Triazole derivatives

BACKGROUND OF THE INVENTION

The invention had the object of finding novel compounds having valuable properties, in particular those which can be used for the preparation of medicaments.

The present invention relates to compounds and to the use of compounds in which the inhibition, regulation and/or modulation of signal transduction by kinases, in particular TGF-beta receptor kinases, plays a role, furthermore to pharmaceutical compositions which comprise these compounds, and to the use of the compounds for the treatment of kinase-induced diseases.

Transforming growth factor beta is the prototype of the TGF-beta superfamily, a family of highly preserved, pleiotrophic growth factors, which carry out important functions both during embryo development and also in the adult organism. In mammals, three isoforms of TGF-beta (TGF-beta 1, 2 and 3) have been identified, TGF-beta 1 being the commonest isoform (Kingsley (1994) Genes Dev 8:133-146). TGF-beta 3 is expressed, for example, only in mesenchymal cells, whereas TGF-beta 1 is found in mesenchymal and epithelial cells. TGF-beta is synthesised as pre-proprotein and is released in inactive form into the extracellular matrix (Derynck (1985) Nature 316: 701-705; Bottinger (1996) PNAS 93: 5877-5882). Besides the proregion cleaved off, which is also known as latency associated peptide (LAP) and remains associated with the mature region, one of the 4 isoforms of the latent TGF-beta binding proteins (LTBP 1-4) may also be bonded to TGF-beta (Gentry (1988) Mol Cell Biol 8: 4162-4168, Munger (1997) Kindey Int 51: 1376-1382). The activation of the inactive complex that is necessary for the development of the biological action of TGF-beta has not yet been clarified in

full. However, proteolytic processing, for example by plasmin, plasma transglutaminase or thrombospondin, is certainly necessary (Munger (1997) Kindey Int 51: 1376-1382). The activated ligand TGF-beta mediates its biological action via three TGF-beta receptors on the membrane, the ubiquitously expressed type I and type II receptors and the type III receptors betaglycan and endoglin, the latter only being expressed in endothelial cells (Gougos (1990) J Biol Chem 264: 8361-8364, Loeps-Casillas (1994) J Cell Biol 124:557-568). Both type III TGF-beta receptors lack an intracellular kinase domain which facilitates signal transmission into the cell. Since the type III TGF-beta receptors bind all three TGF-beta isoforms with high affinity and type II TGF-beta receptor also has higher affinity for ligands bonded to type III receptor, the biological function is thought to consist in regulation of the availability of the ligands for type I and type II TGF-beta receptors (Lastres (1996) J Cell Biol 133:1109-1121; Lopes-Casillas (1993) Cell 73: 1435-1344). The structurally closely related type I and type II receptors have a serine/threonine kinase domain, which is responsible for signal transmission, in the cytoplasmatic region. Type II TGF-beta receptor binds TGF-beta, after which the type I TGF-beta receptor is recruited to this signal-transmitting complex. The serine/threonine kinase domain of the type II receptor is constitutively active and is able to phosphorylate seryl radicals in this complex in the so-called GS domain of the type I receptor. This phosphorylation activates the kinase of the type I receptor, which is now itself able to phosphorylate intracellular signal mediators, the SMAD proteins, and thus initiates intracellular signal transmission (summarised in Derynck (1997) Biochim Biophys Acta 1333: F105-F150).

The proteins of the SMAD family serve as substrates for all TGF-beta family receptor kinases. To date, 8 SMAD proteins have been identified, which can be divided into 3 groups: (1) receptor-associated SMADs (R-SMADs) are direct substrates of the TGF-β receptor kinases (SMAD1, 2, 3, 5, 8); (2) co-SMADs, which associate with the R-Smads during the

signal cascade (SMAD4); and (3) inhibitory SMADs (SMAD6, 7), which inhibit the activity of the above-mentioned SMAD proteins. Of the various R-SMADs, SMAD2 and SMAD3 are the TGF-beta-specific signal mediators. In the TGF-beta signal cascade, SMAD2/SMAD3 are thus phosphorylated by the type I TGF-beta receptor, enabling them to associate with SMAD4. The resultant complex of SMAD2/SMAD3 and SMAD4 can now be translocated into the cell nucleus, where it can initiate the transcription of the TGF-beta-regulated genes directly or via other proteins (summarised in Itoh (2000) Eur J Biochem 267: 6954-6967; Shi (2003) Cell 113: 685-700).

The spectrum of the functions of TGF-beta is wide-ranging and dependent on cell type and differentiation status (Roberts (1990) Handbook of Experimental Pharmacology: 419-472). The cellular functions which are influenced by TGF-beta include: apoptosis, proliferation, differentiation, mobility and cell adhesion. Accordingly, TGF-beta plays an important role in a very wide variety of biological processes. During embryo development, it is expressed at sites of morphogenesis and in particular in areas with epithelial-mesenchymal interaction, where it induces important differentiation processes (Pelton (1991) J Cell Biol 115:1091-1105). TGF-beta also carries out a key function in the self-renewal and maintenance of an undifferentiated state of stem cells (Mishra (2005) Science 310: 68-71). In addition, TGF-beta also fulfils important functions in the regulation of the immune system. It generally has an immunosuppressive action, since it inhibits, inter alia, the proliferation of lymphocytes and restricts the activity of tissue macrophages. TGF-beta thus allows inflammatory reactions to subside again and thus helps to prevent excessive immune reactions (Bogdan (1993) Ann NY Acad Sci 685: 713-739, summarised in Letterio (1998) Annu Rev Immunol 16: 137-161). Another function of TGF-beta is regulation of cell proliferation. TGF-beta inhibits the growth of cells of endothelial, epithelial and haematopoietic origin, but promotes the growth of cells of mesenchymal origin (Tucker (1984) Science 226:705-707, Shipley (1986)

Cancer Res 46:2068-2071, Shipley (1985) PNAS 82: 4147-4151). A further important function of TGF-beta is regulation of cellular adhesion and cell-cell interactions. TGF-beta promotes the build-up of the extracellular matrix by induction of proteins of the extracellular matrix, such as, for example, fibronectin and collagen. In addition, TGF-beta reduces the expression of matrix-degrading metalloproteases and inhibitors of metalloproteases (Roberts (1990) Ann NY Acad Sci 580: 225-232; Ignotz (1986) J Biol Chem 261: 4337-4345; Overall (1989) J Biol Chem 264: 1860-1869); Edwards (1987) EMBO J 6: 1899-1904).

The broad spectrum of action of TGF-beta implies that TGF-beta plays an important role in many physiological situations, such as wound healing, and in pathological processes, such as cancer and fibrosis.

TGF-beta is one of the key growth factors in wound healing (summarised in O'Kane (1997) Int J Biochem Cell Biol 29: 79-89). During the granulation phase, TGF-beta is released from blood platelets at the site of injury. TGF-beta then regulates its own production in macrophages and induces the secretion of other growth factors, for example by monocytes. The most important functions during wound healing include stimulation of chemotaxis of inflammatory cells, the synthesis of extracellular matrix and regulation of the proliferation, differentiation and gene expression of all important cell types involved in the wound-healing process.

Under pathological conditions, these TGF-beta-mediated effects, in particular the regulation of the production of extracellular matrix (ECM), can result in fibrosis or scars in the skin (Border (1994) N Engl J Med 331:1286-1292).

For the fibrotic diseases, diabetic nephropathy and glomeronephritis, it has been shown that TGF-beta promotes renal cell hypertrophy and pathogenic accumulation of the extracellular matrix. Interruption of the TGF-beta signalling pathway by treatment with anti-TGF-beta antibodies prevents expansion of the mesangial matrix, progressive reduction in kidney function and reduces established lesions of diabetic glomerulo-

pathy in diabetic animals (Border (1990) 346: 371-374, Yu (2004) Kindney Int 66: 1774-1784, Fukasawah (2004) Kindney Int 65: 63-74, Sharma (1996) Diabetes 45: 522-530).

TGF-beta also plays an important role in liver fibrosis. The activation, essential for the development of liver fibrosis, of the hepatic stellate cells to give myofibroblasts, the main producer of the extracellular matrix in the course of the development of liver cirrhosis, is stimulated by TGF-beta. It has likewise been shown here that interruption of the TGF-beta signalling pathway reduces fibrosis in experimental models (Yata (2002) Hepatology 35:1022-1030; Arias (2003) BMC Gastroenterol 3:29)

TGF-beta also takes on a key function in the formation of cancer (summarised in Derynck (2001) Nature Genetics: 29: 117-129; Elliott (2005) J Clin Onc 23: 2078-2093). At early stages of the development of cancer, TGF-beta counters the formation of cancer. This tumour-suppressant action is based principally on the ability of TGF-beta to inhibit the division of epithelial cells. By contrast, TGF-beta promotes cancer growth and the formation of metastases at late tumour stages. This can be attributed to the fact that most epithelial tumours develop a resistance to the growth-inhibiting action of TGF-beta, and TGF-beta simultaneously supports growth of the cancer cells via other mechanisms. These mechanisms include promotion of angiogenesis, the immunosuppressant action, which supports tumour cells in avoiding the control function of the immune system (immunosurveillance), and promotion of invasiveness and the formation of metastases. The formation of an invasive phenotype of the tumour cells is a principal prerequisite for the formation of metastases. TGF-beta promotes this process through its ability to regulate cellular adhesion, motility and the formation of the extracellular matrix. Furthermore, TGF-beta induces the transition from an epithelial phenotype of the cell to the invasive mesenchymal phenotype (epithelial mesenchymal transition = EMT). The important role played by TGF-beta in the promotion of cancer growth is also demonstrated by investigations which show a correlation between strong TGF-

beta expression and a poor prognosis. Increased TGF-beta level have been found, inter alia, in patients with prostate, breast, intestinal and lung cancer (Wikström (1998) Prostate 37: 19-29; Hasegawa (2001) Cancer 91: 964-971; Friedman (1995), Cancer Epidemiol Biomarkers Prev. 4:549-54).

Owing to the cancer-promoting actions of TGF-beta described above, inhibition of the TGF-beta signalling pathway, for example via inhibition of the TGF-beta type I receptor, is a possible therapeutic concept. It has been shown in numerous preclinical trials that interruption of the TGF-beta signalling pathway does indeed inhibit cancer growth. Thus, treatment with soluble TGF-beta type II receptor reduces the formation of metastases in transgenic mice, which develop invasive breast cancer in the course of time (Muraoka (2002) J Clin Invest 109: 1551-1559, Yang (2002) J Clin Invest 109: 1607-1615).

Tumour cell lines which express a defective TGF-beta type II receptor exhibit reduced tumour and metastatic growth (Oft (1998) Curr Biol 8: 1243-1252, McEachern (2001) Int J Cancer 91:76-82, Yin (1999) Jclin Invest 103: 197-206).

Conditions "characterised by enhanced TGF-β activity" include those in which TGF-β synthesis is stimulated so that TGF-β is present at increased levels or in which TGF-β latent protein is undesirably activated or converted to active TGF-β protein or in which TGF-β receptors are upregulated or in which the TGF-β protein shows enhanced binding to cells or extracellular matrix in the location of the disease. Thus, in either case "enhanced activity" refers to any condition in which the biological activity of TGF-β is undesirably high, regardless of the cause.

A number of diseases have been associated with TGF-β1 overproduction.

Inhibitors of TGF-β intracellular signaling pathway are useful treatments for fibroproliferative diseases. Specifically, fibroproliferative diseases include kidney disorders associated with unregulated TGF-β activity and excessive fibrosis including glomerulonephritis (GN), such as mesangial proliferative GN, immune GN, and crescentic GN. Other renal conditions include diabetic nephropathy, renal interstitial fibrosis, renal fibrosis in transplant patients receiving cyclosporin, and HIV-associated nephropathy. Collagen vascular disorders include progressive systemic sclerosis, polymyositis, sclerorma, dermatomyositis, eosinophilic fascitis, morphea, or those associated with the occurrence of Raynaud's syndrome. Lung fibroses resulting from excessive TGF-β activity include adult respiratory distress syndrome, idiopathic pulmonary fibrosis, and interstitial pulmonary fibrosis often associated with autoimmune disorders, such as systemic lupus erythematosus and sclerorma, chemical contact, or allergies. Another autoimmune disorder associated with fibroproliferative characteristics is rheumatoid arthritis.

Eye diseases associated with a fibroproliferative condition include retinal reattachment surgery accompanying proliferative vitreoretinopathy, cataract extraction with intraocular lens implantation, and post-glaucoma drainage surgery are associated withTGF-β1 overproduction.

Fibrotic diseases associated with TGF-β1 overproduction can be divided into chronic conditions, such as fibrosis of the kidney, lung and liver, and more acute conditions, such as dermal scarring and restenosis (Chamberlain, J. Cardiovascular Drug Reviews, 19 (4): 329-344). Synthesis and secretion of TGF-β1 by tumor cells can also lead to immune suppression, as seen in patients with aggressive brain or breast tumors (Arteaga, et al. (1993) J. Clin. Invest. 92: 2569-2576). The course of Leishmanial infection in mice is drastically altered by TGF-β1 (Barral-Netto, et al. (1992) Science 257: 545-547). TGF-β1 exacerbated the disease, whereas TGF-β1 anti-

bodies halted the progression of the disease in genetically susceptible mice. Genetically resistant mice became susceptible to Leishmanial infection upon administration of TGF-β1.

The profound effects of TGF-β1 on extracellular matrix deposition have been reviewed (Rocco and Ziyadeh (1991) in Contemporary Issues in Nephrology v. 23, Hormones, autocoids and the kidney. ed. Jay Stein, Churchill Livingston, New York pp. 391-410 ; Roberts, et al. (1988) Rec. Prog. Hormone Res. 44: 157-197) and include the stimulation of the synthesis and the inhibition of degradation of extracellular matrix components. Since the structure and filtration properties of the glomerulus are largely determined by the extracellular matrix composition of the mesangium and glomerular membrane, it is not surprising that TGF-β1 has profound effects on the kidney. The accumulation of mesangial matrix in proliferative glomerulonephritis (Border, et al. (1990) Kidney Int. 37: 689-695) and diabetic nephropathy (Mauer, et al. (1984) J. Clin. Invest. 74: 1143-1155) are clear and dominant pathological features of the diseases. TGF-β1 levels are elevated in human diabetic glomerulosclerosis (advanced neuropathy) (Yamamoto, et al. (1993) Proc. Natl. Acad. Sci. 90: 1814-1818). TGF-β1 is an important mediator in the genesis of renal fibrosis in a number of animal models (Phan, et al. (1990) Kidney Int. 37: 426; Okuda, et al. (1990) J. Clin. Invest. 86: 453). Suppression of experimentally induced glomerulonephritis in rats has been demonstrated by antiserum against TGF-β1 (Border, et al. (1990) Nature 346: 371) and by an extracellular matrix protein, decorin, which can bind TGF-β1 (Border, et al. (1992) Nature 360: 361-363).

