cap. The reaction mixture was shaken at 60 °C using rotating oven [Robbins Scientific] for 12 hours. The resin was collected by filtration, and washed with DMF, then DCM, to provide the first component piece.

A solution of Fmoc-alanine (3 equiv., second component piece, commercially available), HATU (PerSeptive Biosystems, 3 equiv.), and DIEA (3 equiv.) in NMP (Advanced ChemTech) was added to the resin. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF, to thereby add the second component piece to the first component piece.

To the resin was added 20% piperidine in DMF. After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

A solution of *N'*-Fmoc-*N*-methyl-hydrazinocarbonyl chloride (combined third and fourth component pieces, 5 equiv.) obtained in the above step (1), DIEA (5 equiv.) in DCM was added to the resin prepared above. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and DMF.

To the resin was added 20% piperidine in DMF (10 ml for 1 g of the resin). After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

The resin was treated with a mixture of benzyl isocyanate (4 equiv.) and DIEA (4 equiv.) in DCM for 4 hours at room temperature. Then, the resin was collected by filteration and washed with DMF, DCM, and then MeOH. The resin was dried *in vacuo* at room temperature.

The resin was treated with formic acid for 14 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under reduced pressure to give the product as an oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ ppm; 1.48 (d, 3H), 2.98 (s, 3H), 3.18 (m, 1H), 3.46 (m, 1H), 4.37-4.74 (m, 5H), 5.66 (dd, 1H), 6.18 (m, 1H), 7.10-7.40 (m, 10H).

EXAMPLE 3

PREPARATION OF 2,5,7-TRIMETHYL-3,6-DIOXO-HEXAHYDRO-[1,2,4]TRIAZOLO[4,5-A]PYRAZINE-1-CARBOXYLIC ACID BENZYLAMIDE

The title compound is prepared according to the same procedure as described in Example 2, but reacting bromoacetal resin with a solution of methyl amine instead of benzyl amine. ^{1}H-NMR (400 MHz, $CDCl_3$) δ ppm; 1.48 (d, 3H), 2.99 (s, 3H), 3.03 (s, 3H), 3.38 (m, 1H), 3.53 (dd, 1H), 4.36 (dd,

1H), 4.52 (q, 1H), 4.59 (dd, 1H), 5.72 (dd, 1H), 6.19 (br.t, 1H), 7.10-7.38 (m, 5H).

EXAMPLE 4

PREPARATION OF 2-METHYL-5-(*P*-HYDROXYPHENYLMETHYL)-7-NAPHTHYLMETHYL-3,6-DIOXO-HEXAHYDRO-[1,2,4]TRIAZOLO[4,5-A]PYRAZINE-1-CARBOXYLIC ACID BENZYLAMIDE

Bromoacetal resin (30 mg, 0.98 mmol/g) and a solution of naphthylmethyl amine in DMSO (1.5 ml, 2 M) were placed in vial with screw cap. The reaction mixture was shaken at 60°C using rotating oven [Robbins Scientific] for 12 hours. The resin was collected by filtration, and washed with DMF, then DCM to provide the first component piece.

A solution of Fmoc-Tyr(OBut)-OH (3 equiv.), HATU (PerSeptive Biosystems, 3 equiv.), and DIEA (3 equiv.) in NMP (Advanced ChemTech) was added to the resin. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF, to thereby add the second component piece to the first component piece.

To the resin was added 20% piperidine in DMF. After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

A solution of *N'*-Fmoc-*N*-methyl-hydrazinocarbonyl chloride (5 equiv.), DIEA (5 equiv.) in DCM was added to the resin prepared above. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and DMF.

To the resin was added 20% piperidine in DMF (10 ml for 1 g of the resin). After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

The resin was treated with a mixture of benzyl isocyanate (4 equiv.) and DIEA (4 equiv.) in DCM for 4 hours at room temperature. Then, the resin was collected by filteration and washed with DMF, DCM, and then MeOH. The resin was dried *in vacuo* at room temperature.

The resin was treated with formic acid for 14 hours at room temperature. After the resin was removed by filtration, the filtrate was condensed under reduced pressure to give the product as an oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ ppm; 2.80-2.98 (m, 5H), 3.21-3.37 (m, 2H), 4.22-4.52 (m, 2H), 4.59 (t, 1H), 4.71 (d, 1H), 5.02 (dd, 1H), 5.35 (d, 1H), 5.51 (d, 1H), 6.66 (t, 2H), 6.94 (dd, 2H), 7.21-8.21 (m, 12H).

EXAMPLE 5

PREPARATION OF 2-METHYL-6-(*P*-HYDROXYPHENYLMETHYL)-8-NAPHTHYL-4,7-DIOXO-HEXAHYDRO-PYRAZINO[2,1-C][1,2,4]TRIAZINE-1-CARBOXYLIC ACID BENZYLAMIDE

Bromoacetal resin (60 mg, 0.98 mmol/g) and a solution of naphthyl amine in DMSO (2.5 ml, 2 M) were placed in vial with screw cap. The reaction mixture was shaken at 60 °C using rotating oven [Robbins Scientific] for 12 hours. The resin was collected by filtration, and washed with DMF, then DCM.

A solution of Fmoc- Tyr(OBut)-OH (4 equiv.), HATU [PerSeptive Biosystems] (4 equiv.), and DIEA (4 equiv.) in NMP (Advanced ChemTech) was added to the resin. After the reaction mixture was shaken for 4 hours at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

To the resin was added 20% piperidine in DMF. After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

A solution of N^{β}-Fmoc-N^{α}-benzyl-hyrazinoglycine (4 equiv.), HOBT [Advanced ChemTech] (4 equiv.), and DIC (4 equiv.) in DMF was added to the resin prepared above. After the reaction mixture was shaken for 3 hours

at room temperature, the resin was collected by filtration and washed with DMF, and then DCM. To the resin was added 20% piperidine in DMF (10 ml for 1 g of the resin). After the reaction mixture was shaken for 8 min at room temperature, the resin was collected by filtration and washed with DMF, DCM, and then DMF.

The resin was treated with a mixture of benzyl isocyanate (4 equiv.) and DIEA (4 equiv.) in DCM for 4 hours at room temperature. Then, the resin was collected by filteration and washed with DMF, DCM, and then MeOH. After the resin was dried *in vacuo* at room temperatur, the resin was treated with formic acid (2.5 ml) for 18 hours at room temperature. The resin was removed by filtration, and the filtrate was condensed under reduced pressure to give the product as an oil.

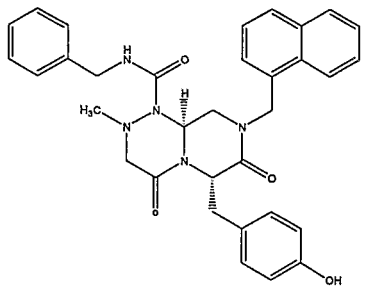
^{1}H-NMR (400 MHz, $CDCl_3$) δ ppm; 2.73 (s, 3H), 3.13 (d, 1H), 3.21-3.38 (m, 3H), 3.55 (d, 1H), 3.75 (t, 1H), 4.22 (dd, 1H), 4.36 (dd, 1H), 4.79 (d, 1H), 5.22 (t, 1H), 5.47 (m, 2H), 6.68 (d, 2H), 6.99 (d, 2H), 7.21-8.21 (m, 12H);

MS (m/z, ESI) 564.1 (MH^+) 586.3 (MNa^+).

EXAMPLE 6

BIOASSAY FOR THE MEASUREMENT OF IC_{50} AGAINST SW480 CELLS AND CYTOTOXICITY TEST ON THE CELL LINES

The test compound (Compound A) used in this example was prepared in Example 4.



a. Reporter Gene Assay

SW480 cells were transfected with the usage of Superfect™ transfect reagent (Qiagen, 301307). Cells were trypsinized briefly 1 day before transfection and plated on 6 well plate (5 x 10^5 cells/well) so that they were 50-80% confluent on the day of transfection.

Four microgram (TOPFlash) and one microgram (pRL-null) of DNAs were diluted in 150 μl of serum-free medium, and 30 μl of Superfect™ transfect reagent was added. The DNA-Superfect mixture was incubated at room temperature for 15 min, and then, 1 ml of 10 % FBS DMEM was added to this complex for an additional 3 hours of incubation. While complexes were forming, cells were washed with PBS twice without antibiotics.

The DNA-Superfect™ transfect reagent complexes were applied to the cells before incubating at 37 °C at 5 % CO_2 for 3 hours. After incubation, recovery medium with 10 % FBS was added to bring the final volume to 1.18 ml. After 3 hours incubation, the cells were harvested and reseeded to 96 well plate (3 x 10^4 cells/well). After overnight incubation at 37 °C at 5 % CO_2, the cells were treated with Compound A for 24 hours. Finally, the activity was checked by means of luciferase assay (Promega, E1960).

Figure 3 illustrates the results of the measurement of IC_{50} of Compound A for SW480 cells.

b. Sulforhodamine B (SRB) assay

Growth inhibitory effect of Compound A on the cells listed below was measured by the sulforhodamine B assay. SW480 cells in 100 μl media were plated in each well of 96-well plate and allowed to attach for 24 hours. Compound A was added to the wells to produce the desired final concentrations, and the plates were incubated at 37 °C for 48 hours. The cells were then fixed by gentle addition of 100 μl of cold (4 °C) 10% trichloroacetic acid to each well, followed by incubation at 4 °C for 1 hour. Plates were washed with deionized water five times and allowed to air dry. The cells were

then stained by addition of 100 µl SRB solution (0.4% SRB(w/v) in 1% acetic acid (v/v)) to wells for 15 min. After staining, the plates were quickly washed five times with 1% acetic acid to remove any unbound dye, and allowed to air dry. Bound dye was solubilized with 10 mmol/L Tris base (pH 10.5) prior to reading the plates. The optical density (OD) was read on a plate reader at a wavelength of 515nm with Molecular Device. Inhibition of growth was expressed as relative viability (% of control) and GI_{50} was calculated from concentration-response curves after log/probit transformation.

Table 6 shows *in vitro* cyctotoxicity (SRB) assay data for Compound A obtained in Example 4. The values in Table 6 are in µg/ml.