Excessive TGF-β1 leads to dermal scar-tissue formation. Neutralising TGF-β1 antibodies injected into the margins of healing wounds in rats have been shown to inhibit scarring without interfering with the rate of wound healing or the tensile strength of the wound (Shah, et al. (1992)

Lancet 339: 213-214). At the same time there was reduced angiogenesis, a reduced number of macrophages and monocytes in the wound, and a reduced amount of disorganised collagen fibre deposition in the scar tissue.

TGF-β1 may be a factor in the progressive thickening of the arterial wall which results from the proliferation of smooth muscle cells and deposition of extracellular matrix in the artery after balloon angioplasty. The diameter of the restenosed artery may be reduced by 90% by this thickening, and since most of the reduction in diameter is due to extracellular matrix rather than smooth muscle cell bodies, it may be possible to open these vessels to 50% simply by reducing extensive extracellular matrix deposition. In undamaged pig arteries transfected in vivo with a TGF-β1 gene, TGF-β1 gene expression was associated with both extracellular matrix synthesis and hyperplasia (Nabel, et al. (1993) Proc. Natl. Acad. Sci. USA 90: 10759-10763). The TGF-β1 induced hyperplasia was not as extensive as that induced with PDGF-BB, but the extracellular matrix was more extensive with TGF-β1 transfectants. No extracellular matrix deposition was associated with hyperplasia induced by FGF-1 (a secreted form of FGF) in this gene transfer pig model (Nabel (1993) Nature 362: 844-846).

There are several types of cancer where TGF-β1 produced by the tumor may be deleterious. MATLyLu rat prostate cancer cells (Steiner and Barrack (1992) Mol. Endocrinol 6: 15-25) and MCF-7 human breast cancer cells (Arteaga, et al. (1993) Cell Growth and Differ. 4: 193-201) became more tumorigenic and metastatic after transfection with a vector expressing the mouse TGF-β1. TGF-β1 has been associated with angiogenesis, metastasis and poor prognosis in human prostate and advanced gastric cancer (Wikstrom, P., et al. (1998) Prostate 37 : 19-29; Saito, H. et al. (1999) Cancer 86: 1455-1462). In breast cancer, poor prognosis is associated with elevated TGF-β (Dickson, et al. (1987) Proc. Natl. Acad. Sci.

USA 84: 837-841; Kasid, et al. (1987) Cancer Res. 47: 5733-5738; Daly, et al. (1990) J. Cell Biochem. 43: 199-211 ; Barrett-Lee, et al. (1990) Br. J Cancer 61: 612-617; King, et al. (1989) J. Steroid Biochem. 34: 133-138; Welch, et al. (1990) Proc. Natl. Acad. Sci. USA 87: 7678-7682; Walker, et al. (1992) Eur. J. Cancer 238 : 641-644) and induction of TGF-β1 by tamoxifen treatment (Butta, et al. (1992) Cancer Res. 52: 4261- 4264) has been associated with failure of tamoxifen treatment for breast cancer (Thompson, et al. (1991) Br. J. Cancer 63: 609-614). Anti-TGF-β1 antibodies inhibit the growth of MDA-231 human breast cancer cells in athymic mice (Arteaga, et al. (1993) J. Clin. Invest. 92: 2569-2576), a treatment which is correlated with an increase in spleen natural killer cell activity. CHO cells transfected with latent TGF-β1 also showed decreased NK activity and increased tumor growth in nude mice (Wallick, et al. (1990) J. Exp. Med. 172: 1777-1784). Thus, TGF-β secreted by breast tumors may cause an endocrine immune suppression. High plasma concentrations of TGF-β1 have been shown to indicate poor prognosis for advanced breast cancer patients (Anscher, et al. (1993) N. Engl. J. Med. 328: 1592-1598). Patients with high circulating TGF-β before high dose chemotherapy and autologous bone marrow transplantation are at high risk of hepatic veno-occlusive disease (15-50% of all patients with a mortality rate up to 50%) and idiopathic interstitial pneumonitis (40-60% of all patients). The implication of these findings is 1) that elevated plasma levels of TGF-β1 can be used to identify at-risk patients and 2) that reduction of TGF-β1 could decrease the morbidity and mortality of these common treatments for breast cancer patients.

Many malignant cells secrete transforming growth factor β (TGF-β), a potent immunosuppressant, suggesting that TGF-β production may represent a significant tumor escape mechanism from host immunosurveillance. Establishment of a leukocyte sub-population with disrupted TGF-β signaling in the tumor-bearing host offers a potential means for immunotherapy

of cancer. A transgenic animal model with disrupted TGF-β signaling in T cells is capable of eradicating a normally lethal TGF-β overexpressing lymphom tumor, EL4 (Gorelik and Flavell, (2001) Nature Medicine 7 (10): 1118-1122).

Downregulation of TGF-β secretion in tumor cells results in restoration of immunogenicity in the host, while T-cell insensitivity to TGF-β results in accelerated differentiation and autoimmunity, elements of which may be required in order to combat self-antigen-expressing tumors in a tolerised host. The immunosuppressive effects of TGF-β have also been implicated in a subpopulation of HIV patients with lower than predicted immune response based on their CD4/CD8 T cell counts (Garba, et al. J. Immunology (2002) 168: 2247-2254). A TGF-β neutralising antibody was capable of reversing the effect in culture, indicating that TGF-β signaling inhibitors may have utility in reversing the immune suppression present in this subset of HIV patients.

During the earliest stages of carcinogenesis, TGF-β1 can act as a potent tumor suppressor and may mediate the actions of some chemopreventive agents. However, at some point during the development and progression of malignant neoplasms, tumor cells appear to escape from TGF-β-dependent growth inhibition in parallel with the appearance of bioactive TGF-β in the microenvironment. The dual tumour suppression/tumour promotion roles of TGF-β have been most clearly elucidated in a transgenic system overexpressing TGF-β in keratinocytes. While the transgenics were more resisitant to formation of benign skin lesions, the rate of metastatic conversion in the transgenics was dramatically increased (Cui, et al (1996) Cell 86 (4): 531-42). The production of TGF-β1 by malignant cells in primary tumours appears to increase with advancing stages of tumour progression. Studies in many of the major epithelial cancers suggest that the increased production of TGF-β by human cancers occurs as

a relatively late event during tumour progression. Further, this tumor-associated TGF-β provides the tumour cells with a selective advantage and promotes tumour progression. The effects of TGF-β1 on cell/cell and cell/stroma interactions result in a greater propensity for invasion and metastasis.

Tumour-associated TGF-β may allow tumour cells to escape from immune surveillance since it is a potent inhibitor of the clonal expansion of activated lymphocytes. TGF-β has also been shown to inhibit the production of angiostatin. Cancer therapeutic modalities, such as radiation therapy and chemotherapy, induce the production of activated TGF-β in the tumour, thereby selecting outgrowth of malignant cells that are resistant to TGF-β growth inhibitory effects. Thus, these anticancer treatments increase the risk and hasten the development of tumours with enhanced growth and invasiveness. In this situation, agents targeting TGF-β-mediated signal transduction might be a very effective therapeutic strategy. The resistance of tumour cells to TGF-β has been shown to negate many of the cytotoxic effects of radiation therapy and chemotherapy, and the treatment-dependent activation of TGF-β in the stroma may even be detrimental as it can make the microenvironment more conducive to tumour progression and contributes to tissue damage leading to fibrosis. The development of a TGF-β signal transduction inhibitors is likely to benefit the treatment of progressed cancer alone and in combination with other therapies.

The compounds are suitable for the treatment of cancer and other disease states influenced by TGF-β by inhibiting TGF-β in a patient in need thereof by administration of said compound(s) to said patient. TGF-β would also be useful against atherosclerosis (T. A. McCaffrey: TGF-ps and TGF-β Receptors in Atherosclerosis: Cytokine and Growth Factor Reviews 2000,11,103-114) and Alzeheimer's (Masliah, E.; Ho, G.; Wyss-Coray, T.: Functional Role of TGF-β in Alzheimer's Disease Microvascular Injury:

Lessons from Trangenic Mice: Neurochemistry International 2001,39,393-400) diseases.

It has been found that the compounds according to the invention and salts thereof have very valuable pharmacological properties while being well tolerated.
In particular, they exhibit TGFβ receptor I kinase-inhibiting properties.

The compounds according to the invention preferably exhibit an advantageous biological activity, which is easily demonstrated in enzyme-based assays, for example assays as described herein. In such enzyme-based assays, the compounds according to the invention preferably exhibit and cause an inhibiting effect, which is usually documented by IC_{50} values in a suitable range, preferably in the micromolar range and more preferably in the nanomolar range.

As discussed herein, these signalling pathways are relevant for various diseases. Accordingly, the compounds according to the invention are useful in the prophylaxis and/or treatment of diseases that are dependent on the said signalling pathways by interaction with one or more of the said signalling pathways.
The present invention therefore relates to compounds according to the invention as promoters or inhibitors, preferably as inhibitors, of the signalling pathways described herein. The invention therefore preferably relates to compounds according to the invention as promoters or inhibitors, preferably as inhibitors, of the TGFβ signalling pathway.

The present invention furthermore relates to the use of one or more compounds according to the invention in the treatment and/or prophylaxis of diseases, preferably the diseases described herein, that are caused, mediated and/or propagated by an increased TGFβ activity.

The present invention therefore relates to compounds according to the invention as medicaments and/or medicament active ingredients in the treatment and/or prophylaxis of the said diseases and to the use of compounds according to the invention for the preparation of a pharmaceutical for the treatment and/or prophylaxis of the said diseases as well as to a method for the treatment of the said diseases comprising the administration of one or more compounds according to the invention to a patient in need of such an administration.

The host or patient can belong to any mammalian species, for example a primate species, particularly humans; rodents, including mice, rats and hamsters; rabbits; horses, cows, dogs, cats, etc. Animal models are of interest for experimental investigations, providing a model for treatment of human disease.

The susceptibility of a particular cell to treatment with the compounds according to the invention can be determined by in vitro tests. Typically, a culture of the cell is combined with a compound according to the invention at various concentrations for a period of time which is sufficient to allow the active agents to induce cell death or to inhibit migration, usually between about one hour and one week. In vitro testing can be carried out using cultivated cells from a biopsy sample. The viable cells remaining after the treatment are then counted.

The dose varies depending on the specific compound used, the specific disease, the patient status, etc. A therapeutic dose is typically sufficient considerably to reduce the undesired cell population in the target tissue while the viability of the patient is maintained. The treatment is generally continued until a considerable reduction has occurred, for example an at least about 50% reduction in the cell burden, and may be continued until essentially no more undesired cells are detected in the body.

For identification of a signal transduction pathway and for detection of interactions between various signal transduction pathways, various scientists have developed suitable models or model systems, for example cell culture models (for example Khwaja et al., EMBO, 1997, 16, 2783-93) and models of transgenic animals (for example White et al., Oncogene, 2001, 20, 7064-7072). For the determination of certain stages in the signal transduction cascade, interacting compounds can be utilised in order to modulate the signal (for example Stephens et al., Biochemical J., 2000, 351, 95-105). The compounds according to the invention can also be used as reagents for testing kinase-dependent signal transduction pathways in animals and/or cell culture models or in the clinical diseases mentioned in this application.

Measurement of the kinase activity is a technique which is well known to the person skilled in the art. Generic test systems for the determination of the kinase activity using substrates, for example histone (for example Alessi et al., FEBS Lett. 1996, 399, 3, pages 333-338) or the basic myelin protein, are described in the literature (for example Campos-González, R. and Glenney, Jr., J.R. 1992, J. Biol. Chem. 267, page 14535).

For the identification of kinase inhibitors, various assay systems are available. In scintillation proximity assay (Sorg et al., J. of. Biomolecular Screening, 2002, 7, 11-19) and flashplate assay, the radioactive phosphorylation of a protein or peptide as substrate with γATP is measured. In the presence of an inhibitory compound, a decreased radioactive signal, or none at all, is detectable. Furthermore, homogeneous time-resolved fluorescence resonance energy transfer (HTR-FRET) and fluorescence polarisation (FP) technologies are suitable as assay methods (Sills et al., J. of Biomolecular Screening, 2002, 191-214).

Other non-radioactive ELISA assay methods use specific phospho-antibodies (phospho-ABs). The phospho-AB binds only the phosphorylated

substrate. This binding can be detected by chemiluminescence using a second peroxidase-conjugated anti-sheep antibody (Ross et al., 2002, Biochem. J.) just about to be published, manuscript BJ20020786).

PRIOR ART

Compounds "B2", "B3", "B4", "B5", "B8", "B9", "B10", "B12", "B14", "B16", "B17", "B19", "B20" are described in DE 2 409 308 as medicament active ingredients having an analgesic and/or inflammatory effect.

Compounds "B1", "B6", "B7", "B11", "B13", "B15", "B18", "B21", "B22" have been described by E. Szarvasi et al. in Eur. J. Med. 1978, 13, 113-119, as medicament active ingredients having an analgesic and/or anti-inflammatory action.

Other triazolo-1,5-benzodiazepines are known from DE 2 318 673.

L. Kosychova et al. in Chemistry of Heterocyclic Compounds, Vol. 40, 811-815 (2004) describe other 5,6-dihydro-4*H*-1,2,4-triazolo-*a*]-1,5benzo-diazepine for combating tumours.

V. Ambrogi et al. in J. Heterocyclic Chem. 31, 1349-1352 (1994) described sulfur-containing 4,5-dihydro-*s*-triazolo[3,4-*d*]-1,5-benzothiazepine derivatives.

V. Ambrogi et al. in Il Farmaco 48, 665-676 (1993) describe 1,4-benzo-thiazines and 1,5-benzothiazepines having an action on the central nervous system.

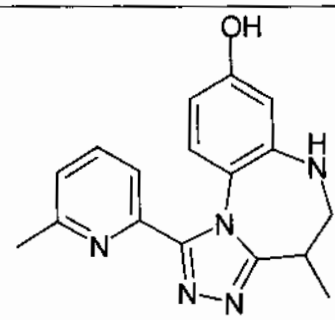
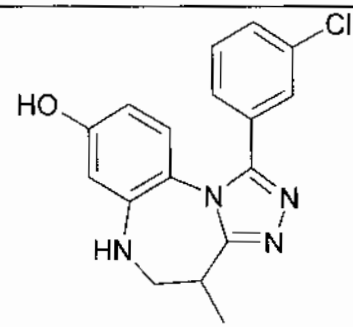
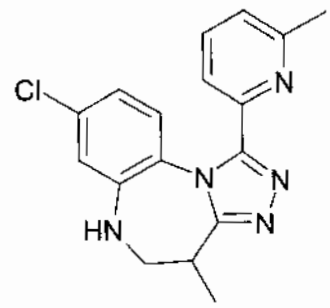
Other triazole derivatives are disclosed as TGF-beta inhibitors in WO 03/042211 A1.

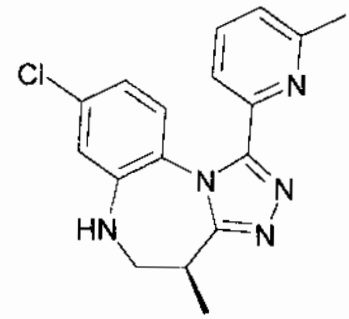
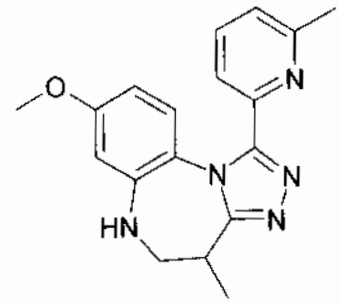
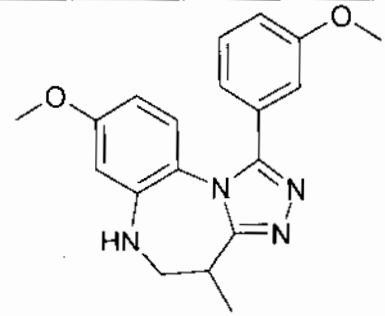
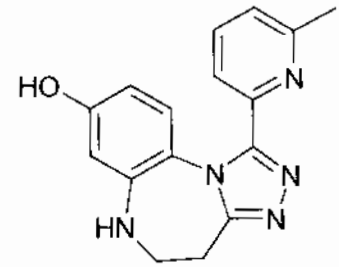
Still other triazole derivatives are known as TGF-beta inhibitors WO 2004/026307 A1.

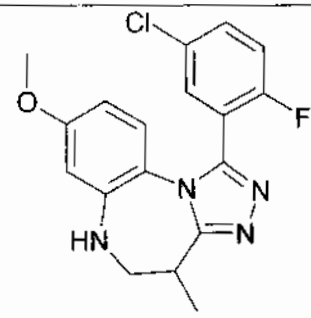
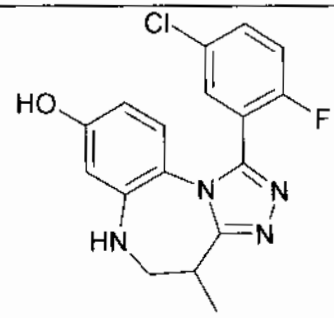
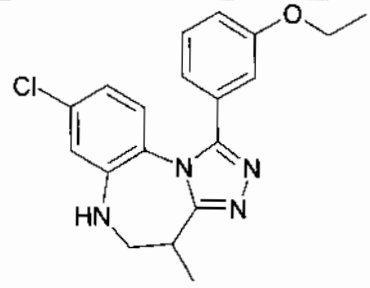
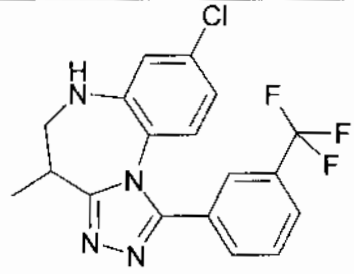
Bicyclic pyrrole derivatives are described as TGF-beta inhibitors in WO 02/094833.

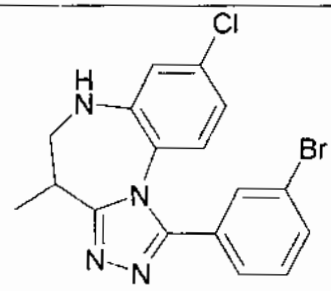
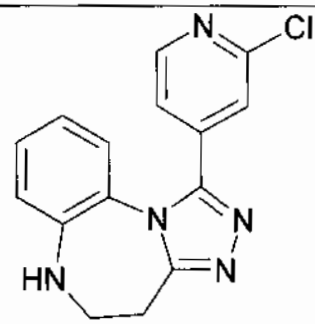
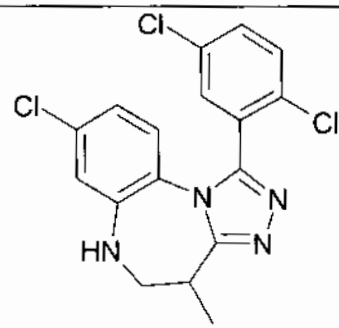
SUMMARY OF THE INVENTION

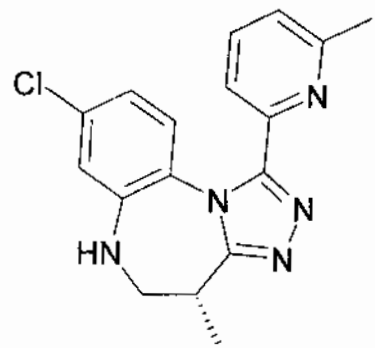
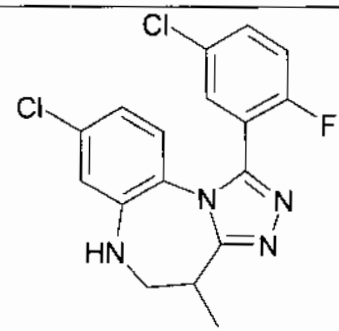
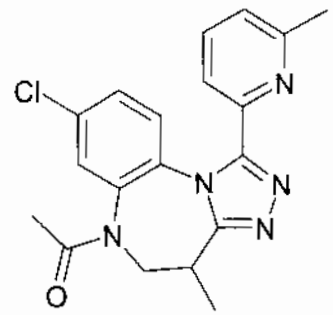
The invention relates to compounds selected from the group

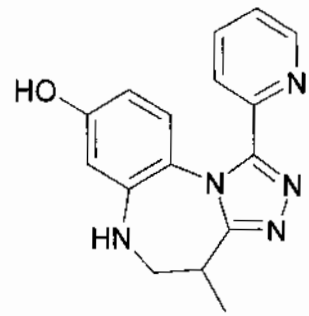
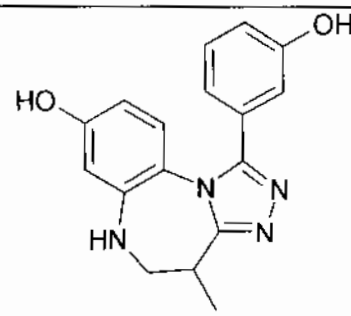
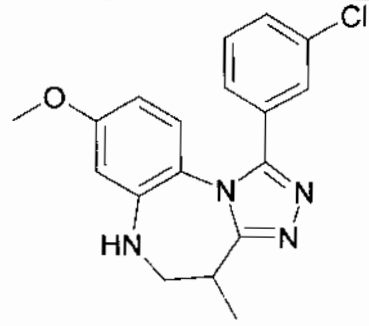
Compound No.	Structure / name
"A1"	 (*R,S*)-8-Hydroxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A2"	 (R,S)-1-(3-Chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A3"	 (R,S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

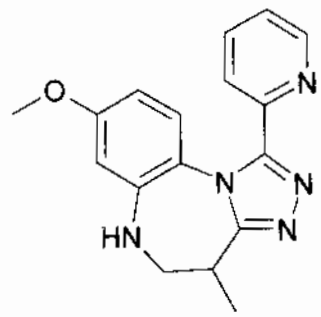
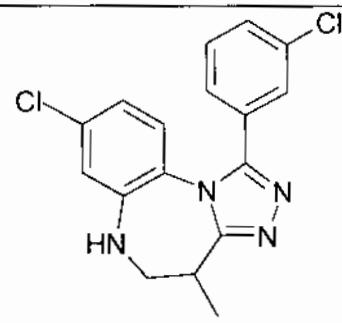
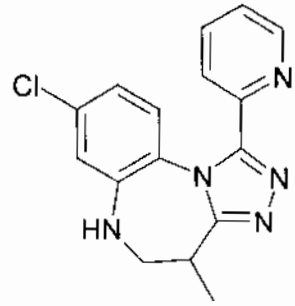
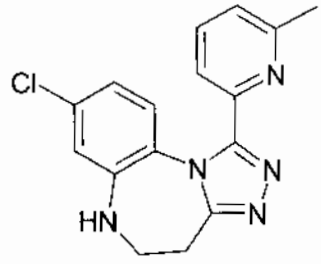
"A4"	 (+)-(S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A5"	 (R,S)-8-Methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A6"	 (R,S)-8-Methoxy-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A7"	 1-(6-Methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

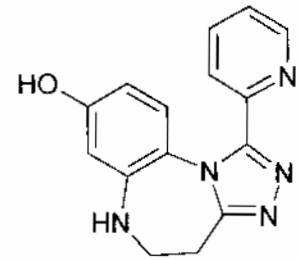
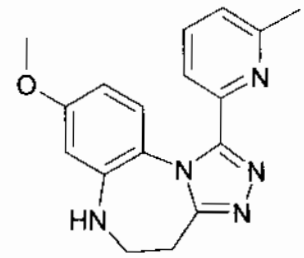
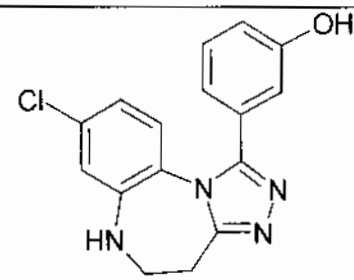
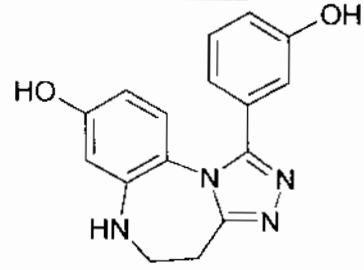
"A8"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A9"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A10"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A11"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethylphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

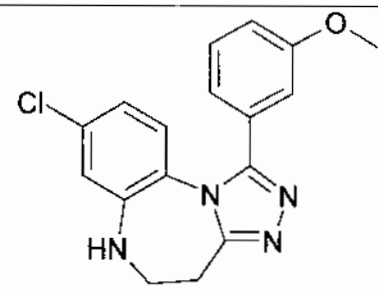
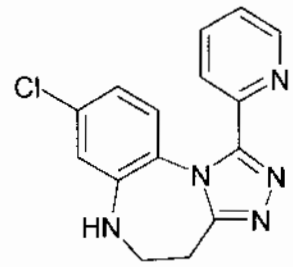
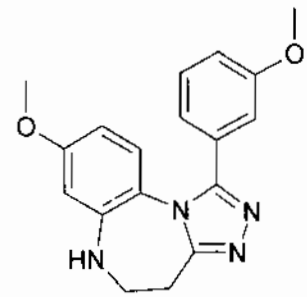
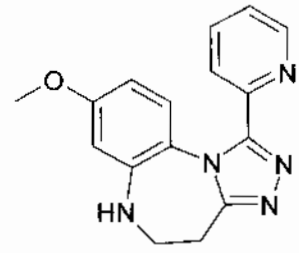
"A12"	 (R,S)-1-(3-Bromophenyl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulene
"A13"	 1-(2-Chloropyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A14"	 (R,S)-8-Chloro-1-(2,5-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulene

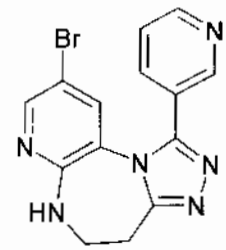
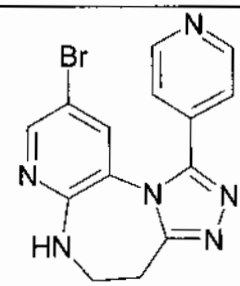
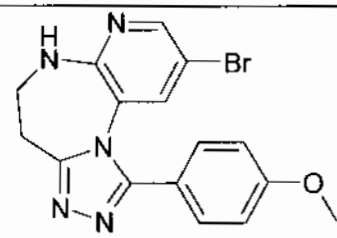
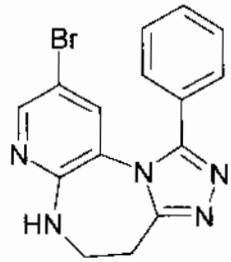
"A15"	 (-)-(R)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A16"	 (R,S)-8-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A17"	 (R,S)-1-[8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulen-6-yl]ethanone

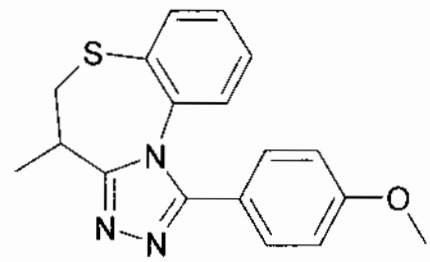
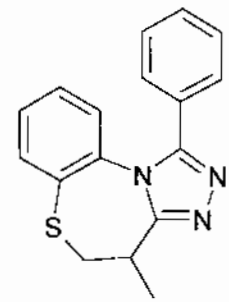
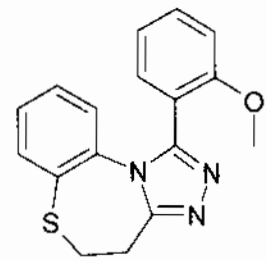
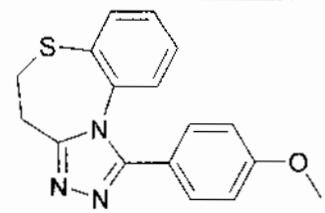
"A18"	 (R,S)-4-Methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A19"	 (R,S)-1-(3-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A20"	 (R,S)-1-(3-Chlorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