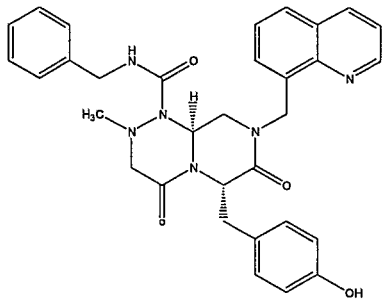
TABLE 6

Origin	Cell	Example 4	Cisplatin	5-FU
Colon	T84	1.134	> 10	1.816
	LOVO	0.532	> 10	1.029
	HT29	1.694	> 10	5.334
	DLD-1	1.775	> 10	> 10
	COLO205	1.136	> 10	1.130
	CACO-2	1.201	> 10	0.451
	SW480-Kribb	1.137	> 10	> 10
	SW480-CWP	0.980	4.502	> 10
	SW620	1.426	> 10	5.570
	KM12	1.451	> 10	2.729
	HCT15	2.042	> 10	1.179
	HCT116	0.96	> 10	1.039
	HCC2998	1.047	> 10	5.486
	786-0	1.417	3.347	0.584
Leukemia	HL60	1.243	> 10	7.010
	RPMI8226	1.1.177	> 10	> 10
	K562/VIN	1.640	> 10	7.071
	K562/ADR	7.682	> 10	> 10
	K562	1.247	> 10	6.133
Prostate	PC3	1.207	> 10	> 10
	HT1080	1.469	> 10	0.798
Lung	A549	1.386	> 10	1.007
	NCI H460	1.498	> 10	1.397
	NCI H23	1.296	5.176	2.254
Renal	293	0.731	6.641	2.015
	CAKI-1	0.467	> 10	0.925
	ACHN	1.263	5.019	5.062
Melanoma	RPMI7951	0.936	5.010	0.920
	M14	2.289	3.447	1.225
	HMV-II	4.834	3.190	0.695
	HMV-I	1.153	5.478	2.110
	G361	0.584	4.827	1.539
	CRL1579	1.830	0.699	> 10
	A431	1.083	3.722	0.404
	A253	1.398	2.084	2.926
	UACC62	0.563	> 10	1.093
	SK-MEL-28	1.291	> 10	> 10
	SK-MEL-5	0.888	> 10	2.434
	LOX-IMVI	1.526	> 10	> 10
	A375	1.391	> 10	1.464
Breast	MCF7/ADR	9.487	9.907	> 10
	MCF7	7.355	> 10	1.751

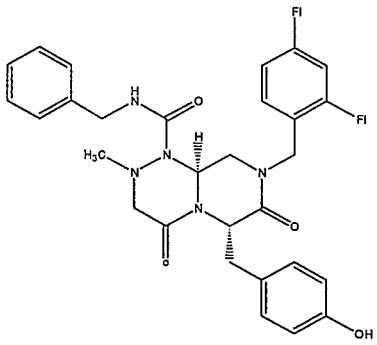
EXAMPLE 7

MIN MOUSE MODEL

Selected compounds of the present invention (Compound B and Compound C) were evaluated in the min mouse model to evaluate their efficacy as anit-cancer agents.



Compound B



Compound C

The min mouse model is a widely used model to test for this type of efficacy. The numbers of polyp formed in small intestine and colon of these mice after various treatments were measured (Table 7). The data shown that both compounds, when administered at about 300 mpk, reduce the number of polyp in min mice compared to those in the control mice treated with vehicle only.

TABLE 7

MIN MOUSE MODEL DATA

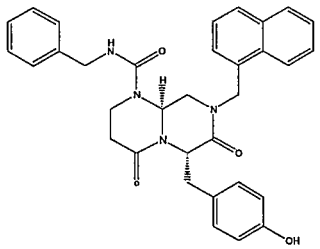
Group	Polyp Number (Mean ± S.D.)	*P* (total)	% Inhibition

	Small Intestine	Colon	Total	Vs. VH	vs. VH
Wild Type	0.0±0.0	0.0±0.0	0.0±0.0	-	-
Vehicle	65.8±15.9	1.8±1.5	67.7±15.3	-	-
Compound C -100 mpk	69.2±20.8	1.7±1.5	71.4±23.0	-	-
Compound C -300 mpk	46.1±17.1	1.1±1.2	47.0±16.9	<0.01	31
Compound B -300 mpk	45.2±22.1	1.4±0.9	46.8±17.0	<0.01	31
Sulindac -160 ppm	48.0±20.7	0.5±0.5	48.5±20.9	<0.05	28

EXAMPLE 8

CHEMOGENOMIC INHIBITION OF CBP/β-CATENIN INTERACTION RESCUES DEFECTS IN NEURONAL DIFFERENTIATION CAUSED BY A PRESENILIN-1 MUTATION

The following compound (Compound D) was used in this example:



Materials and Methods

Plasmids. TOPFLASH and FOPFLASH reporter constructs were transformed into DH5α competent cells by standard protocol. Plasmids used for transfection assays were isolated and purified using EndoFree Maxi Kit (Qiagen, Valencia, CA).

PC-12 Cell Culture. PC-12 cells were maintained in RPMI 1640 supplemented with 10% horse serum, 5% fetal bovine serum, 4.5 g/L glucose,

2 mM L-glutamine, 1.0 mM sodium pyruvate and 10 µg/ml penicillin-streptomycin.

Cell Differentiation. Cell culture dishes were pre-coated overnight with 0.25 mg/ml collagen (Cohesion, CA), 10 µg/ml Poly-L-Lysine (Sigma-Aldrich, St. Louis, MO) and 12 µg/ml Polyethyleneimine (ICN, La Mesa, CA). Cells were cultured on coated dishes at 15,000 cells/cm^2, and differentiated into a neuron-like phenotype by incubation in medium with reduced serum (1% fetal bovine serum), containing 50 ng/ml nerve growth factor (NGF) (Sigma-Aldrich) for 10 days. NGF-containing medium was changed every 2-3 days.

Treatment with Compound D. Compound D, a small molecule inhibitor of β-catenin/CBP interaction, was dissolved in DMSO at a stock concentration of 100 mM. Differentiated PC-12/L286V cells were treated with increasing concentrations of this compound for 4 hours. Transfection was then initiated after this treatment period. For cell differentiation experiments, Compound D was added at a concentration of 10 µM, together with NGF, for the entire differentiation period.

Transfection. PC-12 cells were cultured and differentiated on 60-mm dishes. At the end of the 10-day differentiation period, cells were transfected with 2 µg reporter constructs, TOPFLASH and FOPFLASH, per 60-mm dish. Transfections were performed using Superfect (Qiagen) according to manufacturer's instructions.

Luciferase Assays. Cells were lysed, 6 hours after transfections, in 100 µl of Cell Culture Lysis Reagent (Promega, Madison, WI), and scraped into microcentrifuge tubes. Tubes were then centrifuged briefly (about 10 seconds) at 12000 rpm to pellet cell debris. Luciferase activity was measured on 20 µl of cell lysate and 100 µl substrate from the Luciferase Assay System (Promega). Luciferase activity was measure using Packard LumiCount. (Hewlett Packard). Quantitation of luciferase was performed in triplicates, and repeated in at least three independent experiments.

Immunofluorescence. Cells were plated at a density of 10,000 cells/cm^2 on sterile coated 22x22 mm coverslips in a 6-well culture plate. Differentiation was initiated, as previously described, for 10 days. The differentiated cells were then fixed in methanol for 15 minutes at -20°C. This is followed by a 15 minutes incubation with PBS + 0.1% Triton X-100. The coverslips were incubated with antibodies raised against Ephrin B2 Receptor (Santa Cruz Biotechnology) and Gap-43 (Novus Biologicals) for 40 minutes at 37°C. After a series of washes with PBS-Triton X-100, secondary antibody conjugated to FITC (Jackson ImmunoResearch, Westgrove, PA) was applied. All slides images were acquired using a Nikon PCM2000 Laser Scanning Confocal Microscope mounted on a Nikon Eclipse E600 upright microscope (Nikon, Melville, NY).

Quantitation of Neurite Outgrowth. Cell counts were taken from six randomly chosen microscopic fields (10x). In each field, total number of cells, as well as cells that displayed neurites greater than twice the length of the cell body was determined. The number of cells with such outgrowths was then expressed as a percentage of the total number of cells. Values obtained were from duplicates of three independent experiments.

RT-PCR. To analyze the mRNA levels for Ephrin B2 (EphB2) receptor, total RNA was isolated using Trizol (Invitrogen-GIBCO-BRL, Baltimore, MD) from differentiated cells. 2 µg RNA was reverse transcribed in a total volume of 20 µl with random hexamer (50 ng), and using the Superscript II reverse transcription system (Invitrogen-GIBCO-BRL), according to manufacturer's guidelines. PCR was carried out in a 50 µl volume containing 5 µl cDNA, 100 pmol primers, 100 µM dNTPs, 1X *Taq* buffer and 1.5 mM $MgCl_2$. Reaction mixtures were heated to 80°C for 10 min, after which *Taq* was added. cDNAs were amplified for 25 (EphB2 receptor) or 15 (GAPDH) cycles. One round of amplification consisted of 1 min at 94°C, 2 min at 60°C, and 2 min at 72°C, with a final extension time of 10 min at 72°C. The PCR products were resolved and visualized by electrophoresis in a 2% gel, stained with ethidium

bromide. EphB2 receptor PCR primers used were, 5' – CACTACTGGACCGCACGATAC – 3' and 5' – TCTACCGACTGGATCTGGTTCA – 3'. Primer pairs for GAPDH were 5' – GGTGCTGAGTATGTCGTGGA – 3' and 5' – ACAGTGTTCTGGGTGGCAGT – 3'.

Results

Rat PC-12 cells are derived from the neural crest lineage and upon nerve growth factor (NGF) treatment, undergo differentiation to a neurite-bearing sympathetic-like neuron (Greene and Tischler, *Proc Natl Acad Sci U S A* **73,** 2424 (1976)). Utilizing a PC-12 cell based model, the effects of an early-onset FAD associated PS-1 mutation, PS-1/L286V, on TCF/β-catenin mediated transcription and neuronal differentiation were characterized. It has been demonstrated that specifically blocking transcription mediated by TCF/β-catenin/CBP alleviates PS-1 induced defects in neuronal differentiation.

PC-12 cells stably overexpressing either wild type PS-1 (PS-1/WT) or mutant PS-1 (PS-1/L286V) and a vector-transfected control cell line (Guo *et al.*, *Neuroreport,* **8,** 379 (1996)) were plated on dishes coated with collagen, poly-L-lysine and poly-etheleneimine. Differentiation was induced by treatment with 50ng/ml of NGF for 10 days. Overexpressing PS-1/WT cells or the vector-transfected cells had extensive neurite formation (similar to PC-12 cell clones from ATCC), whereas the PS-1/L286V mutant cells had only stubby neurite formation (Fig.4 A-C). Additionally, vector-transfected PC-12 control and PS-1/WT cells displayed extensive expression of the neuronal differentiation marker GAP-43 (Gorgels *et al.*, *Neurosci Lett.* **83,** 59 (1987)) (Fig.4 D,E), whereas the PS-1/L286V cells were essentially devoid of this marker (Fig.4 F).

To assess the effects of the PS-1/L286V mutation on canonical Wnt/β-catenin signaling, we transiently transfected NGF treated PC-12 cells with Topflash, a Wnt/β-catenin signaling reporter construct (Morin *et al.*,

Science **275**, 1787 (1997)). As seen in Figure 4F, the overexpressing PS-1/WT cells had similar levels of TCF/β-catenin signaling compared to the vector control cells. However, the PS-1/L286V mutant cells displayed significantly (10-fold) increased Topflash expression. In contrast, the negative control reporter construct Fopflash did not show any significant differences.

It was hypothesized that dysregulated TCF/β-catenin signaling in the PS-1/L286V mutant cells was responsible for the defective differentiation and neurite outgrowth. To test this hypothesis, a specific small molecule inhibitor of TCF/β-catenin signaling, Compound D (Emami *et al.,* Cancer Cell, in press), was used. This small molecule selectively blocks the β-catenin/CBP interaction, but not the β-catenin/p300 interaction, thereby interrupting a subset of TCF/β-catenin transcription. Treatment of the PS-1/L286V mutant cells with 10μM Compound D plus NGF decreased TCF/β-catenin reporter gene transcription, and led to essentially normal neurite outgrowth and differentiation (Fig.5 A), similar to that seen in the overexpressing PS-1/WT cells (Figs.5 A, B), as compared to the untreated cells (Fig.4 C). Furthermore, PS-1/L286V mutants treated with Compound D showed similar intense GAP-43 staining to the PS-1/WT and vector-transfected cells (Fig.4 B). To demonstrate that Compound D treated mutant cells develop neurites similar to that of the vector control or PS-1/WT cells, cells that had neurites greater than twice the length of the cell body were counted. Treatment with Compound D substantially increased the percentage of cells bearing neurites to levels similar to that of the vector-transfected and overexpressing PS-1/WT cells (Fig.5 C). It is concluded that blocking transcription mediated by TCF/β-catenin/CBP corrects many of the phenotypic defects in neurite outgrowth and neuronal differentiation due to the PS-1/L286V mutation.