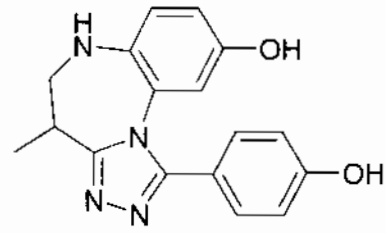
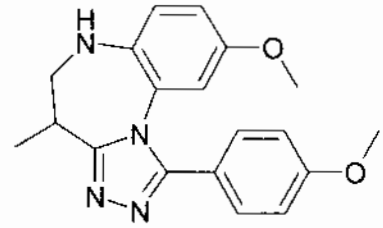
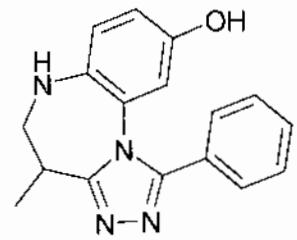
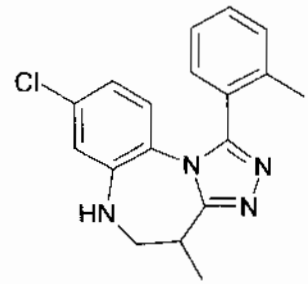
"A21"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A22"	 (R,S)-8-Chloro-1-(3-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A23"	 (R,S)-8-Chloro-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A24"	 8-Chloro-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

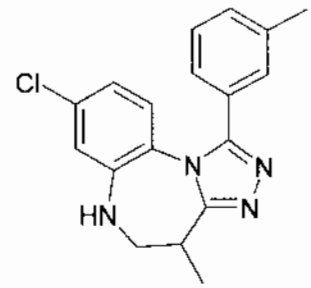
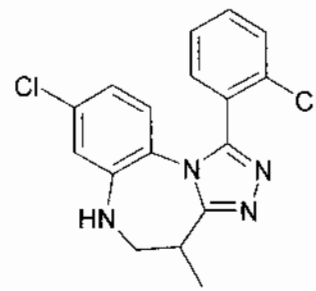
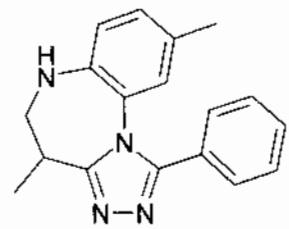
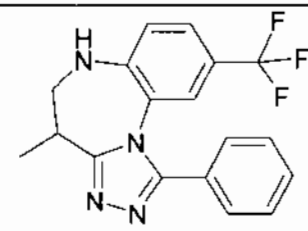
"A25"	 1-Pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol
"A26"	 8-Methoxy-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A27"	 3-(8-Chloro-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)phenol
"A28"	 1-(3-Hydroxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

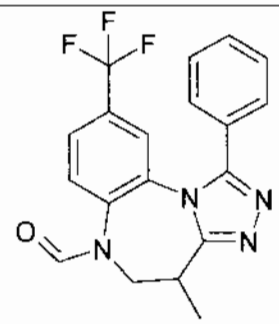
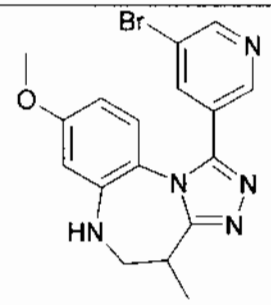
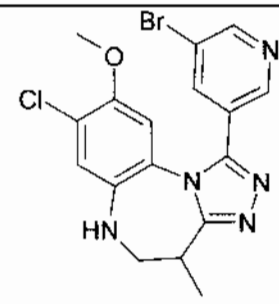
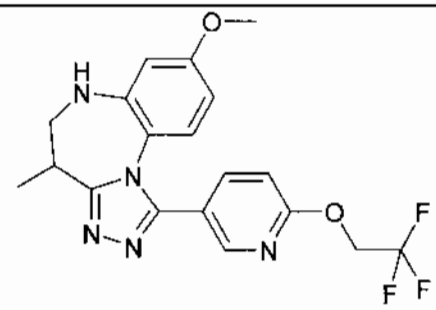
"A29"	 8-Chloro-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A30"	 8-Chloro-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A31"	 8-Methoxy-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A32"	 8-Methoxy-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene

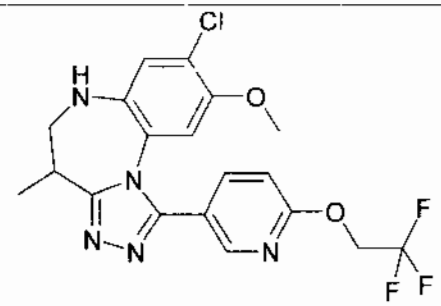
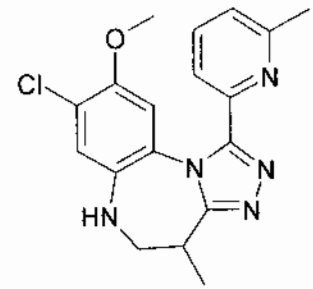
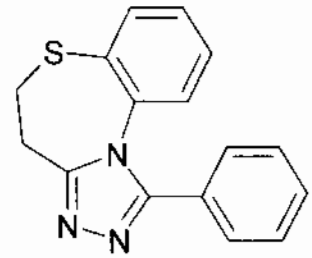
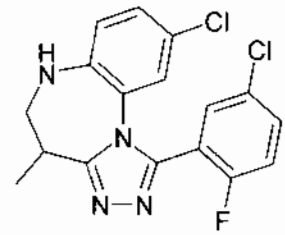
"A33"	 9-Bromo-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A34"	 9-Bromo-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A35"	 9-Bromo-1-(4-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene
"A36"	 9-Bromo-1-phenyl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene

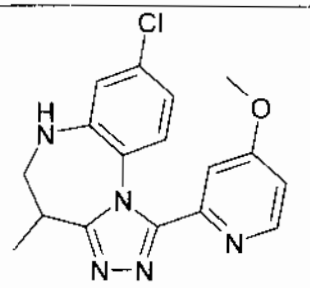
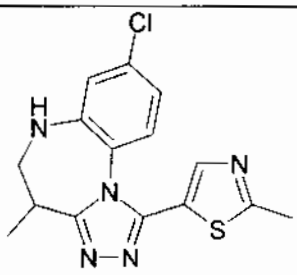
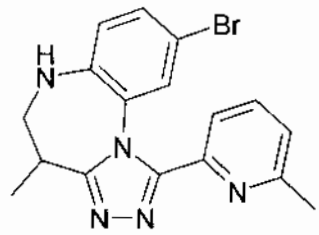
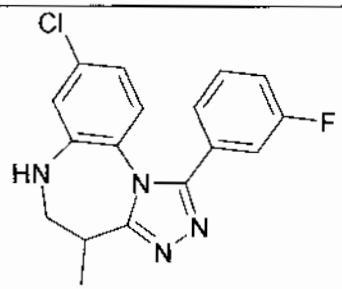
"A37"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A38"	 (R,S)-4-Methyl-1-phenyl-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A39"	 1-(2-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A40"	 1-(4-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene

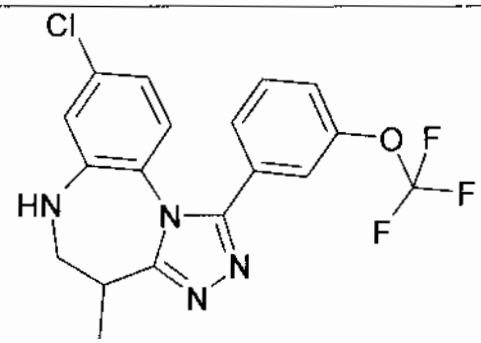
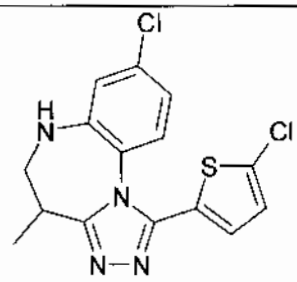
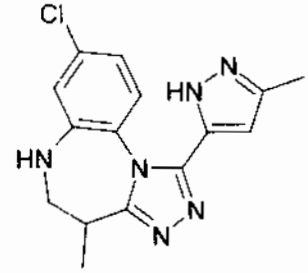
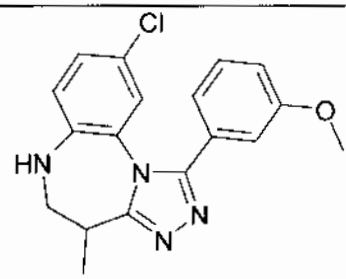
"A41"	 (R,S)-1-(4-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A42"	 (R,S)-9-Methoxy-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A43"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol
"A44"	 (R,S)-8-Chloro-4-methyl-1-*o*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

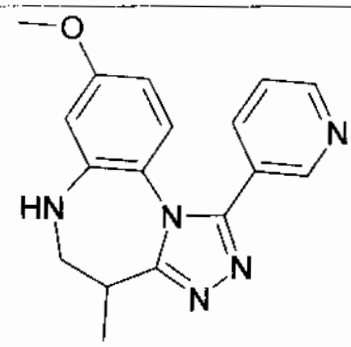
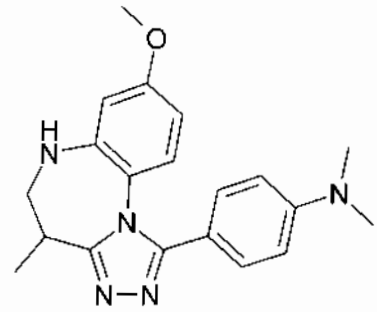
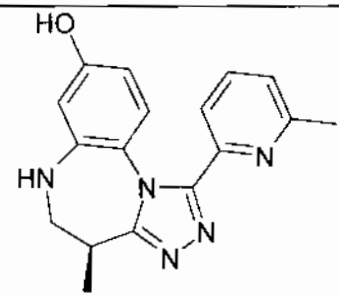
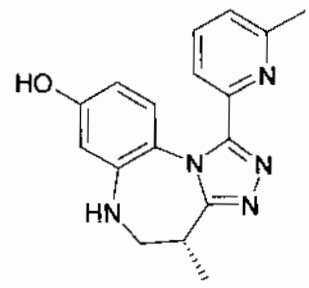
"A45"	 (R,S)-8-Chloro-4-methyl-1-*m*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A46"	 (R,S)-8-Chloro-1-(2-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A47"	 (R,S)-4,9-Dimethyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A48"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

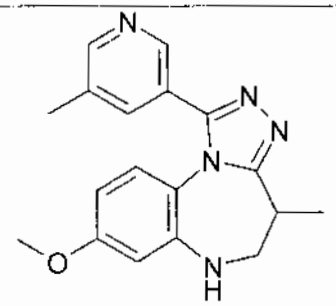
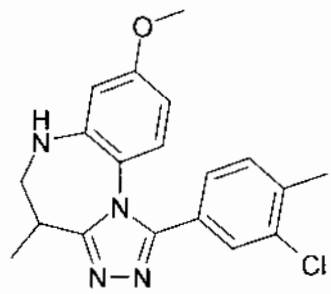
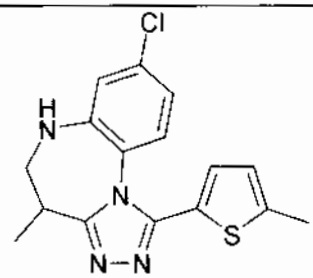
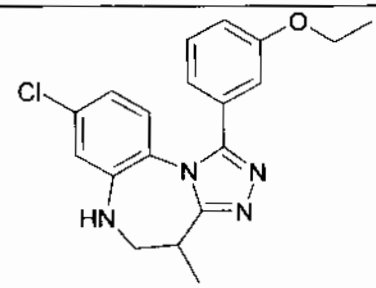
"A49"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulene-6-carbaldehyde
"A50"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A51"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-chloro-9-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A52"	 (R,S)-8-Methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

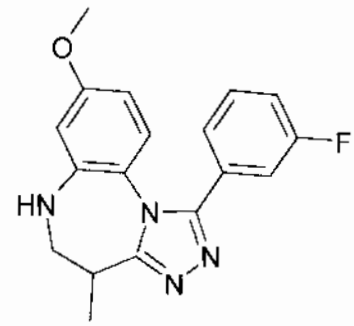
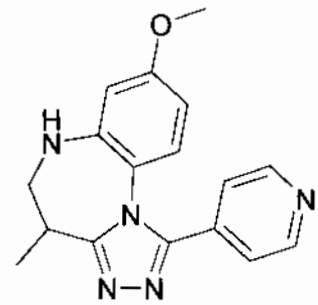
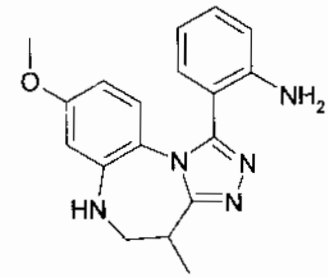
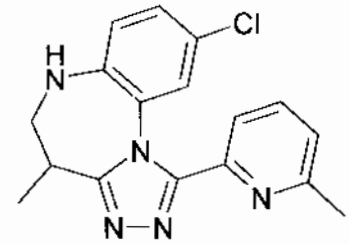
"A53"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-[6-(2,2,2-trifluoro-ethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A54"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A55"	 1-Phenyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A56"	 (R,S)-9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

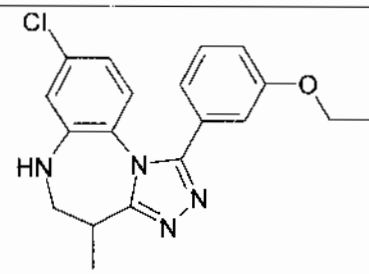
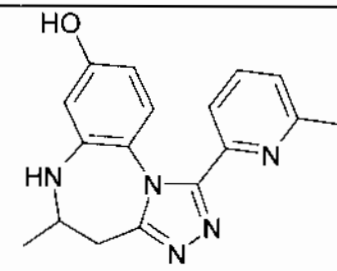
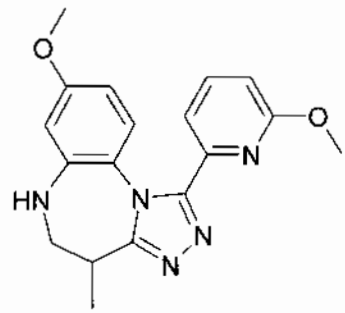
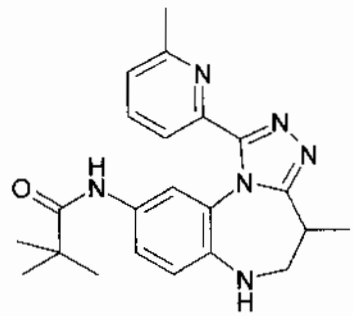
"A57"	 (R,S)-8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A58"	 (R,S)-8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A59"	 (R,S)-9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A60"	 (R,S)-8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

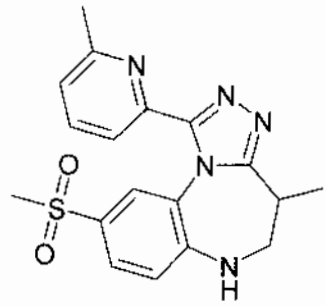
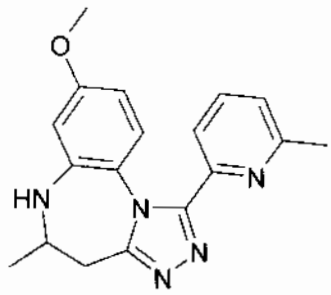
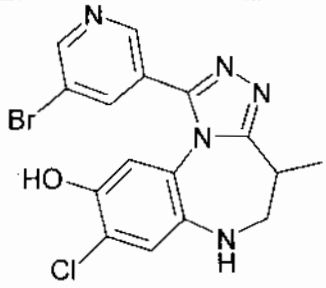
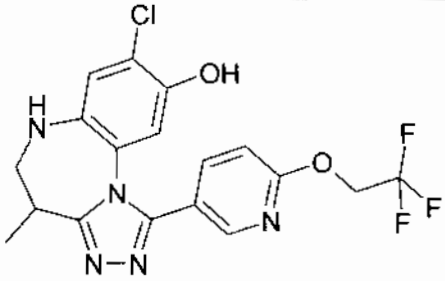
"A61"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A62"	 (R,S)-8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A63"	 (R,S)-8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A64"	 (R,S)-9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

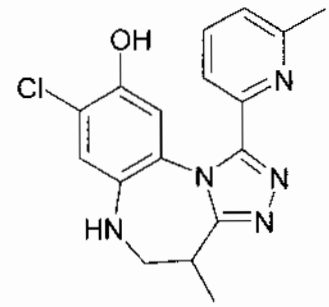
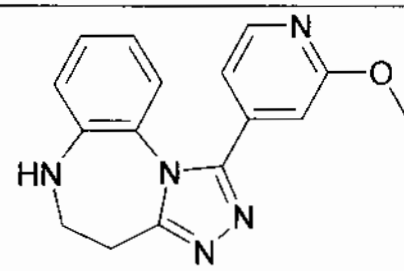
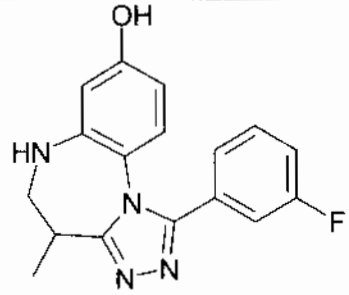
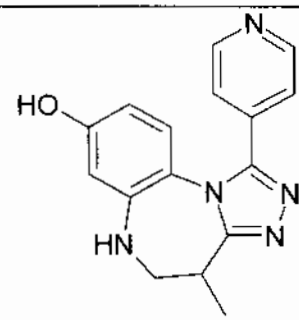
"A65"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A66"	 (R,S)-[4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenyl]dimethylamine
"A67"	 (S)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A68"	 (R)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol

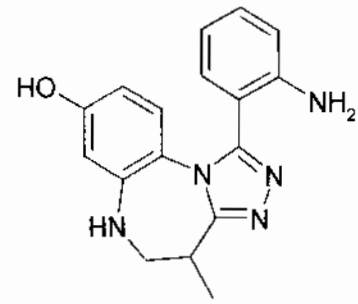
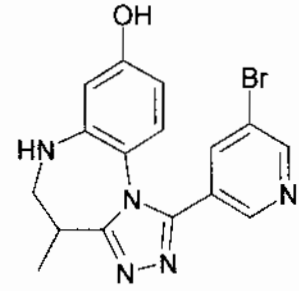
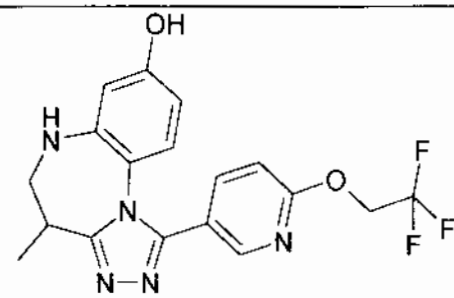
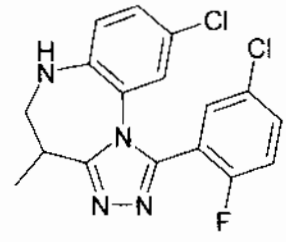
"A69"	 (R,S)-8-Methoxy-4-methyl-1-(5-methylpyridin-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A70"	 (R,S)-1-(3-Chloro-4-methylphenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A71"	 (R,S)-8-Chloro-4-methyl-1-(5-methylthiophen-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A72"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

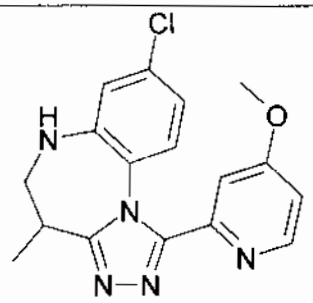
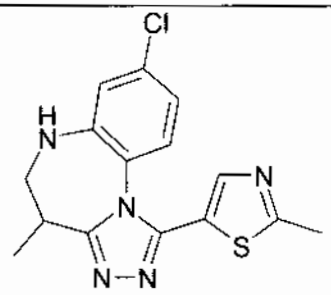
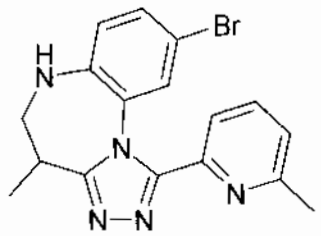
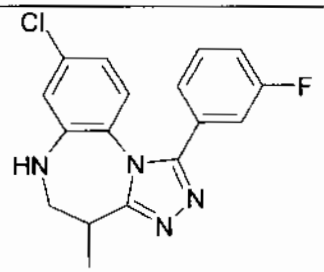
"A73"	 (R,S)-1-(3-Fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A74"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A75"	 (R,S)-2-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenylamine
"A76"	 (R,S)-9-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene bistrifluoroacetate

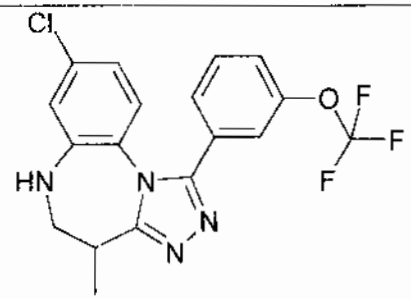
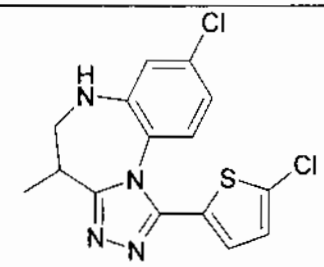
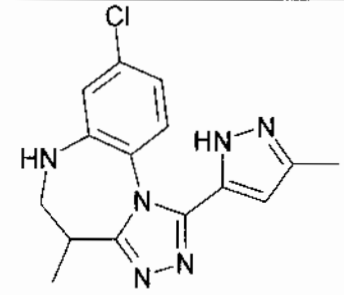
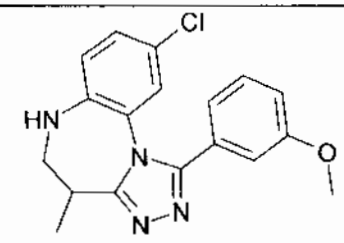
"A77"	 8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A78"	 5-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A79"	 8-Methoxy-1-(6-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A80"	 2,2-Dimethyl-N-[4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-yl]propion-amide

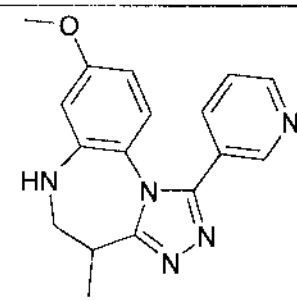
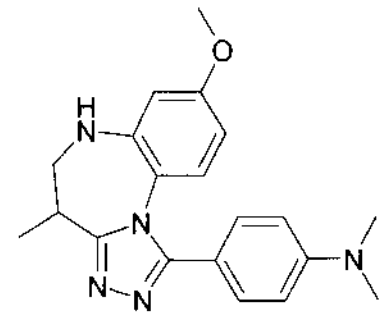
"A81"	 9-Methanesulfonyl-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A82"	 8-Methoxy-5-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A83"	 1-(5-Bromopyridin-3-yl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A84"	 8-Chloro-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol

"A85"	 8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A86"	 1-(2-Methoxypyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A87"	 1-(3-Fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A88"	 4-Methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

"A89"	 1-(2-Aminophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A90"	 1-(5-Bromopyridin-3-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A91"	 4-Methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A92"	 9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"A93"	 8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A94"	 8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A95"	 9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A96"	 8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"A97"	 8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A98"	 8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A99"	 8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A100"	 9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"A101"	 8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A102"	 [4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)phenyl]dimethylamine

and pharmaceutically usable derivatives, solvates, salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

The invention also relates to the optically active forms (stereoisomers), the enantiomers, the racemates, the diastereomers and the hydrates and solvates of these compounds. The term solvates of the compounds is taken to mean adductions of inert solvent molecules onto the compounds which form owing to their mutual attractive force. solvates are, for example, mono- or dihydrates or alkoxides.

The term pharmaceutically usable derivatives is taken to mean, for example, the salts of the compounds according to the invention and also so-called prodrug compounds.

The term prodrug derivatives is taken to mean compounds according to the invention which have been modified by means of, for example, alkyl or

acyl groups, sugars or oligopeptides and which are rapidly cleaved in the organism to form the effective compounds according to the invention. These also include biodegradable polymer derivatives of the compounds according to the invention, as described, for example, in Int. J. Pharm. 115, 61-67 (1995).

The expression "effective amount" denotes the amount of a medicament or of a pharmaceutical active ingredient which causes in a tissue, system, animal or human a biological or medical response which is sought or desired, for example, by a researcher or physician.
In addition, the expression "therapeutically effective amount" denotes an amount which, compared with a corresponding subject who has not received this amount, has the following consequence:
improved treatment, healing, prevention or elimination of a disease, syndrome, condition, complaint, disorder or side-effects or also the reduction in the advance of a disease, complaint or disorder.
The expression "therapeutically effective amount" also encompasses the amounts which are effective for increasing normal physiological function.

The invention also relates to the use of mixtures of the compounds according to the invention, for example mixtures of two diastereomers, for example in the ratio 1:1, 1:2, 1:3, 1:4, 1:5, 1:10, 1:100 or 1:1000.
These are particularly preferably mixtures of stereoisomeric compounds.

The compounds according to the invention and also the starting materials for their preparation are, in addition, prepared by methods known per se, as described in the literature (for example in the standard works, such as Houben-Weyl, Methoden der organischen Chemie [Methods of Organic Chemistry], Georg-Thieme-Verlag, Stuttgart), to be precise under reaction conditions which are known and suitable for the said reactions. Use can also be made here of variants known per se which are not mentioned here in greater detail.

The compounds according to the invention can preferably be obtained by reacting tetrahydrobenzo[*b*][1,4]diazepine-2-thione derivatives with carbohydrazides

The reaction is generally carried out in an inert solvent.
Depending on the conditions used, the reaction time is between a few minutes and 14 days, the reaction temperature is between about -15° and 150°, normally between 30° and 130°, particularly preferably between 60° and 120°C.

Suitable inert solvents are, for example, hydrocarbons, such as hexane, petroleum ether, benzene, toluene or xylene; chlorinated hydrocarbons, such as trichloroethylene, 1,2-dichloroethane, carbon tetrachloride, chloroform or dichloromethane; alcohols, such as methanol, ethanol, isopropanol, n-propanol, n-butanol or tert-butanol; ethers, such as diethyl ether, diisopropyl ether, tetrahydrofuran (THF) or dioxane; glycol ethers, such as ethylene glycol monomethyl or monoethyl ether, ethylene glycol dimethyl ether (diglyme); ketones, such as acetone or butanone; amides, such as acetamide, dimethylacetamide or dimethylformamide (DMF); nitriles, such as acetonitrile; sulfoxides, such as dimethyl sulfoxide (DMSO); carbon disulfide; carboxylic acids, such as formic acid or acetic acid; nitro compounds, such as nitromethane or nitrobenzene; esters, such as ethyl acetate, or mixtures of the said solvents.
Particular preference is given to 1-butanol.

Suitable for the cleavage of ethers is treatment with boron tribromide under standard conditions.

<u>Pharmaceutical salts and other forms</u>
The said compounds according to the invention can be used in their final non-salt form. On the other hand, the present invention also encompasses

the use of these compounds in the form of their pharmaceutically acceptable salts, which can be derived from various organic and inorganic acids and bases by procedures known in the art. Pharmaceutically acceptable salt forms of the compounds according to the invention are for the most part prepared by conventional methods. If the compound according to the invention contains a carboxyl group, one of its suitable salts can be formed by reacting the compound with a suitable base to give the corresponding base-addition salt. Such bases are, for example, alkali metal hydroxides, including potassium hydroxide, sodium hydroxide and lithium hydroxide; alkaline earth metal hydroxides, such as barium hydroxide and calcium hydroxide; alkali metal alkoxides, for example potassium ethoxide and sodium propoxide; and various organic bases, such as piperidine, diethanolamine and N-methylglutamine. The aluminium salts of the compounds according to the invention are likewise included. In the case of certain compounds according to the invention, acid-addition salts can be formed by treating these compounds with pharmaceutically acceptable organic and inorganic acids, for example hydrogen halides, such as hydrogen chloride, hydrogen bromide or hydrogen iodide, other mineral acids and corresponding salts thereof, such as sulfate, nitrate or phosphate and the like, and alkyl- and monoarylsulfonates, such as ethanesulfonate, toluenesulfonate and benzenesulfonate, and other organic acids and corresponding salts thereof, such as acetate, trifluoroacetate, tartrate, maleate, succinate, citrate, benzoate, salicylate, ascorbate and the like. Accordingly, pharmaceutically acceptable acid-addition salts of the compounds according to the invention include the following: acetate, adipate, alginate, arginate, aspartate, benzoate, benzenesulfonate (besylate), bisulfate, bisulfite, bromide, butyrate, camphorate, camphorsulfonate, caprylate, chloride, chlorobenzoate, citrate, cyclopentanepropionate, digluconate, dihydrogenphosphate, dinitrobenzoate, dodecylsulfate, ethanesulfonate, fumarate, galacterate (from mucic acid), galacturonate, glucoheptanoate, gluconate, glutamate, glycerophosphate, hemisuccinate, hemisulfate, heptanoate, hexanoate, hippurate, hydrochloride, hydro-

bromide, hydroiodide, 2-hydroxyethanesulfonate, iodide, isethionate, isobutyrate, lactate, lactobionate, malate, maleate, malonate, mandelate, metaphosphate, methanesulfonate, methylbenzoate, monohydrogenphosphate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, oleate, palmoate, pectinate, persulfate, phenylacetate, 3-phenylpropionate, phosphate, phosphonate, phthalate, but this does not represent a restriction.