Ephrin B2 receptors (EphB2) have been implicated in synapse formation (Wilkinson, *Nat. Rev. Neurosci.* **2,** 155 (2001)) and the Ephrin A family has recently been shown to play a role in hippocampal dendritic spine morphology (Murai *et al.*, *Nat. Neurosci.* **6,** 153 (2003)). Focused EphB2

expression was observed, which localized with neuronal processes in the vector and PS-1/WT-transfected cells (Fig.6 A, B), whereas the PS-1/L286V mutant cells demonstrated very weak and diffuse EphB2 signal (Fig. 6 C). Increased TCF/β-catenin signaling in PS-1/L286V mutant cells manifested itself in decreased EphB2 expression as judged by RT-PCR (Fig.6 E, lane 3). Furthermore, addition of 10μM Compound D led to increased EphB2 message (Fig.6 E, lane 4) as well as EphB2 expression in these cells (Fig.6 D). These results are consistent with the data of Batlle and colleagues (Batlle *et al.*, *Cell* **111,** 251 (2002)) who recently showed that expression of EphB2/EphB3 receptors and their ligand ephrin-B1 is inversely controlled in colonic crypts via TCF/β-catenin transcription, and that proper regulation is important for appropriate cell proliferation, differentiation and sorting. We present evidence that the PS-1/L286V mutation via increased TCF/β-catenin signaling, decreased the expression of EphB2 receptors and this is corrected by Compound D mediated inhibition of the β-catenin/CBP interaction.

EXAMPLE 9

COMPOUND D CAUSES A G1/S-PHASE ARREST AND ACTIVATES CASPASE ACTIVITY

Flow Cytometric Analysis (FACS)

For FACS analysis, approx. 5 X 10^6 cells from Compound D-treated or vehicle-treated were fixed with 70% chilled ethanol and stored at -20 °C for at least 30 minutes. The cells were washed once with 1x PBS and incubated with propidium iodine (PI) solution (85 μg/ml propidium iodine, 0.1% Nonidet P-40, 10 mg/ml RNAse) for 30 minutes at room temperature. 10,000 stained cells for each sample were acquired using Beckman Coulter EPICS XL-MCL Flow Cytometry and the percentage of cells in different phase of the cell cycle was determined by Expo32 ADC software (Coulter Corporation, Miami, Florida, 33196).

Caspase-3 Activity Assay

SW480, HCT116, and CCD18Co cells were plated at 10^5 cells per well (96-well plates) for 24 hours prior to treatment. 25 μM of Compound D or control (0.5% DMSO) was added to each well. 24 hours post treatment, cells were lysed and caspase activity was measured using a caspase-3/7 activity kit (Apo-One Homogeneous caspase-3/7 assay, #G77905, Promega). Relative fluorescence units (RFU) were obtained by subtracting the unit values of the blank (control, without cells) from the experimental measured values.

Compound D Causes a G_1/S-Phase Arrest and Activates Caspase Activity

It has been shown that inhibition of the expression of the *cyclin D1* gene causes arrest at the G_1/S-phase of the cell cycle (Shintani et al., "Infrequent alternations of RB pathway (Rb-p16INK4A-cyclin D1) in adenoid cystic carcinoma of salivary glands," *Anticancer Res. 20*:2169-75 (2000)). HCT116 (Figure 7A, upper panel) and SW480 (Figure 7A, lower panel) cells were treated with Compound D (25 μM) (Figure 7A, right) or control (0.5% DMSO) (Figure 7A, left) for 24 hours. The cells were subsequently stained with propidium iodide (PI) and analyzed for DNA content by FACS cytofluorometry. As expected, the control cells, (Figure 7A, left), were cycling normally whereas the Compound D treated cells (Figure 7A, right) showed increased accumulation at G_1/S-phase of the cell cycle. Thus, it can be seen that Compound D causes arrest of cells at the G_1 phase.

Caspases are cysteine proteases that are generally activated in a given population of cells triggered by apoptotic stimuli. To assess apoptotic induction in SW480, HCT116, and wild-type colonocytes (CCD18Co cells), the cells were treated with either Compound D (25 μM) or control (0.5% DMSO) for 24 hours, followed by an assay for caspase-3/7 activity. As shown in Figure 7B, Compound D specifically and significantly activated the caspase-3/7 pathway in SW480 and HCT116 cells compared to CCD18Co cells.

EXAMPLE 10

COMPOUND D REDUCES PROLIFERATION OF TRANSFORMED COLORECTAL CELLS

Soft Agar Assays

The soft agar colony formation assay was conducted with SW480 cells by some modification of the procedure previously described (Moody et al., "A vasoactive intestinal peptide antagonist inhibits non-small cell lung cancer growth," *Proc. Natl. Acad. Sci. USA. 90*:4345-49 (1993)).

Each well (35mm) of a 6-well plate (Nalge Nunc International, Roskide, Denmark) was coated with 1ml of 0.8 % bottom agar in DMEM medium containing 10% fetal bovine serum. After it was solidified, 1ml of DMEM medium containing 0.4 % top agar, 10% fetal bovine serum, compound doubly concentrated, and 5,000 single viable cells was added to each well. The cultures were incubated at 37 °C in humidified 5% CO_2 incubator. Colonies in soft agar were monitored daily and photographed after incubation for 8 days. Colonies > 60 μm in diameter were counted.

Compound D Reduces Proliferation of Transformed Colorectal Cells

Soft agar colony forming assays were performed using SW480 cells treated with Compound D (0.25-5 μM) and 5-fluorouracil (5-FU) (0.5-32 μM). As shown in Figure 8A, Compound D shows a dose dependent decrease in the number of colonies formed. IC_{50} value of Compound D and 5-FU was 0.87 ± 0.11 μM and 1.98 ± 0.17 μM, respectively. Thus, Compound D increased caspase activity and reduced growth *in vitro* of colorectal cells that are transformed by mutations that activate β-catenin signaling.

EXAMPLE 11

COMPOUND C REDUCES TUMOR GROWTH IN NUDE MOUSE MODEL

SW620 cells ($9X10^6$ cells/mouse) were grafted into nude mice subcutaneously on Day 0. Mice received 200 mg/kg of Compound C intraperitoneally every other day until Day 21 after 4 times of 300 mg/kg every other day starting Day 1. Compound C reduces the tumor growth in the treated mice compared to the vehicle control mice (Figure 9A), and slightly reduces body weights of the treated mice compared to those of the vehicle control mice (Figure 9B).

EXAMPLE 12

COMPOUND D SUPRRESSES SURVIVIN EXPRESSION

The effect of Compound D on survivin expression was studied at both transcriptional and translational levels. The methods used at the transcriptional level include cDNA microarray analysis, RT-PCR, survivin reporter assays and chromotin immunoprecipitation (ChIP). The methods used at translational levels include Western blot analysis and immunochemistry.

A plasmid containing luciferase under the control of survivin promoter was constructed and transfected into wild type, CBP+/-, or p300+/- 3T3 cells. The results (Figure 10) show that Wnt 1 stimulates expression of the survivin gene in all three types of cells, whereas Compound D reduces expression of the survivin gene and decreases the stimulation of the survinin gene expression by Wnt1 in those cells. Similarly, Compound D and its analog (Comound A) were shown to inhibit expression of survivin in SW480 cells (Figure 11).

Real time reverse transcription-PCR analysis was performed according to the protocol provided with the SYBR Green PCR Master Mix Kit (Perkin Elmer Biosystems, Shelton, ST). Total RNA templates for the RT-PCR reactions were extracted with the RNeasy Midi Kit (Qiagen) from cells treated with Compound D (25 μM) or control (0.5% DMSO) 24 hours after treatment. The primers used for the RT-PCR reactions were 5'-AGCCCTTTCTCAAGGACCAC-3' and 5'-GCACTTTCTTCGCAGTTTCC-3'. Table 8 shows the results of the analysis. A ratio less than 0.5 indicates a significant decrease of gene expression due to the treatment of Compound D, whereas a ratio greater than 1.5 indicates a significant increase of gene expression. A ratio about 1 indicates no change. As indicated in Table 8 and Figure 12, the expression of the survivin gene is significantly reduced in the presence of Compound D compared to the control.

Table 8. Gene Expression with and without Compound D

Gene	Ratio (Treated/DMSO Control)
Ubiquitin	0.98
GADPH	0.98
HLAC	1.01
Survivin	0.30
PCNA	0.33
Antigen KI-67	0.45
MIC-1	7.0
GADD-153	7.00

ChIP assays on SW 480 cells treated with either Compound D (25 μM) or control (0.5% DMSO) were performed. As shown in Figure 13, the

survivin promoter is occuried by CBP, β-catenin, Tcf4 and acetylated histone in control treated cells. Treatment with Compound D decreases the association of all these proteins with the survivin promoter.

To characterize the effect of Compound D on the survivin expression at the translational level, Western blot analysis of extracts of cells treated with vehicle (0.5% DMSO) alone, 10 μM or 25 μM Compound D, or 5 μM 5-FU was performed using survivin 6E4 monoclonal antibody (Cell Signaling Technolgy). The results (Figure 14A) show that the treatments with Compound D at both concentrations and the treatment with 5-FU reduced the amount of the survivin protein. The treatments with Compound D at both concentrations were more effective in reducing the survivin expression than the treatment with 5-FU, and the treatment with Compound D at the higher concentration (*i.e.*, 25 μM) was most effective.

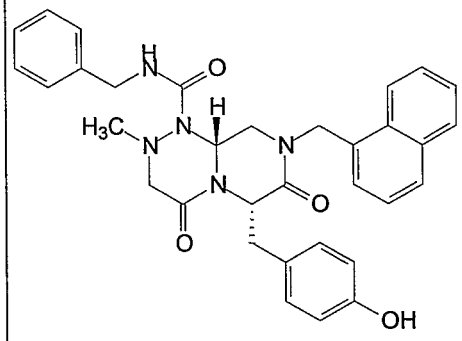
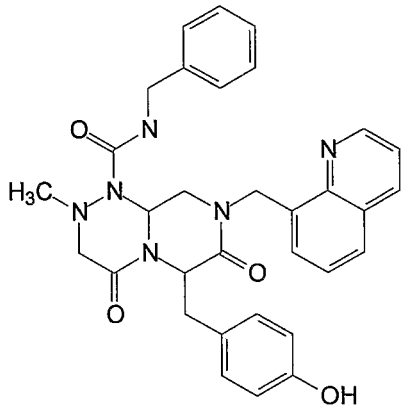
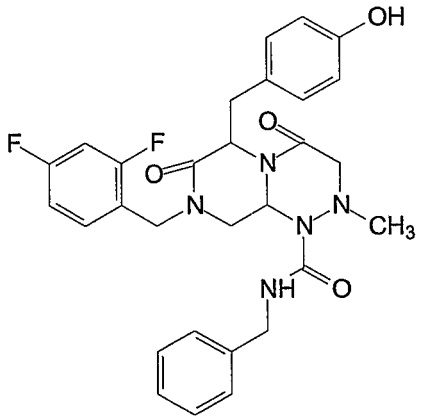
The effect of Compound D on the survivin expression at the translational level was further characterized using immunofluorescence microscopy. In the absence of Compound D, survivin localizes to the mitotic spindle apparatus, consistent with the notion that survivin is involved in chromosomal separation (Figure 14B). This expression pattern was not observed in SW480 cells after the treatment of Compound D as little or no survivin protein was detected (Figure 14C).

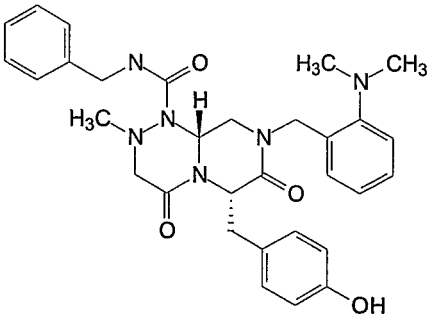
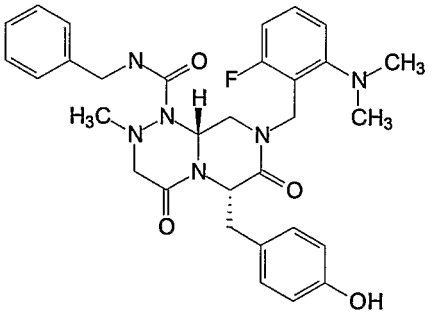
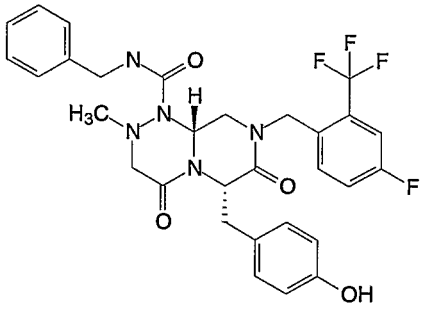
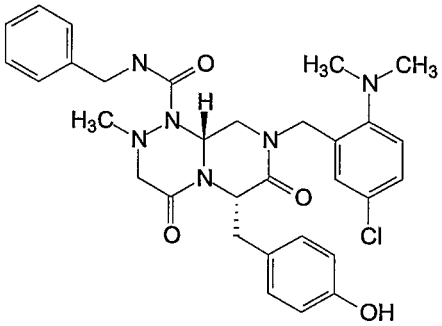
EXAMPLE 13

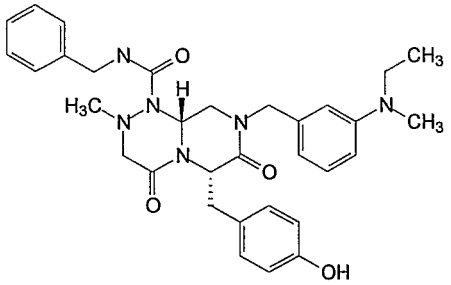
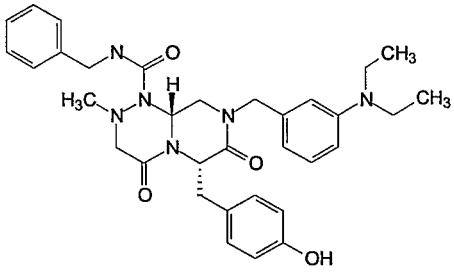
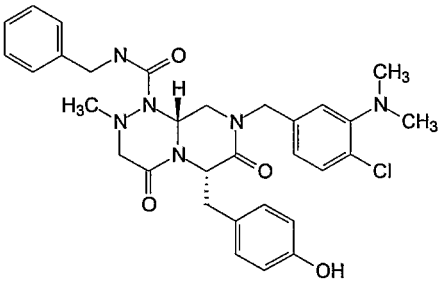
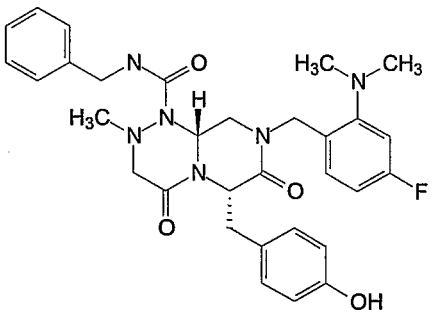
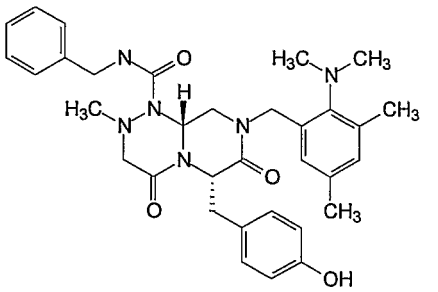
EFFECTS OF VARIOUS COMPOUNDS ON SURVIVIN AND TCF4 EXPRESSION

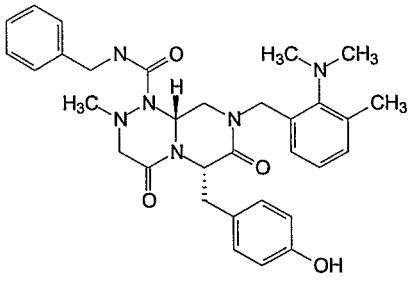
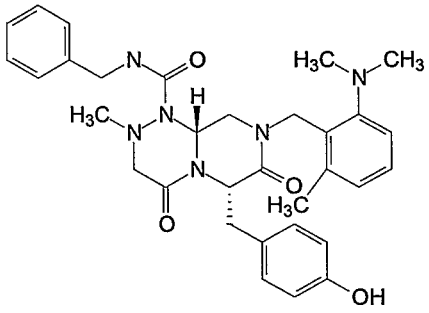
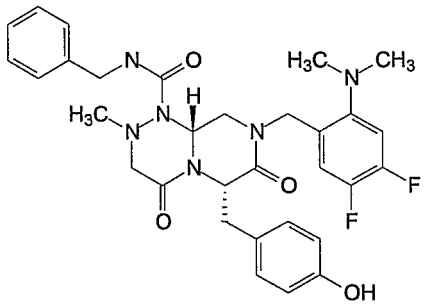
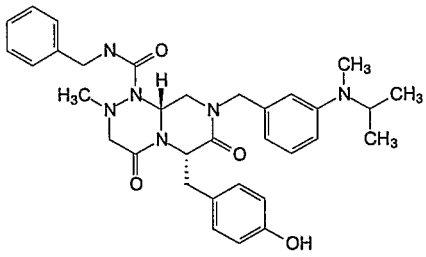
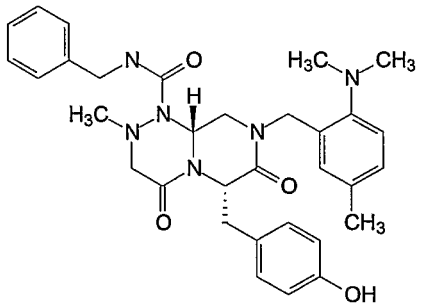
The effects of various compounds having general formula (I) on survivin and TCF4 expression were characterized. The results are shown in Table 9.

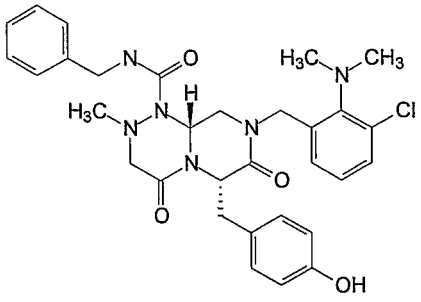
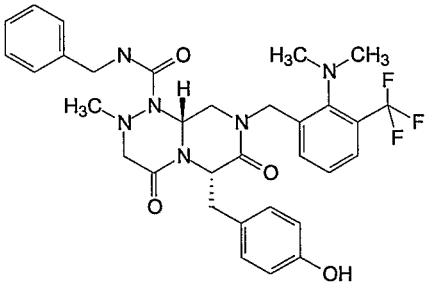
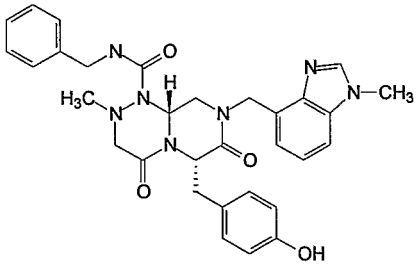
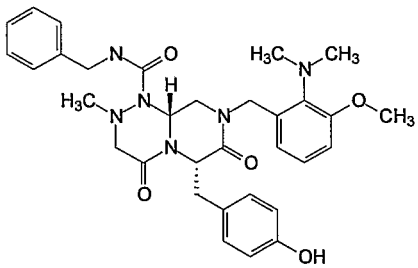
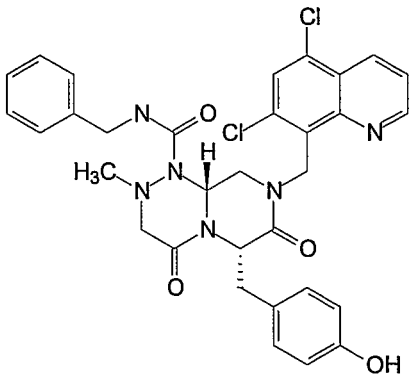
Table 9. Effects of compounds on survivin and TCF4 expression

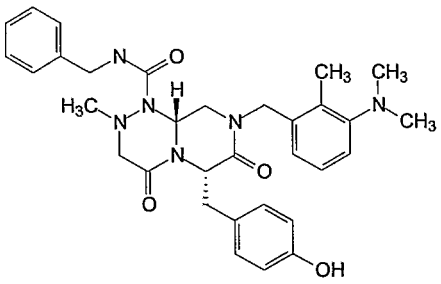
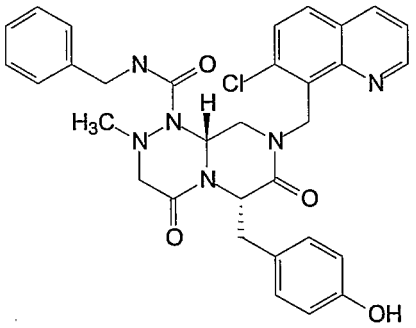
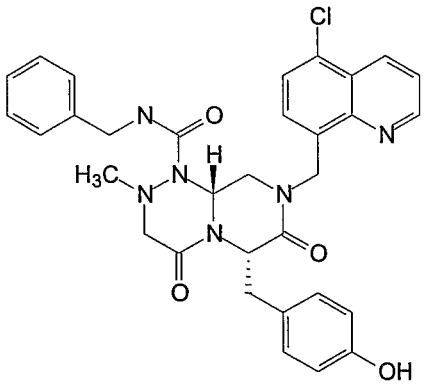
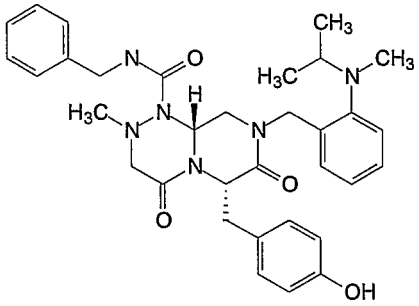
	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	100	99	~2
	97	100	~2.2
	51	93	~6.3