Furthermore, the base salts of the compounds according to the invention include aluminium, ammonium, calcium, copper, iron(III), iron(II), lithium, magnesium, manganese(III), manganese(II), potassium, sodium and zinc salts, but this is not intended to represent a restriction. Of the above-mentioned salts, preference is given to ammonium; the alkali metal salts sodium and potassium, and the alkaline earth metal salts calcium and magnesium. Salts of the compounds according to the invention which are derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary and tertiary amines, substituted amines, also including naturally occurring substituted amines, cyclic amines, and basic ion exchanger resins, for example arginine, betaine, caffeine, chloroprocaine, choline, N,N'-dibenzylethylenediamine (benzathine), dicyclohexylamine, diethanolamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lidocaine, lysine, meglumine, N-methyl-D-glucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethanolamine, triethylamine, trimethylamine, tripropylamine and tris(hydroxymethyl)methylamine (tromethamine), but this is not intended to represent a restriction.

Compounds of the present invention which contain basic nitrogen-containing groups can be quaternised using agents such as (C_1-C_4)alkyl halides, for example methyl, ethyl, isopropyl and tert-butyl chloride, bromide and iodide; di(C_1-C_4)alkyl sulfates, for example dimethyl, diethyl and diamyl

sulfate; (C_{10}-C_{18})alkyl halides, for example decyl, dodecyl, lauryl, myristyl and stearyl chloride, bromide and iodide; and aryl(C_1-C_4)alkyl halides, for example benzyl chloride and phenethyl bromide. Both water- and oil-soluble compounds according to the invention can be prepared using such salts.

The above-mentioned pharmaceutical salts which are preferred include acetate, trifluoroacetate, besylate, citrate, fumarate, gluconate, hemisuccinate, hippurate, hydrochloride, hydrobromide, isethionate, mandelate, meglumine, nitrate, oleate, phosphonate, pivalate, sodium phosphate, stearate, sulfate, sulfosalicylate, tartrate, thiomalate, tosylate and tromethamine, but this is not intended to represent a restriction.

The acid-addition salts of basic compounds according to the invention are prepared by bringing the free base form into contact with a sufficient amount of the desired acid, causing the formation of the salt in a conventional manner. The free base can be regenerated by bringing the salt form into contact with a base and isolating the free base in a conventional manner. The free base forms differ in a certain respect from the corresponding salt forms thereof with respect to certain physical properties, such as solubility in polar solvents; for the purposes of the invention, however, the salts otherwise correspond to the respective free base forms thereof.

As mentioned, the pharmaceutically acceptable base-addition salts of the compounds according to the invention are formed with metals or amines, such as alkali metals and alkaline earth metals or organic amines. Preferred metals are sodium, potassium, magnesium and calcium. Preferred organic amines are N,N'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, N-methyl-D-glucamine and procaine.

The base-addition salts of acidic compounds according to the invention are prepared by bringing the free acid form into contact with a sufficient

amount of the desired base, causing the formation of the salt in a conventional manner. The free acid can be regenerated by bringing the salt form into contact with an acid and isolating the free acid in a conventional manner. The free acid forms differ in a certain respect from the corresponding salt forms thereof with respect to certain physical properties, such as solubility in polar solvents; for the purposes of the invention, however, the salts otherwise correspond to the respective free acid forms thereof.

If a compound according to the invention contains more than one group which is capable of forming pharmaceutically acceptable salts of this type, the invention also encompasses multiple salts. Typical multiple salt forms include, for example, bitartrate, diacetate, difumarate, dimeglumine, diphosphate, disodium and trihydrochloride, but this is not intended to represent a restriction.

With regard to that stated above, it can be seen that the expression "pharmaceutically acceptable salt" in the present connection is taken to mean an active ingredient which comprises a compound according to the invention in the form of one of its salts, in particular if this salt form imparts improved pharmacokinetic properties on the active ingredient compared with the free form of the active ingredient or any other salt form of the active ingredient used earlier. The pharmaceutically acceptable salt form of the active ingredient can also provide this active ingredient for the first time with a desired pharmacokinetic property which it did not have earlier and can even have a positive influence on the pharmacodynamics of this active ingredient with respect to its therapeutic efficacy in the body.

The invention furthermore relates to medicaments comprising at least one compound according to the invention and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

Pharmaceutical formulations can be administered in the form of dosage units which comprise a predetermined amount of active ingredient per dosage unit. Such a unit can comprise, for example, 0.5 mg to 1 g, preferably 1 mg to 700 mg, particularly preferably 5 mg to 100 mg, of a compound according to the invention, depending on the condition treated, the method of administration and the age, weight and condition of the patient, or pharmaceutical formulations can be administered in the form of dosage units which comprise a predetermined amount of active ingredient per dosage unit. Preferred dosage unit formulations are those which comprise a daily dose or part-dose, as indicated above, or a corresponding fraction thereof of an active ingredient. Furthermore, pharmaceutical formulations of this type can be prepared using a process which is generally known in the pharmaceutical art.

Pharmaceutical formulations can be adapted for administration via any desired suitable method, for example by oral (including buccal or sublingual), rectal, nasal, topical (including buccal, sublingual or transdermal), vaginal or parenteral (including subcutaneous, intramuscular, intravenous or intradermal) methods. Such formulations can be prepared using all processes known in the pharmaceutical art by, for example, combining the active ingredient with the excipient(s) or adjuvant(s).

Pharmaceutical formulations adapted for oral administration can be administered as separate units, such as, for example, capsules or tablets; powders or granules; solutions or suspensions in aqueous or non-aqueous liquids; edible foams or foam foods; or oil-in-water liquid emulsions or water-in-oil liquid emulsions.

Thus, for example, in the case of oral administration in the form of a tablet or capsule, the active-ingredient component can be combined with an oral, non-toxic and pharmaceutically acceptable inert excipient, such as, for example, ethanol, glycerol, water and the like. Powders are prepared by

comminuting the compound to a suitable fine size and mixing it with a pharmaceutical excipient comminuted in a similar manner, such as, for example, an edible carbohydrate, such as, for example, starch or mannitol. A flavour, preservative, dispersant and dye may likewise be present.

Capsules are produced by preparing a powder mixture as described above and filling shaped gelatine shells therewith. Glidants and lubricants, such as, for example, highly disperse silicic acid, talc, magnesium stearate, calcium stearate or polyethylene glycol in solid form, can be added to the powder mixture before the filling operation. A disintegrant or solubiliser, such as, for example, agar-agar, calcium carbonate or sodium carbonate, may likewise be added in order to improve the availability of the medicament after the capsule has been taken.

In addition, if desired or necessary, suitable binders, lubricants and disintegrants as well as dyes can likewise be incorporated into the mixture. Suitable binders include starch, gelatine, natural sugars, such as, for example, glucose or beta-lactose, sweeteners made from maize, natural and synthetic rubber, such as, for example, acacia, tragacanth or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. The lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride and the like. The disintegrants include, without being restricted thereto, starch, methylcellulose, agar, bentonite, xanthan gum and the like. The tablets are formulated by, for example, preparing a powder mixture, granulating or dry-pressing the mixture, adding a lubricant and a disintegrant and pressing the entire mixture to give tablets. A powder mixture is prepared by mixing the compound comminuted in a suitable manner with a diluent or a base, as described above, and optionally with a binder, such as, for example, carboxymethylcellulose, an alginate, gelatine or polyvinylpyrrolidone, a dissolution retardant, such as, for example, paraffin, an absorption accelerator, such as, for example, a quaternary salt, and/or an

absorbant, such as, for example, bentonite, kaolin or dicalcium phosphate. The powder mixture can be granulated by wetting it with a binder, such as, for example, syrup, starch paste, acadia mucilage or solutions of cellulose or polymer materials and pressing it through a sieve. As an alternative to granulation, the powder mixture can be run through a tableting machine, giving lumps of non-uniform shape, which are broken up to form granules. The granules can be lubricated by addition of stearic acid, a stearate salt, talc or mineral oil in order to prevent sticking to the tablet casting moulds. The lubricated mixture is then pressed to give tablets. The compounds according to the invention can also be combined with a free-flowing inert excipient and then pressed directly to give tablets without carrying out the granulation or dry-pressing steps. A transparent or opaque protective layer consisting of a shellac sealing layer, a layer of sugar or polymer material and a gloss layer of wax may be present. Dyes can be added to these coatings in order to be able to differentiate between different dosage units.

Oral liquids, such as, for example, solution, syrups and elixirs, can be prepared in the form of dosage units so that a given quantity comprises a prespecified amount of the compound. Syrups can be prepared by dissolving the compound in an aqueous solution with a suitable flavour, while elixirs are prepared using a non-toxic alcoholic vehicle. Suspensions can be formulated by dispersion of the compound in a non-toxic vehicle. Solubilisers and emulsifiers, such as, for example, ethoxylated isostearyl alcohols and polyoxyethylene sorbitol ethers, preservatives, flavour additives, such as, for example, peppermint oil or natural sweeteners or saccharin, or other artificial sweeteners and the like, can likewise be added.

The dosage unit formulations for oral administration can, if desired, be encapsulated in microcapsules. The formulation can also be prepared in such a way that the release is extended or retarded, such as, for example, by coating or embedding of particulate material in polymers, wax and the like.

The compounds according to the invention and salts, solvates and physiologically functional derivatives thereof can also be administered in the form of liposome delivery systems, such as, for example, small unilamellar vesicles, large unilamellar vesicles and multilamellar vesicles. Liposomes can be formed from various phospholipids, such as, for example, cholesterol, stearylamine or phosphatidylcholines.

The compounds according to the invention and the salts, solvates and physiologically functional derivatives thereof can also be delivered using monoclonal antibodies as individual carriers to which the compound molecules are coupled. The compounds can also be coupled to soluble polymers as targeted medicament carriers. Such polymers may encompass polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidophenol, polyhydroxyethylaspartamidophenol or polyethylene oxide polylysine, substituted by palmitoyl radicals. The compounds may furthermore be coupled to a class of biodegradable polymers which are suitable for achieving controlled release of a medicament, for example polylactic acid, poly-epsilon-caprolactone, polyhydroxybutyric acid, polyorthoesters, polyacetals, polydihydroxypyrans, polycyanoacrylates and crosslinked or amphipathic block copolymers of hydrogels.

Pharmaceutical formulations adapted for transdermal administration can be administered as independent plasters for extended, close contact with the epidermis of the recipient. Thus, for example, the active ingredient can be delivered from the plaster by iontophoresis, as described in general terms in Pharmaceutical Research, 3(6), 318 (1986).

Pharmaceutical compounds adapted for topical administration can be formulated as ointments, creams, suspensions, lotions, powders, solutions, pastes, gels, sprays, aerosols or oils.

For the treatment of the eye or other external tissue, for example mouth and skin, the formulations are preferably applied as topical ointment or cream. In the case of formulation to give an ointment, the active ingredient can be employed either with a paraffinic or a water-miscible cream base. Alternatively, the active ingredient can be formulated to give a cream with an oil-in-water cream base or a water-in-oil base.

Pharmaceutical formulations adapted for topical application to the eye include eye drops, in which the active ingredient is dissolved or suspended in a suitable carrier, in particular an aqueous solvent.

Pharmaceutical formulations adapted for topical application in the mouth encompass lozenges, pastilles and mouthwashes.

Pharmaceutical formulations adapted for rectal administration can be administered in the form of suppositories or enemas.

Pharmaceutical formulations adapted for nasal administration in which the carrier substance is a solid comprise a coarse powder having a particle size, for example, in the range 20-500 microns, which is administered in the manner in which snuff is taken, i.e. by rapid inhalation via the nasal passages from a container containing the powder held close to the nose. Suitable formulations for administration as nasal spray or nose drops with a liquid as carrier substance encompass active-ingredient solutions in water or oil.

Pharmaceutical formulations adapted for administration by inhalation encompass finely particulate dusts or mists, which can be generated by various types of pressurised dispensers with aerosols, nebulisers or insufflators.

Pharmaceutical formulations adapted for vaginal administration can be administered as pessaries, tampons, creams, gels, pastes, foams or spray formulations.

Pharmaceutical formulations adapted for parenteral administration include aqueous and non-aqueous sterile injection solutions comprising antioxidants, buffers, bacteriostatics and solutes, by means of which the formulation is rendered isotonic with the blood of the recipient to be treated; and aqueous and non-aqueous sterile suspensions, which may comprise suspension media and thickeners. The formulations can be administered in single-dose or multidose containers, for example sealed ampoules and vials, and stored in freeze-dried (lyophilised) state, so that only the addition of the sterile carrier liquid, for example water for injection purposes, immediately before use is necessary. Injection solutions and suspensions prepared in accordance with the recipe can be prepared from sterile powders, granules and tablets.

It goes without saying that, in addition to the above particularly mentioned constituents, the formulations may also comprise other agents usual in the art with respect to the particular type of formulation; thus, for example, formulations which are suitable for oral administration may comprise flavours.

A therapeutically effective amount of a compound according to the invention depends on a number of factors, including, for example, the age and weight of the animal, the precise condition that requires treatment, and its severity, the nature of the formulation and the method of administration, and is ultimately determined by the treating doctor or vet. However, an effective amount of a compound according to the invention for the treatment of neoplastic growth, for example colon or breast carcinoma, is generally in the range from 0.1 to 100 mg/kg of body weight of the recipient (mammal) per day and particularly typically in the range from 1 to 10 mg/kg

of body weight per day. Thus, the actual amount per day for an adult mammal weighing 70 kg is usually between 70 and 700 mg, where this amount can be administered as a single dose per day or usually in a series of part-doses (such as, for example, two, three, four, five or six) per day, so that the total daily dose is the same. An effective amount of a salt or solvate or of a physiologically functional derivative thereof can be determined as the fraction of the effective amount of the compound according to the invention *per se*. It can be assumed that similar doses are suitable for the treatment of other conditions mentioned above.

The invention furthermore relates to medicaments comprising at least one compound according to the invention and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

The invention also relates to a set (kit) consisting of separate packs of

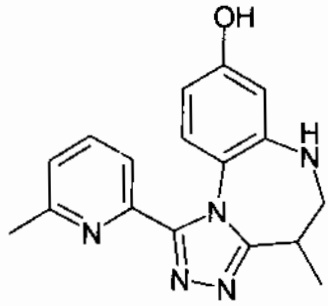
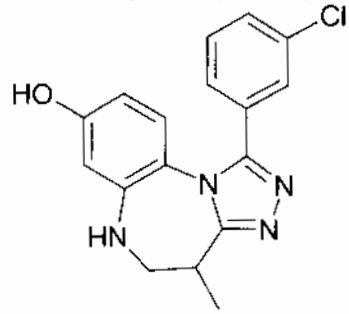
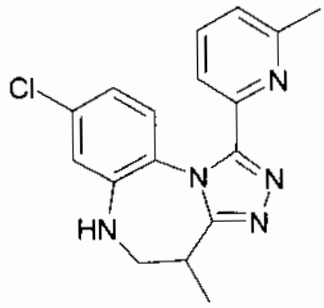
(a) an effective amount of a compound according to the invention and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios,
and

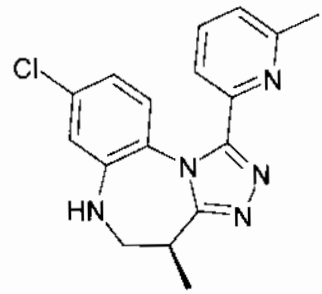
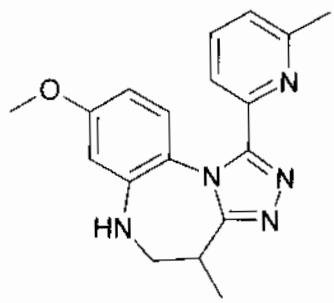
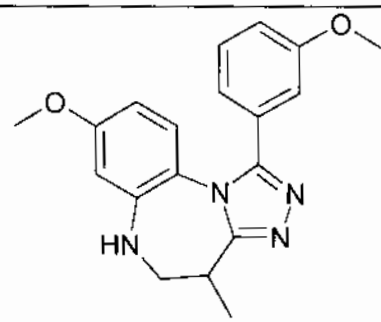
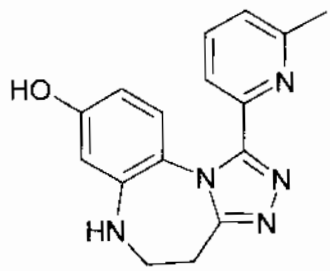
(b) an effective amount of a further medicament active ingredient.

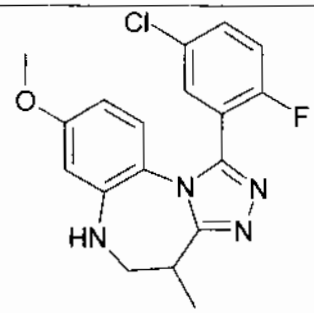
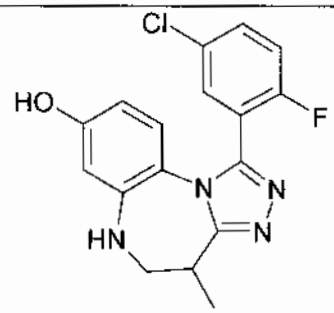
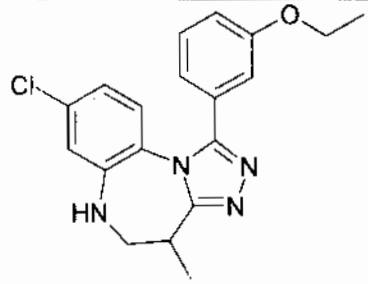
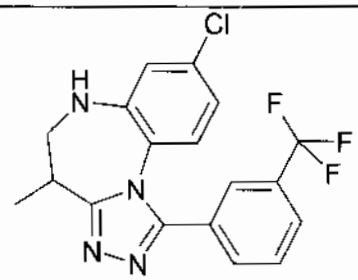
The set comprises suitable containers, such as boxes, individual bottles, bags or ampoules. The set may, for example, comprise separate ampoules, each containing an effective amount of a compound according to the invention and/or pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and an effective amount of a further medicament active ingredient in dissolved or lyophilised form.

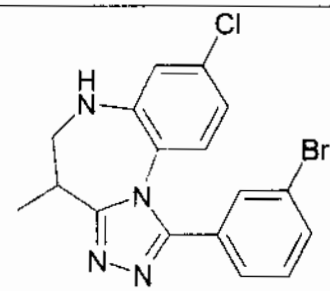
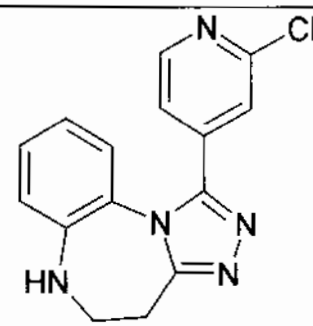
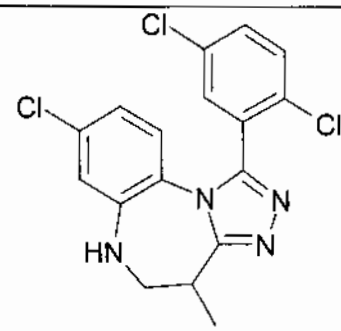
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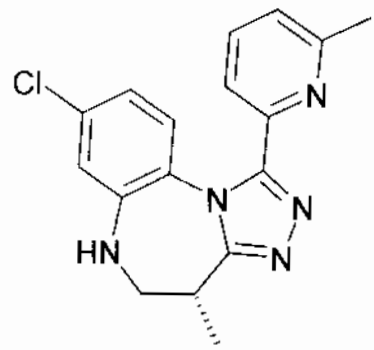
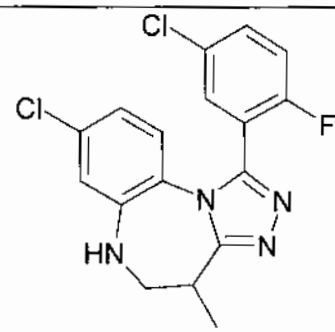
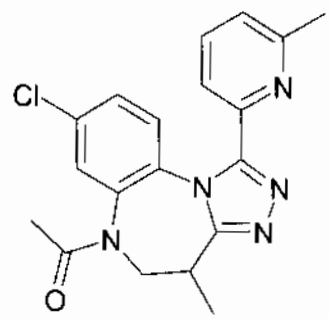
The present compounds selected from the group

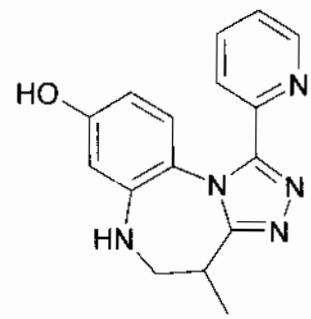
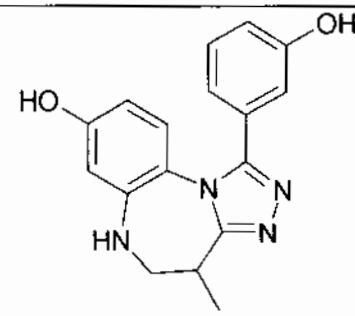
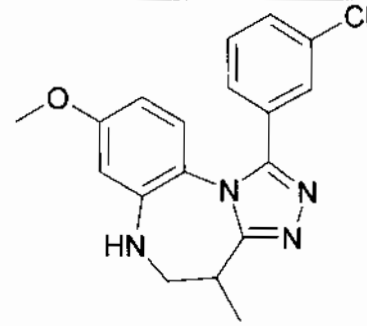
Compound No.	Structure / name
"A1"	 (*R*,*S*)-8-Hydroxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A2"	 (R,S)-1-(3-Chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A3"	 (R,S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

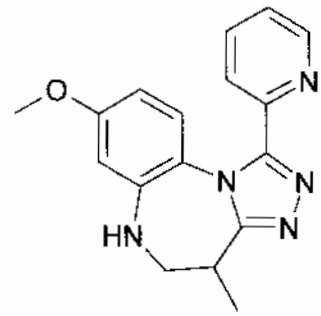
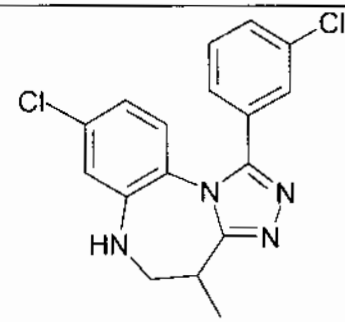
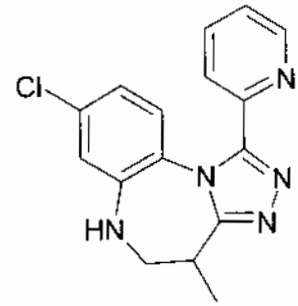
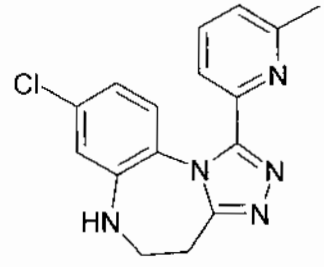
"A4"	 (+)-(S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A5"	 (R,S)-8-Methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A6"	 (R,S)-8-Methoxy-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A7"	 1-(6-Methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

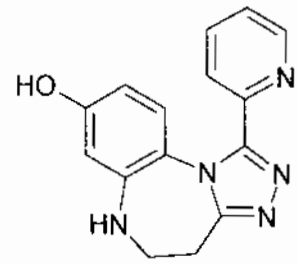
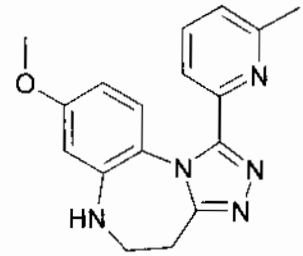
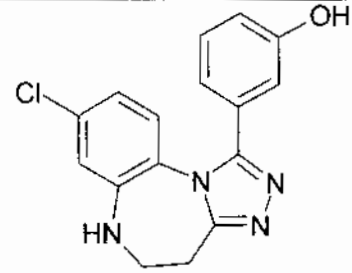
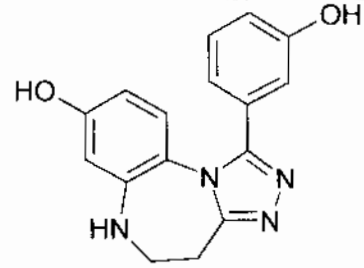
"A8"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A9"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A10"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A11"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethylphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

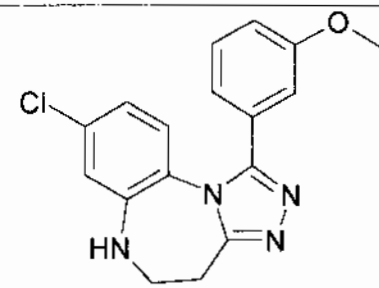
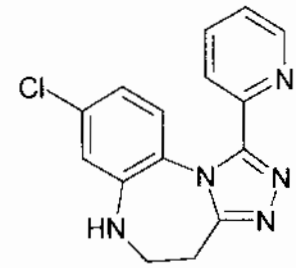
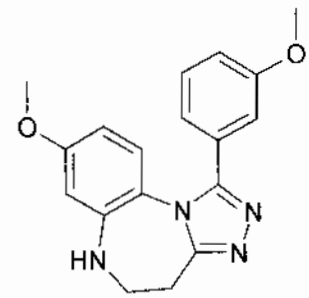
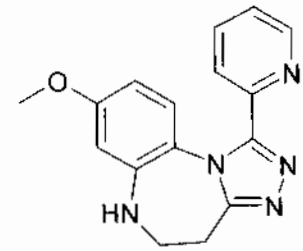
"A12"	 (R,S)-1-(3-Bromophenyl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulene
"A13"	 1-(2-Chloropyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A14"	 (R,S)-8-Chloro-1-(2,5-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

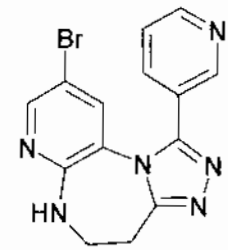
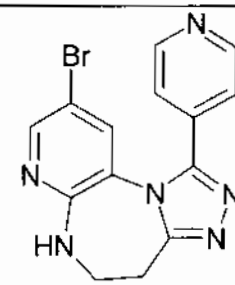
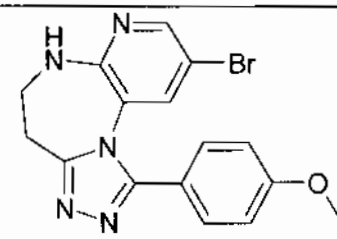
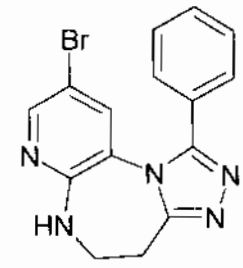
"A15"	 (-)-(R)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A16"	 (R,S)-8-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A17"	 (R,S)-1-[8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulen-6-yl]ethanon

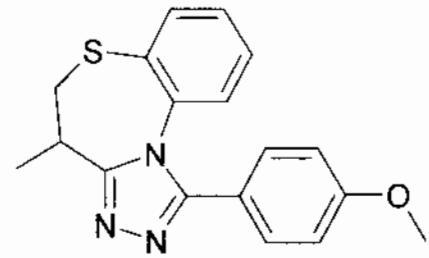
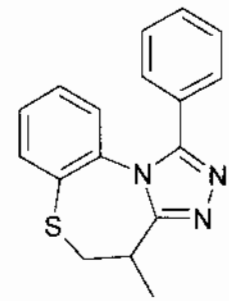
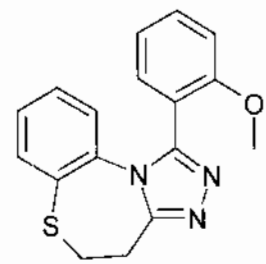
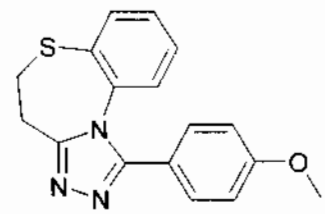
"A18"	 (R,S)-4-Methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A19"	 (R,S)-1-(3-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A20"	 (R,S)-1-(3-Chlorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