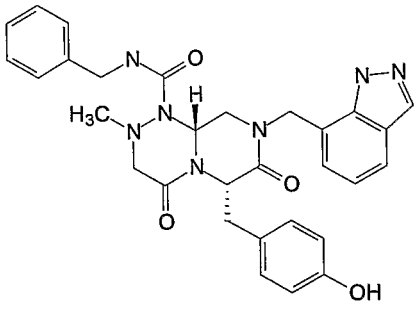
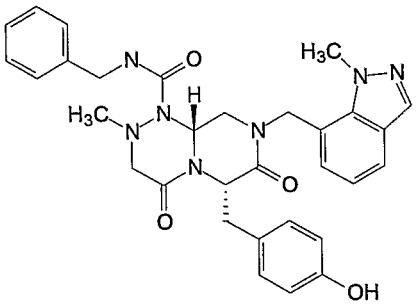
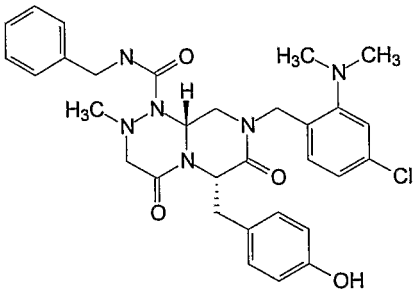
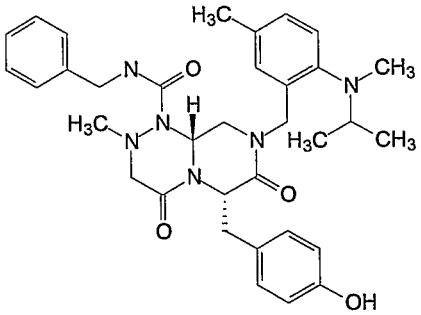
	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	41	92	5.2 ± 0.7
	0	6	18.2 ± 2.4
	0	80	1.3 ± 0.1
	0	93	2.2 ± 0.2

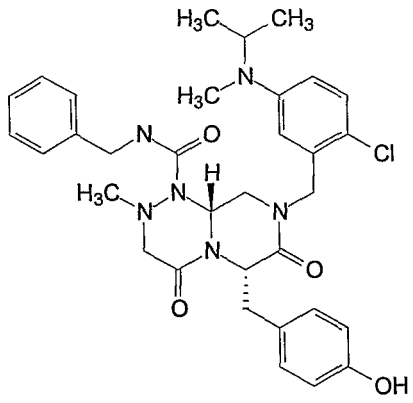
	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	46	96	4.4 ± 0.6
	0	77	3.5 ± 0.3
	0	92	7.3 ± 0.6
	79	81	1.7 ± 0.2
	0	84	4.8 ± 0.4

	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	0	68	10.9 ± 1.3
	8	4	NA
	9	91	1.4 ± 0.2
	5	91	6.3 ± 0.431
	0	94	2.6 ± 0.4

	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	0	21	7.3 ± 1.1
	0	91	5.2 ± 1.1
	45	88	13.2 ± 4.1
	9	92	5.9 ± 0.5
	6	58	11.2 ± 1.5

	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	48	96	3.9 ± 0.55
	0	32	50.4 ± 7.0
	86	91	2.6 ± 0.6
	27	98	10.7 ± 1.7

	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	80	97	4.6 ± 0.7
	82	97	2.8 ± 0.4
	6	89	13.9 ± 2.3
	14	99	10.7 ± 1.9

	Survivin %inhibition		TCF4 IC50 (uM)
	5uM	25uM	
	25	44	27.1 ± 4.6

EXAMPLE 14

COMPOUND D PROMOTES APOPTOSIS VIA SUPPRESSION OF SURVIVIN EXPRESSION

To determine the effect of Compound D on apoptosis and the role of survivin in such an effect, the activities of caspases 2 and 3 in cultured tumor cells treated with either Compound D or control were measured. The results (Figure 15) show that (1) Compound D (at 2.5 μM or 5.0 μM) activated the caspase 3 activity, but not the caspase 2 activity; (2) stausporine (0.5 μM) increased both the caspase 2 and caspase 3 activities; (3) the co-treatment of stausporine and Compound D produced a synergic stimuation of the caspase 3 activity, but not a synergic stimuation of the caspase 2 activity; and (4) transfection of the survivin gene decreased the activiation of the caspase 3 activity induced by the treatment of stausporine or Compound D, and the synergic stimulation of the caspase 3 activity induced by the co-treatment of stausporine and Compound D. The above results suggest that Compound D stimulate the caspase 3 activity via suppression of the expression of the survivin gene.

The effect of compound D on apoptosis and the role of survivin in such an effect were further characterized by measuring cell death of cultured tumor cells treated with staurosporine (0.5 μM), Compound D (5.0 μM) or both. The results (Figure 16) showed that both Compound D and stausporine promote cell death, and that transfection of the survivin gene decreased the increase in cell death induced by the treatment of stausporine, Compound D, or both. The above results suggest that Compound D promote apoptosis via suppression of the expression of the survivin gene.

To determine the effect of Compound D on cell cycle and the role of survivin in such an effect, FACS analysis was performed on cultured tumor cells with or without transfection of a construct containing the survivin gene and further treated with stausporine (0.5 μM), Compound D (5 μM), or both. The results (Figure 17) show that both stausporine and Compound D increase the number of cells in G_0, and that overexpression of survivin in the cells decreases the effect of the treatment of stausporine, Compound D, or both. These results suggest that the effect of Compound D on cell cycle may be at least partially via suppression of the expression of the survivin gene.

EXAMPLE 15

PREPARATION AND ACTIVITY OF PRODRUGS

(1) General procedure for preparing prodrugs by phosphorylation of phenol group

The starting phenol (26.06 mmol) was dissolved in tetrahydrofuran (130 ml), followed by addition of triethylamine (TEA) (10.9 ml, 78.18 mmol) at room temperature. The reaction mixture was cooled to 5 °C, and then $POCl_3$ (12.2 ml, 130.3 mmol) was added slowly. After addition was finished, the mixture was allowed to warm to room temperature, and stirred at this temperature for 5 hours. After the reaction was completed, the mixture

was poured into celite-pad filter funnel to remove TEA-HCl salt. Organics was diluted with water (130 ml) at 5°C, followed by adjusting pH 7~8 using sodium bicarbonate (50 g), and the resulting basic solution was stirred overnight at room temperature. The resulting aqueous layer was washed with EtOAc (100 ml), and then lyophilized. The crude product was dissolved in methylene chloride (100 ml), followed by for 1 hour at room temperature. Inorganic salts were removed by filtration using celite pad, then solvent was evaporated. The crude product was purified by recrystallization (EA/Ether) to get 9.5 g of phosphorylated product as an off-white solid.

(2) Typical work-up procedure for the free form of phosphate

After washing the resulting basic aqueous layer, the solution was acidified to pH 3~4 using 1N HCl, and then the phosphate free form was extracted twice with chloroform (300 ml). The organic layer was dried over sodium sulfate, and the crude product was purified by recrystallization.

(3) Converting method from free form to di-sodium form

A. Titration method

Free form of phosphate can be transformed to di-sodium salt form by titration, which could use many inorganic bases. For example, sodium carbonate, sodium bicarbonate, and sodium hydroxide are used in this experiment to produce di-sodium form. Other cations can be used to make different di-salt forms.

1. Analytical method and instrument for titration

a. Instrument: TitraLab (RADIOMETER COPENHAGEN)
Electrode: pHG201 pH glass electrode
(RADIOMETER COPENHAGEN, 945-462)

REF201 reference electrode with KCl salt-bridge solution (RADIOMETER COPENHAGEN, 945-463)

Titrant: 10 M Na_2CO_3

Burette speed (titration speed): 15% (=1.5 ml/min)

Sample: 50 mg dissolved in distilled water (30 ml)

b. Results

pH 4 (start pH=2)

n	start pH	EP1		EP2	
		pH	Titrant (ml)	pH	Titrant (ml)
1	2.10	4.21	9.50	8.15	19.03
2	2.08	4.26	10.28	8.02	19.12
Mean	2.09	4.24	9.89	8.09	19.08

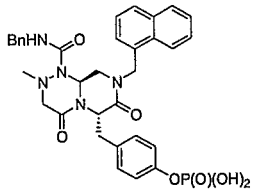
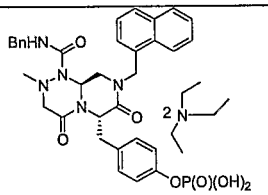
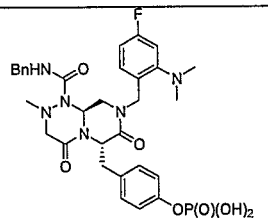
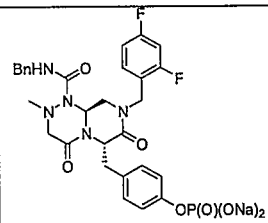
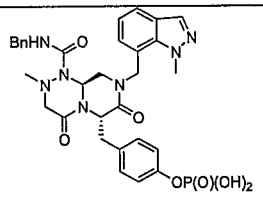
B. Using organic sodium donor

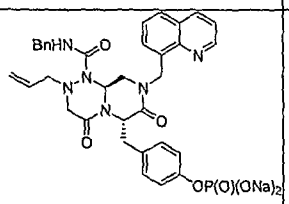
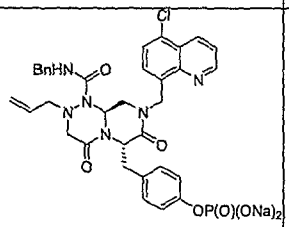
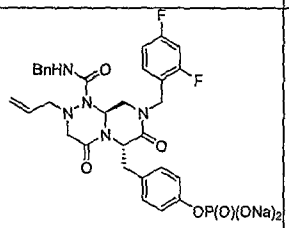
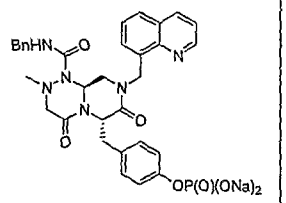
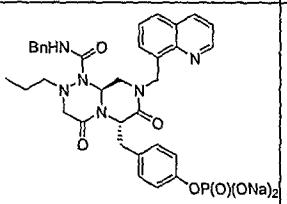
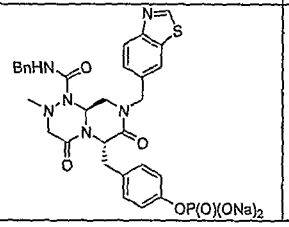
The basic drawback of titration using inorganic base is that the water must be used for the solvent. So searching the sodium donor dissolved freely in normal organic solvent is the easiest way to solve the problem. Several reagents such as sodium acetate and sodium ethylhexanoic acid were tested and found to be useful for making a di-sodium salt form.

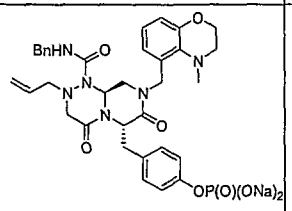
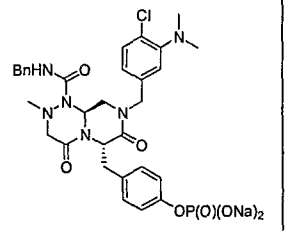
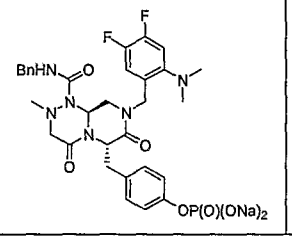
Table 10 shows compounds for bioactivity test selected from the prodrugs of the present invention and IC_{50} values thereof, which are measured by the reporter gene assay (RGA) and oncogenic activity by MTS or Sulforhodamine B assay as described in Example 6. The compound numbers on Table 10 are unrelated to those in Table 4 or 5.

Table 10

THE REPORTER GENE ASSAY AND ONCOGENIC ACTIVITY BY MTS OR SULFORHODAMINE B ASSAY FOR SELECTED PRODRUG COMPOUNDS

No	Structure	Assay					
		RGA, TopF IC50, uM	RGA, Surviv in IC50, uM	MTS, SW480 (uM)		MTS, HCT116 (uM)	
				LD50	GI50	LD50	GI50
1		4.2	6.4	17.0	2.0	16.1	2.2
2		3.5	5.7	8.2	3.1	23.2	6.6
3		11.5		ND up to 50uM	3.0	41.9	3.1
4		7.3	6.5	ND up to 50uM	6.9	49.3	11.4
5		26.0		34.0	5.2	ND up to 50uM	16.5

No	Structure	Assay					
		RGA, TopF IC50, uM	RGA, Surviv in IC50, uM	MTS, SW480 (uM)		MTS, HCT116 (uM)	
				LD50	GI50	LD50	GI50
6		0.8	0.1	9.2	0.5	6.4	0.4
7		2.3	1.0	12.9	2.2	12.0	1.8
8		1.4	0.9	21.6	2.1	23.2	1.9
9		9.6	6.0	ND up to 50uM	7.6	ND up to 50uM	14.7
10		2.8	1.7	9.4	0.9	7.9	0.8
11		10.3	6.7	ND up to 50uM	6.5	ND up to 50uM	6.3

No	Structure	Assay					
		RGA, TopF IC50, uM	RGA, Surviv in IC50, uM	MTS, SW480 (uM)		MTS, HCT116 (uM)	
				LD50	GI50	LD50	GI50
12		1.0	0.7	ND up to 50uM	1.0	19.3	1.2
13		1.8	0.9	21.1	2.3	20.0	1.7
14		1.7	1.2	21.1	2.3	16.0	2.1

EXAMPLE 16

SOLUBILITY OF SELECTED PRODRUGS

General procedure for Solubility test of Prodrugs

About 2 mg of each prodrug was dissolved in 1 ml of JP1 or JP2 solution as indicated below. Incubating at a temperature of 37°C, 200 ul of samples were withdrawn at 0 hour, 2 hour and 20 hour. Withdrawn samples were filtered through 0.45 µm syringe filters and analyzed by HPLC system.

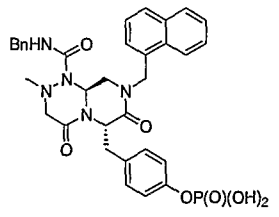
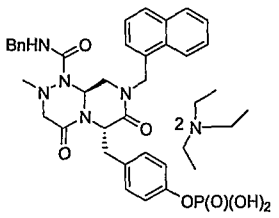
Composition of artificial gastro-intestinal fluids (JP1, JP2)

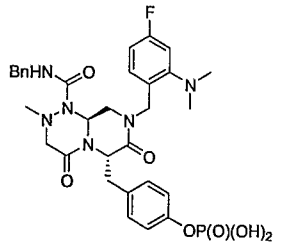
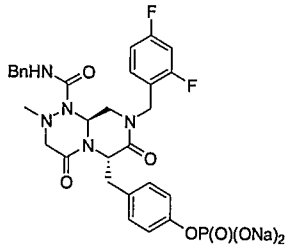
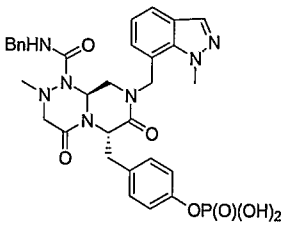
JP1		JP2	
PH	1.2	pH	6.8
NaCl	2.0 g	0.2 M KH_2PO_4	250 ml
10% HCl	24.0 ml	0.2N NaOH	118 ml
Distilled H_2O	Adjusted to 1 L	Distilled H_2O	Adjusted to 1 L

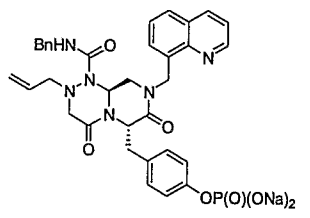
Table 11 below shows the results of solubility test of selected prodrugs. The compound numbers on Table 11 are unrelated to those in Table 4, 5 or 10.

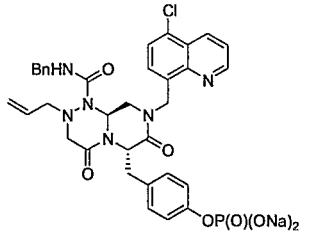
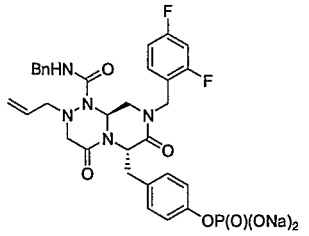
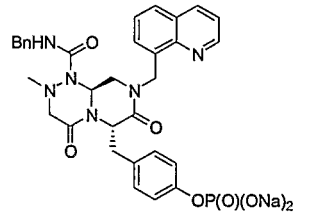
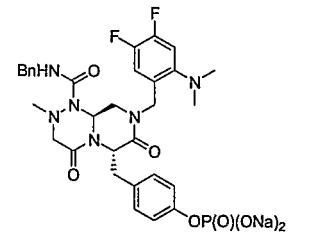
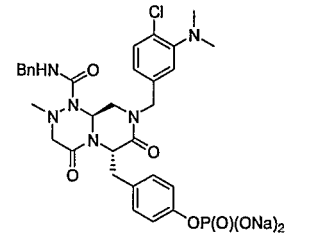
Table 11

AQUEOUS SOLUBILITY FOR SELECTED PRODRUG COMPOUNDS

No	Structure	Solubility (37oC, ug/mL) 0 hr, 2 hr, 20 hr	
		JP1 (pH 1.2)	JP2 (pH 6.8)
1		60.1 87.3 92.8	1797 1867 1894
2		122 173 160	1950 1939 1940

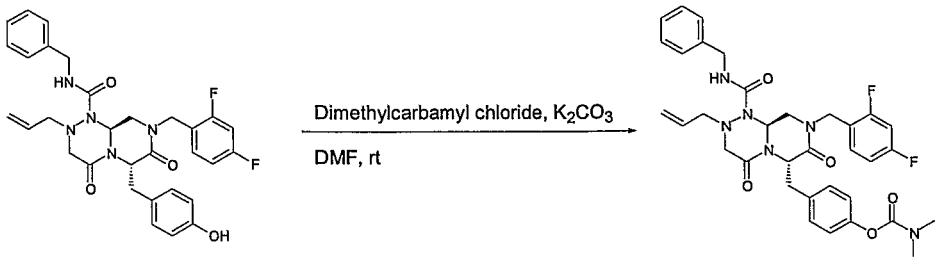
No	Structure	Solubility (37oC, ug/mL) 0 hr, 2 hr, 20 hr	
		JP1 (pH 1.2)	JP2 (pH 6.8)
3		1878 1971 2036	1325 1902 2005
4		554 646 756	1982 2014 2030
5		406 532 684	1761 1778 1758

No	Structure	Solubility (37 oC, ug/mL) 0 hr, 2 hr, 20 hr	
		JP1 (pH 1.2)	JP2 (pH 6.8)
6		1453 1724 1787	1829 1864 1867

No	Structure	Solubility (37 oC, ug/mL) 0 hr, 2 hr, 20 hr	
		JP1 (pH 1.2)	JP2 (pH 6.8)
7		309 446 521	2145 2221 2239
8		671 775 921	2295 2317 2272
9		2251 2275 2403	2322 2353 2421
10		2292 2274 2327	2028 2055 2027
11		2006 2000 1998	1636 1654 1651

EXAMPLE 17

PREPARATION OF DIMETHYL-CARBAMIC ACID 4-[2-ALLYL-1BENZYLCARBAMOYL-8-(2,4-DIFLUORO-BENZYL)-4.7-DIOXO-OCTAHYDRO-PYRAZINO[2,1-C][1,2,4]TRIAZIN-6-YLMETHYL]-PHENYL ESTER



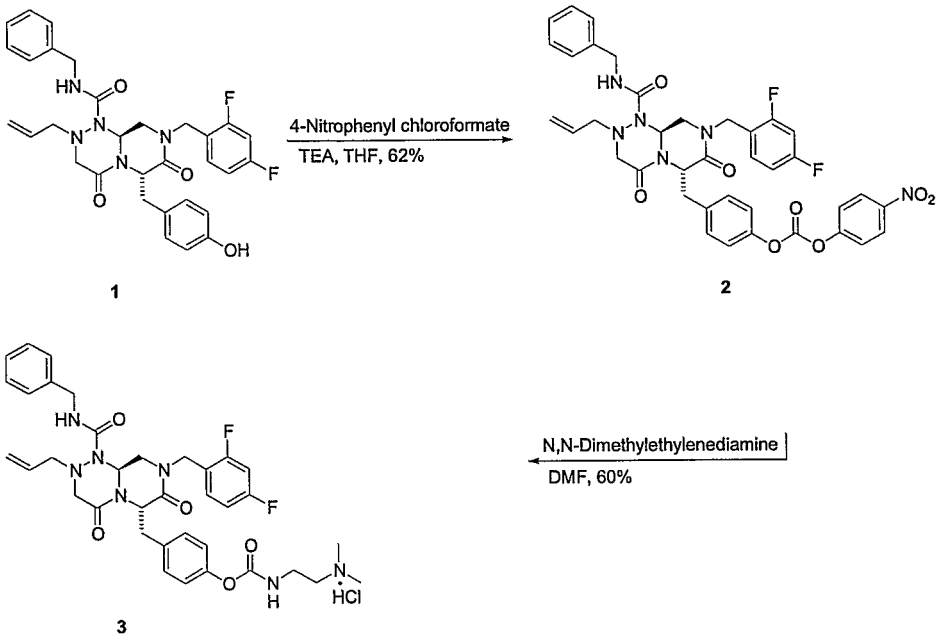
To a stirred solution of starting material (SM) (8.0 g, 13.9 mmol) and potassium carbonate (5.8 g, 41.7 mmol) in dimethylformamide was added dimethylcarbamyl chloride (3.0 g, 27.8 mmol). The reaction mixture was stirred overnight and then dissolved in EtOAc, washed with water five times. The combined organic layer was washed with brine, dried over sodium sulfate, concentrated *in vacuo*. The residue was chromatographed on silica gel with neat EtOAc to afford product (4.2 g, 32%). The data from analyzing the resulting product by mass spectrometry and NMR are:

MS (ESI) : m/e 647 (M+1), 669 (M+Na).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.27-7.39 (6H, m), 6.78-7.13 (6H, m), 6.68 (1H, t, *J*=6.0 Hz), 5.61-5.70 (2H, m), 5.34 (1H, t, *J*=6.0 Hz), 5.06-5.20 (2H, m), 4.31-4.69 (4H, m), 3.24-3.58 (8H, m), 3.07 (3H, s), and 2.99 (3H, s).

EXAMPLE 18

PREPARATION OF CARBONIC ACID 4-[2-ALLYL-1-BENZYLCARBAMOYL-8-(2,4-DIFLUORO-BENZYL)-4,7-DIOXO-OCTAHYDRO-PYRAZINO[2,1-C][1,2,4]TRIAZIN-6-YLMETHYL]-PHENYL ESTER 4-NITRO-PHENYL ESTER **(2)**



To a stirred solution of 2-Allyl-8-(2,4-difluoro-benzyl)-6-(4-hydroxy-benzyl)-4,7-dioxohexahydro-pyrazino[2,1-c][1,2,4]triazine-1-carboxylic acid benzylamine **(1)** (2 g, 3.47mmol) in THF(40 ml) was added Triethylamine(0.97 ml, 6.95mmol) and 4-nitrophenylchloroformate (0.7 g, 3.47 mmol). After stirring at room temperature for overnight, the solvent was removed under reduced pressure. The crude compound was purified by chromatography (Hexane, EtOAc 1:1) to give the compound (1.59 g, 62%). The data from analyzing the purified compound by TLC system and NMR are:

TLC System: R_f = 0.3 (*n*-Hexane:EtOAc 1:1)

^{1}H NMR (300MHz, $CDCl_3$): δ 3.25-3.60 (m, 8H), 4.35 (dd, J=14.9 Hz, 5.7 Hz, 1H), 4.43 (dd, J=14.8 Hz, 6.1 Hz,1H), 4.52 (d, 14.5 Hz, 1H), 4.68 (d, 14.1H), 5.10 (d, 17.1 Hz, 1H), 5.21 (d, 10.3 Hz, 1H), 5.34 (t, J=6.1 Hz, 1H), 5.58 (dd, J=11.1 Hz , 4.1 Hz, 1H), 5.67 (m, 1H), 6.71 (t, J=6.1 Hz, NH), 6.75-6.98 (m,

2H), 7.13 (d, J=8.4 Hz, 2H), 7.21 (d, J=8.7 Hz, 2H), 7.23-7.39 (m, 6H), 7.46 (d, J=9.5 Hz, 2H), and 8.30 (d, J=9.5 Hz, 2H).

EXAMPLE 19

PREPARATION OF (2-DIMETHYLAMINO-ETHYL)-CARBAMIC ACID 4-[2-ALLYL-1-BENZYLCARBAMOYL-8-(2,4-DIFLUORO-BENZYL)-4,7-DIOXO-OCTAHYDRO-PYRAZINE[2,1-C][1,2,4]TRIAZINE-6-YLMETHYL]-PHENYL ESTER HYDROCHLORIDE SALT (3)

To a stirred solution of carbonic acid 4-[2-allyl-1-benzylcarbamoyl-8-(2,4-difluoro-benzyl)-4,7-dioxo-octahydro-pyrazino[2,1-c][1,2,4]triazin-6-ylmethyl]-phenyl ester 4-nitro-phenyl ester (2) (1.2 g, 1.62 mmol) in DMF(25 ml) was added N,N-Dimethylethylenediamine (0.26 ml, 2.43 mmol). After stirring at room temperature for overnight, the solvent was removed under reduced pressure. The residue was diluted with EtOAc and washed with water, brine. The organic layer was dried with Na_2SO_4 and concentrated in *vacuo*. The crude compound was purified by chromatography (*n*-Hexane:EtOAc, 1:1; EtOAc; CH_2Cl_2: MeOH, 9:1). The compound was poured with water and was maintained pH 5-6 with 1N aq. HCl to make HCl salt and then lyophilized to get the compound (0.75g, 60%). The data from analyzing the resulting compound by TLC system and NMR are:

TLC System: R_f = 0.35 (CH_2Cl_2:MeOH, 9:1)

ESI-MS: M + H^+ 690.39

^1H NMR (300MHz, $CDCl_3$): δ 2.56 (d, J=4.6 Hz, 6H), 3.18 (bm, 4H), 3.41-3.58 (m, 4H), 3.75 (t, J=10.3 Hz, 1H), 4.21 (bt, 2H), 4.35 (d, J=14.9Hz 1H), 4.70 (d, J=14.9 Hz 1H), 5.05 (m, 1H), 5.12 (m, 1H), 5.42 (m, 6H), 5.80 (m, 1H), 6.91 (d, J=7.6 Hz, 2H), 7.04 (d, J=7.3, 2H), 7.09 (m, 1H), 7.18-7.26 (m, 6H), 7.31 (d, J=6.9 Hz, 2H), 7.33 (m, 1H), 7.84 (bt, NH), 7.98 (bt, NH), 10.7 (bs, 1H)

EXAMPLE 20

MOUSE IN VIVO PK STUDY OF PRODRUG A AFTER SINGLE I.V. BOLUS INJECTION

Animal experiment

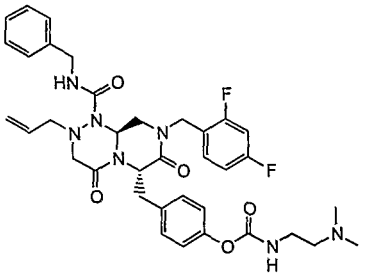
Drugs were prepared 10mg/kg/5ml in 10% Tween 80. Studies were performed in ICR mice. After i.v. bolus injection through the tail vein, blood samples were acquired from inferior vena cava at several time points and separated to plasma by centrifugation. Plasma samples were preserved at –20°C until they were analyzed. Bleeding time points were 3, 6, 9, 17, 34, 67, 134, 202, 302 min. N=4.

Sample preparation

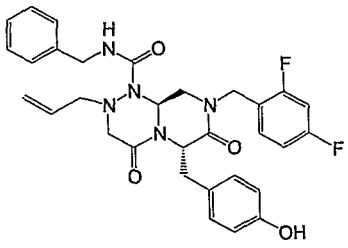
For calibration curve, 98 ul aliquots of control mouse plasma were added 2 ul of drug stock solution and added 2 ul internal standard stock solution, 5 ug/ml of internal standard. Final concentrations of calibration samples were 1, 10, 100, 1000 ng/ml and 10 ug/ml. For plasma sample from animal experiment, 100 ul of plasma were added 2 ul of internal standard. Then, all the samples were added 500 ul of acetonitrile, 500 ul of ethylacetate and 100 ul of DW. Samples were mixed for 10 min and centrifuged. The supernatants were transferred another tubes and evaporated. Adding 200 ul of 40% acetonitrile, they were reconstituted and analyzed by LC-MS system.

Results

The changes of concentrations of prodrug A and its parent compound in mouse plasma with the increase of time after i.v. bolus injection of prodrug A are shown in Figure 18. Square: parent compound; Diamond: prodrug A.



Prodrug A



Parent

It will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without departing from the spirit and scope of the invention. Accordingly, the invention is not limited except by the appended claims.

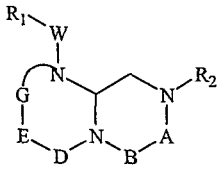
All of the above U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet, including U.S. patent application serial no. 10/087,443 filed on March 01, 2002, and U.S. patent application serial no. 09/976,470 filed on October 12, 2001, are incorporated herein by reference.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

We claim:

1. A compound having the following general formula (I):



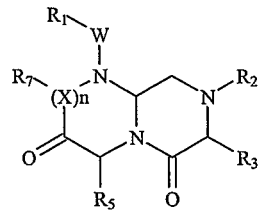
(I)

wherein A is -(CHR_3)- or -(C=O)-, B is -(CHR_4)-, -(C=O)-, D is –(CHR_5)- or –(C=O)-, E is –(ZR_6)-, -(C=O)-, G is –(XR_7)$_n$-, -(CHR_7)-(NR_8)-, -(C=O)-(XR_9)-, or -(C=O)-, W is -Y(C=O)-, -(C=O)NH-, -(SO_2)- or nothing, Y is oxygen, sulfur or -NH-, X and Z is independently nitrogen or CH, n=0 or 1; and R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are the same or different and independently selected from an amino acid side chain moiety or derivative thereof, the remainder of the molecule, a linker and a solid support, and stereoisomers thereof.

2. The compound of claim 1, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are independently selected from the group consisting of aminoC_{2-5}alkyl, guanidinoC_{2-5}alkyl, C_{1-4}alkylguanidinoC_{2-5}alkyl, diC_{1-4}alkylguanidino-C_{2-5}alkyl, amidinoC_{2-5}alkyl, C_{1-4}alkylamidinoC_{2-5}alkyl, diC_{1-4}alkylamidinoC_{2-5}alkyl, C_{1-3}alkoxy, Phenyl, substituted phenyl(where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), benzyl, substituted benzyl (where the substituents on the benzyl are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), naphthyl, substituted naphthyl (where the substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or

ıydroxyl), bis-phenyl methyl, substituted bis-phenyl methyl (where the substituents ıre independently selected from one or more of amino, amidino, guanidino, ıydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), pyridyl, substituted ›yridyl, (where the substituents are independently selected from one or more of ımino amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, ıalogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or ıydroxyl), pyridylC_{1-4}alkyl, substituted pyridylC_{1-4}alkyl (where the pyridine ;ubstituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, ›erfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), ›yrimidylC_{1-4}alkyl, substituted pyrimidylC_{1-4}alkyl (where the pyrimidine substituents ıre independently selected from one or more of amino, amidino, guanidino, ıydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy or nitro, carboxy, cyano, sulfuryl or hydroxyl), triazin-2-yl-C_{1-} ;alkyl, substituted triazin-2-yl-C_{1-4}alkyl (where the triazine substituents are ndependently selected from one or more of amino, amidino, guanidino, hydrazino, ımidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl or hydroxyl), imidazoC_{1-4}alkyl, substituted midazol C_{1-4}alkl (where the imidazole sustituents are independently selected from ›ne or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, ;yano, sulfuryl or hydroxyl), imidazolinylC_{1-4}alkyl, N-amidinopiperazinyl-N-C_{0-4}alkyl, ıydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, hydroxyC_{2-5}alkyl, C_{1-5}alkylaminoC_{2-5}alkyl, C_{1-5}dialkylaminoC_{2-5}alkyl, N-amidinopiperidinylC_{1-4}alkyl and 4-aminocyclohexylC_{0-} ;alkyl.

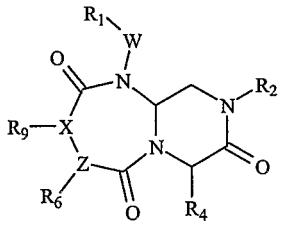
3. The compound of claim 1, wherein A is $-(CHR_3)-$, B is $-(C=O)-$,) is $-(CHR_5)-$, E is $-(C=O)-$, G is $-(XR_7)_n-$, and the compound has the following ;eneral formula (II):



(II)

wherein R_1, R_2, R_3, R_5, R_7, W, X and n are as defined in claim 1.

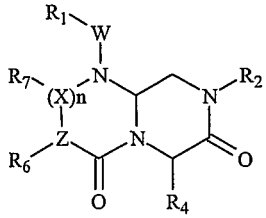
4. The compound of claim 1, wherein A is –(C=O)-, B is -(CHR_4)-, D is –(C=O)-, E is –(ZR_6)-, G is –(C=O)-(XR_9)-, and the compound has the following general formula (III):



(III)

wherein R_1, R_2, R_4, R_6, R_9, W and X are as defined in claim 1, Z is nitrogen or CH (when Z is CH, then X is nitrogen).

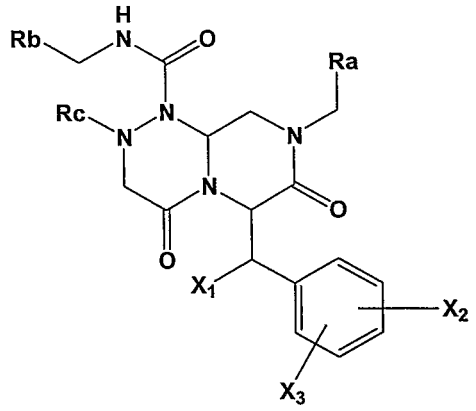
5. The compound of claim 1, wherein A is –(C=O)-, B is –(CHR_4)-, D is –(C=O)-, E is –(ZR_6)-, G is $(XR_7)_n$-, and the compound has the following general formula (IV):



(IV)

wherein R_1, R_2, R_4, R_6, R_7, W, X and n are as defined in claim 1, and Z is nitrogen or CH, with the proviso that when Z is nitrogen, then n is zero, and when Z is CH, then X is nitrogen and n is not zero.

6. The compound of claim 5, wherein the compound has the ollowing general formula (VI):



vherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl group with one or more substituents where the one or more substituents are independently selected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a bicyclic aryl group having 8 to 11 ring members, which may have 1 to 3 heteroatoms selected from nitrogen, oxygen or sulfur; R_b is a monocyclic aryl group having 5 to 7 ring members, which may have 1 to 2 heteroatoms selected from nitrogen, oxygen or sulfur, and aryl ring in the compound may have one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups; Rc is a saturated or unsaturated C_{1-6}alkyl, C_{1-6}alkoxy, perfluoro C_{1-6}alkyl group; and X_1, X_2, and X_3 may be the same or different and independently selected from hydrogen, hydroxyl, and halide.

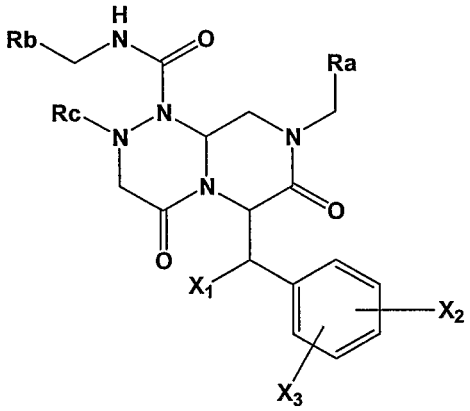
7. The compound of claim 6, wherein R_a is a wherein R_a is a phenyl group; a substituted phenyl group having one or more substituents wherein

ıe one or more substituents are independently selected from one or more of amino, midino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, alogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, sulfuryl, and ydroxyl groups; a benzyl group; a substituted benzyl group with one or more ubstituents where the one or more substituents are independently selected from ıne or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-3}alkoxy, nitro, carboxy, cyano, ulfuryl, and hydroxyl group; a naphthyl group; a quinolinyl group; an indazolyl group; ır a benzpyrazolyl group; an isoquinolinyl group; and R_b is phenyl, pyridyl or ıiperidyl, all of which may be substituted with one or more substituents selected from ı group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups.

8. A compound having the following general formula (VII)

$$(VI)\text{-}Y\text{-}R_{10}$$

wherein (VI) is the general formula:



wherein R_a is a phenyl group; a substituted phenyl group having ɔne or more substituents wherein the one or more substituents are independently ɜelected from one or more of amino, amidino, guanidino, hydrazino, amidazonyl, C_{1-} ıalkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkyl, C_{1-3}alkoxy, nitro, ɔarboxy, cyano, sulfuryl, and hydroxyl groups; a benzyl group; a substituted benzyl ɡroup with one or more substituents where the one or more substituents are ndependently selected from one or more of amino, amidino, guanidino, hydrazino,

imidazonyl, C_{1-4}alkylamino, C_{1-4}dialkylamino, halogen, perfluoro C_{1-4}alkyl, C_{1-4}alkoxy, nitro, carboxy, cyano, sulfuryl, and hydroxyl group; or a bicyclic aryl group having 8 to 11 ring members, which may have 1 to 3 heteroatoms selected from nitrogen, oxygen or sulfur;

R_b is a monocyclic aryl group having 5 to 7 ring members, which may have 1 to 2 heteroatoms selected from nitrogen, oxygen or sulfur, and aryl ring in the compound may have one or more substituents selected from a group consisting of halide, hydroxy, cyano, lower alkyl, and lower alkoxy groups;

Rc is a saturated or unsaturated C_{1-6}alkyl, C_{1-6}alkoxy, perfluoro C_{1-6}alkyl group; and

X_1, X_2, and X_3 may be the same or different and independently selected from hydrogen, hydroxyl, and halide;

Y is oxygen, sulfur, or nitrogen of a group selected from R_a, R_b, R_c, X_1, X_2 and X_3;

R_{10} is phosphate, hemisuccinate, hemimalate, phosphoryloxymethyloxycarbonyl, dimethylaminoacetate, dimethylaminoalkylcarbamates, hydroxyalkyls, amino acid, glycosyl, substituted or unsubstituted piperidine oxycarbonyl, or a salt thereof; and

the compound having general formula (VII) is capable of serving as a substrate for a phosphatase or a carboxylase and is thereby converted to a compound having general formula (VI).

9. The compound of claim 1, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

10. The compound of claim 2, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

11. The compound of claim 3, wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8 or R_9 is joined to a solid support or solid support derivatives.

12. A pharmaceutical composition comprising a compound according to any one of claims 1-8 and pharmaceutically acceptable carrier.

13. A pharmaceutical composition of claim 12, the composition comprising a safe and effective amount of the compound.

14. A library of compounds, comprising at least one compound according to any one of claims 1-8.

15. A method of identifying a biologically active compound, comprising contacting the library of claim 14 with a target to detect or screen the biologically active compound.

16. A method for carrying out a binding assay, comprising:

a) providing a composition comprising a first co-activator and an interacting protein, said first co-activator comprising a binding motif of LXXLL, LXXLI or FXXFF wherein X is any amino acid;

b) combining the first co-activator and the interacting protein with a test compound; and

c) detecting alteration in binding between the first co-activator and the interacting protein in the presence of the compound;

wherein the test compound is selected from a compound of any one of claims 1-8.

17. The method of claim 16, wherein said interacting protein is a transcription factor or a second co-activator.

18. The method of claim 16, wherein said interacting protein is selected from the group consisting of RIP140; SRC-1 (NCoA-1); TIF2 (GRIP-1; SRC-2); p (CIP; RAC3; ACTR; AIB-1; TRAM-1; SRC-3); CBP (p300); TRAPs (DRIPs);

'GC-1; CARM-1; PRIP (ASC-2; AIB3; RAP250; NRC); GT-198; and SHARP (CoAA; 68; p72).

19. The method of claim 16, wherein said interacting protein is elected from the group consisting of TAL 1; p73; MDm2; TBP; HIF-1; Ets-1; RXR; 65; AP-1; Pit-1; HNF-4; Stat2; HPV E2; BRCA1; p45 (NF-E2); c-Jun; c-myb; Tax; ap 1; YY1; SREBP; ATF-1; ATF-4; Cubitus; Interruptus; Gli3; MRF; AFT-2; JMY; Mad; PyLT: HPV E6; CITTA; Tat; SF-1; E2F; junB; RNA helicase A; C/EBP β; ATA-1; Neuro D; Microphthalimia; E1A; TFIIB; p53; P/CAF; Twist; Myo D; pp9O SK; c-Fos; and SV40 Large T.

20. The method of claim 16, wherein said interacting protein is elected from the group consisting of ERAP140; RIP140; RIP160; Trip1; SWI1 SNF); ARA70; RAP46; TIF1; TIF2; GRIP1; and TRAP.

21. The method of claim 16, wherein said interacting protein is elected from the group consisting of VP16; VP64; p300; CBP; PCAF; SRC1 PvALF; AtHD2A; ERF-2; OsGAI; HALF-1; C1; AP-1; ARF-5; ARF-6; ARF-7; ARF-8; CPRF1; CPRF4; MYC-RP/GP; and TRAB1.

22. The method of claim 16, wherein said first co-activator is CBP or 300.

23. A method for inhibiting tumor growth comprising administering to a mammalian subject having a tumor a compound according to any one of claims 1-3, or a composition according to claim 12 or claim 13, in an amount effective to nhibit the growth of the tumor in the mammalian subject.

24. The method of claim 23 wherein the tumor is cancerous.

25. The method of claim 23 wherein the tumor is colorectal cancer.

26. A method of treating or preventing cancer comprising dministering to a subject in need thereof a compound according to any one of laims 1-8, or a composition according to claim 12 or claim 13, in an amount ffective to treat or prevent the cancer.

27. The method of claim 26 wherein the cancer is colorectal cancer.

28. The method of claim 26 wherein the compound or the omposition is administered in combination with an anti-neoplastic agent.

29. The method of claim 28 wherein the anti-neoplastic agent is elected from the group consisting of 5-FU, taxol, cisplatin, mitomycin C, tegafur, altitrexed, capecitabine, and irinotecan.

30. A method of treating or preventing restenosis associated with ngioplasty comprising administering to a subject in need thereof an amount of a ompound according to any one of claims 1-8, or a composition according to claim 2 or claim 13, where the amount is effective to prevent the restenosis.

31. A method of treating or preventing polycystic kidney disease omprising administering to a subject in need thereof an amount of a compound ccording to any one of claims 1-8, or a composition according to claims 12 or 13, here the amount is effective to treat the polycystic kidney disease.

32. A method of treating or preventing aberrant angiogenesis disease comprising administering to a subject in need thereof an amount of a ompound according to any one of claims 1-8, or a composition according to claim

? or claim 13, where the amount is effective to treat the aberrant angiogenesis sease.

33. A method of treating or preventing rheumatoid arthritis disease)mprising administering to a subject in need thereof an amount of a compound :cording to any one of claims 1-8, or a composition according to claim 12 or claim 3, where the amount is effective to treat the rheumatoid arthritis disease.

34. A method of treating or preventing ulcerative colitis comprising dministering to a subject in need thereof an amount of a compound according to ny one of claims 1-8, or a composition according to claim 12 or claim 13, where the nount is effective to treat the ulcerative colitis.

35. A method for treating or preventing tuberous sclerosis complex "SC) comprising administering to a subject in need thereof an amount of a)mpound of any of claims 1-8, or a composition of claim 12 or claim 13, where the nount is effective to treat or prevent TSC.

36. A method for treating or preventing a KSHV-associated tumor)mprising administering to a subject in need thereof an amount of a compound of ny of claims 1-8, or a composition of claim 12 or claim 13, where the amount is ffective to treat or prevent the KSHV-associated tumor.

37. A method for modulating hair growth comprising administering to subject in need thereof an amount of a compound of any of claims 1-8, or a)mposition of claim 12 or claim 13, where the amount is effective to modulate hair rowth on the subject.

38. A method of treating or preventing Alzheimer's disease)mprising administering to a subject in need thereof an amount of a compound

according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to treat or prevent Alzheimer's disease.

39. A method for promoting neurite outgrowth, comprising contacting a neuron with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to promote neurite outgrowth.

40. A method for promoting differentiation of a neural stem cell comprising contacting a neural stem cell with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, where the amount is effective to promote differentiation of the neural stem cell.

41. A method for promoting apoptosis in cancer cells comprising contacting cancer cells with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to promote apoptosis in the cancer cells.

42. A method for inhibiting survivin expression in a cell comprising contacting a survivin-expressing cell with a compound according to any one of claims 1-8, or a composition according to claim 12 or claim 13, in an amount effective to inhibit survivin expression.