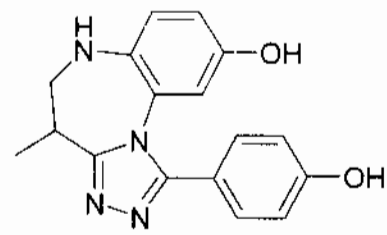
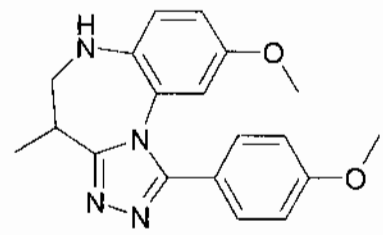
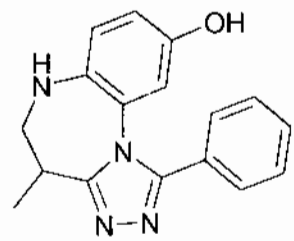
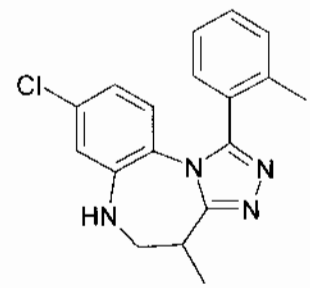
"A21"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A22"	 (R,S)-8-Chloro-1-(3-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A23"	 (R,S)-8-Chloro-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A24"	 8-Chloro-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

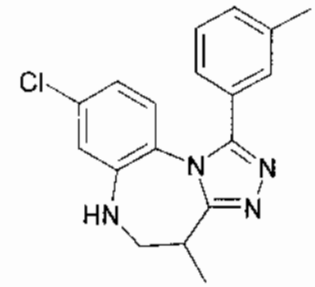
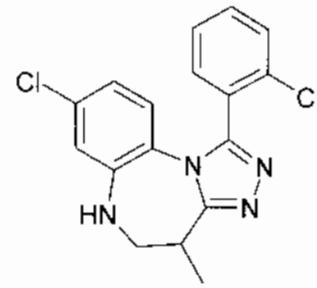
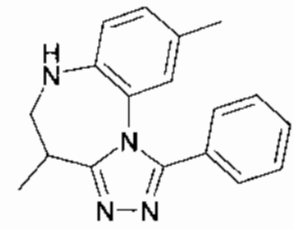
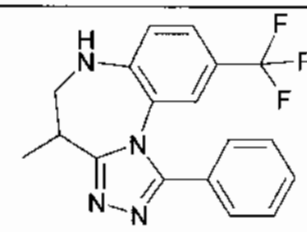
"A25"	 1-Pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol
"A26"	 8-Methoxy-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A27"	 3-(8-Chloro-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)-phenol
"A28"	 1-(3-Hydroxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

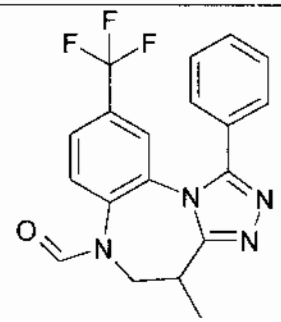
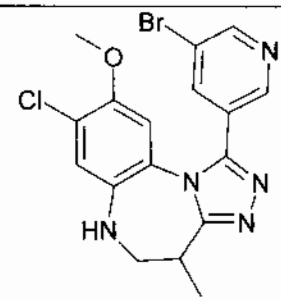
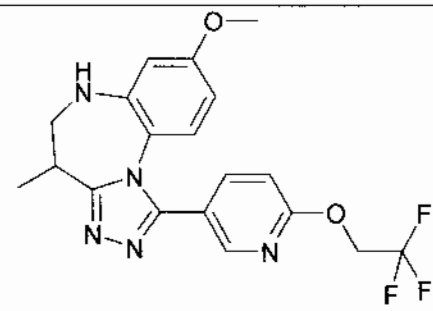
"A29"	 8-Chloro-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A30"	 8-Chloro-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A31"	 8-Methoxy-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A32"	 8-Methoxy-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene

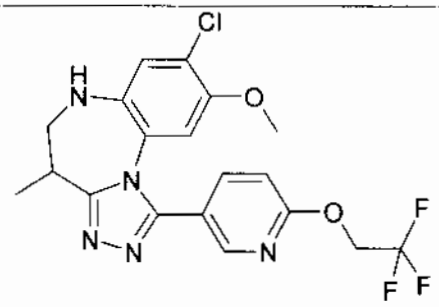
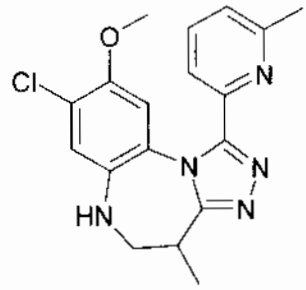
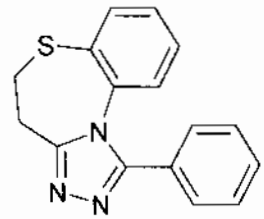
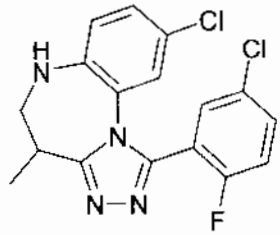
"A33"	 9-Bromo-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A34"	 9-Bromo-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A35"	 9-Bromo-1-(4-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene
"A36"	 9-Bromo-1-phenyl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene

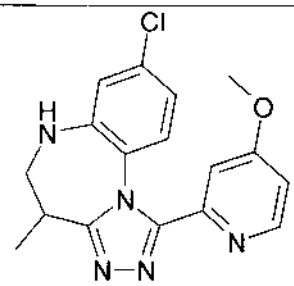
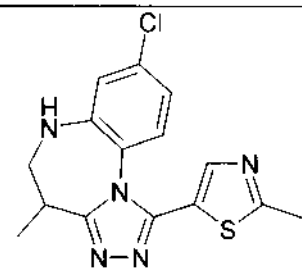
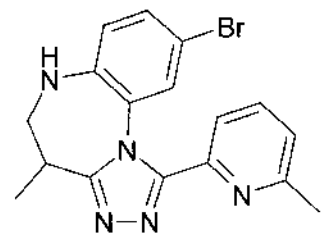
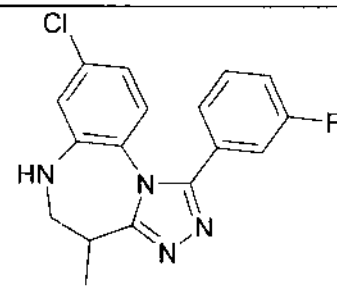
"A37"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A38"	 (R,S)-4-Methyl-1-phenyl-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A39"	 1-(2-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A40"	 1-(4-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene

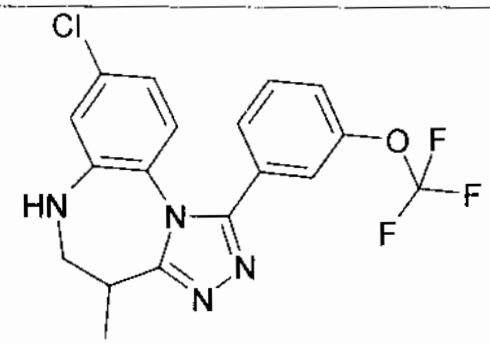
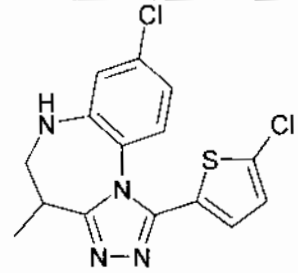
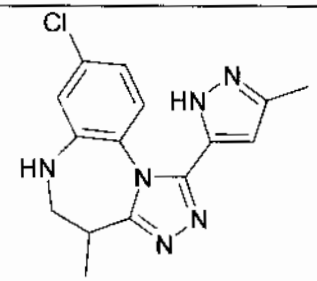
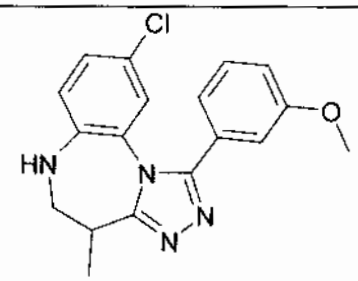
"A41"	 (R,S)-1-(4-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A42"	 (R,S)-9-Methoxy-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A43"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol
"A44"	 (R,S)-8-Chloro-4-methyl-1-*o*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

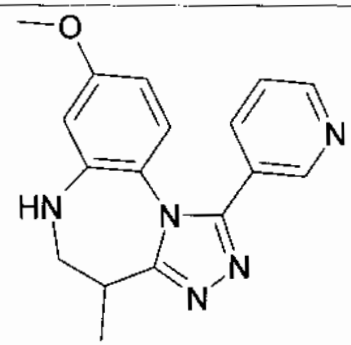
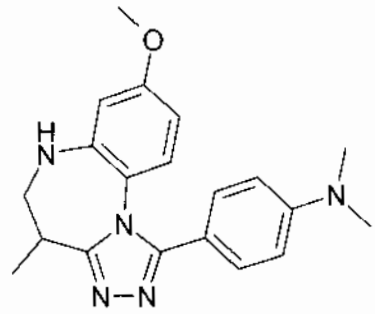
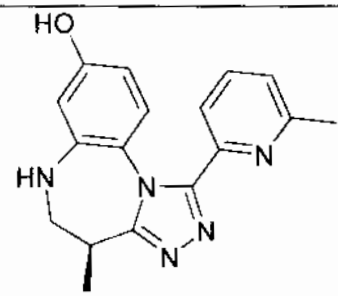
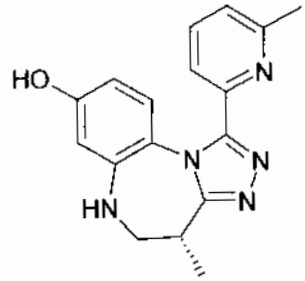
"A45"	 (R,S)-8-Chloro-4-methyl-1-*m*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A46"	 (R,S)-8-Chloro-1-(2-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A47"	 (R,S)-4,9-Dimethyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A48"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

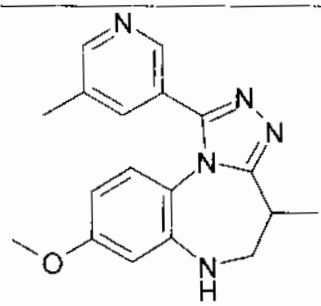
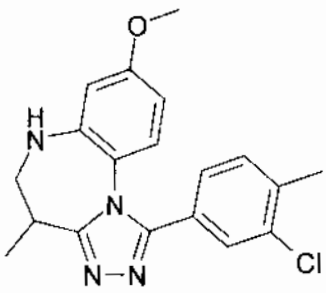
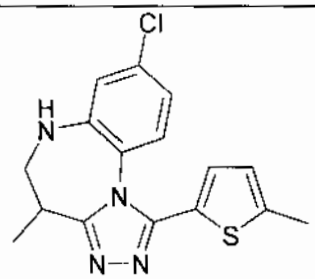
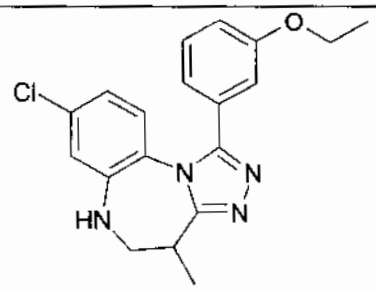
"A49"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulene-6-carbaldehyde
"A50"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A51"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-chloro-9-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A52"	 (R,S)-8-Methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

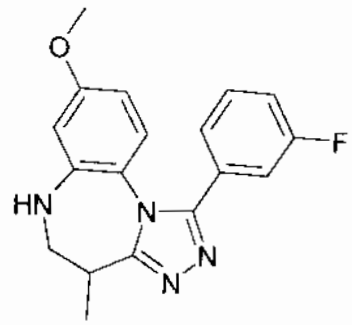
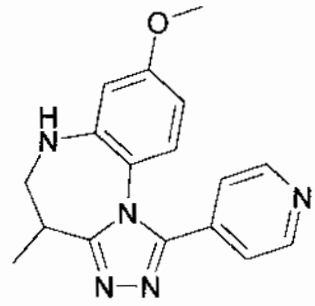
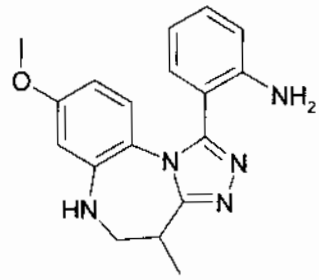
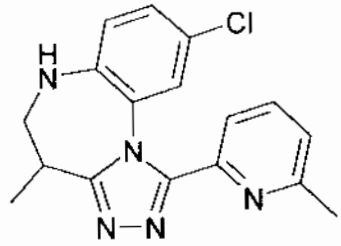
"A53"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-[6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A54"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A55"	 1-Phenyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A56"	 (R,S)-9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

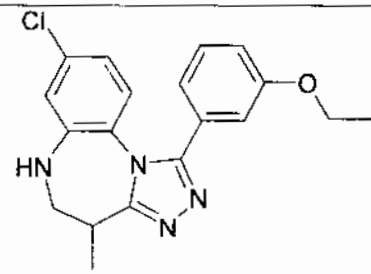
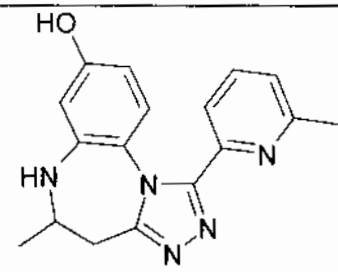
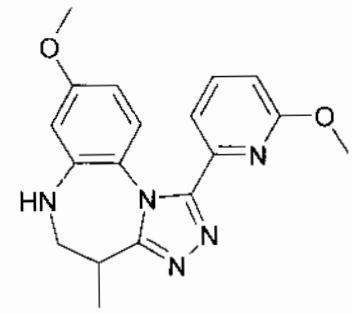
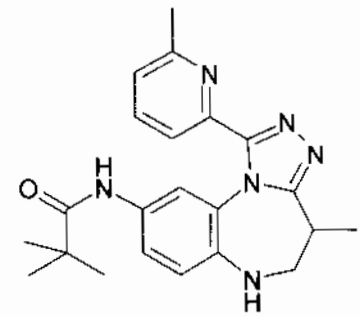
"A57"	 (R,S)-8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulenee
"A58"	 (R,S)-8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A59"	 (R,S)-9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A60"	 (R,S)-8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

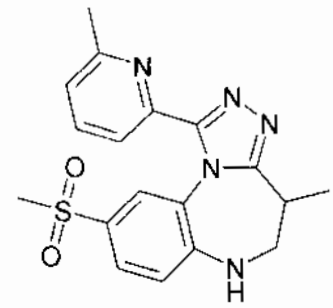
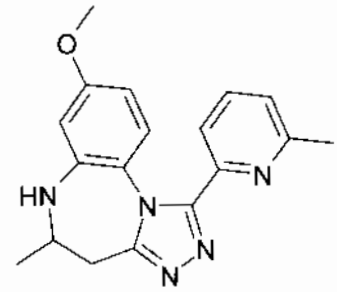
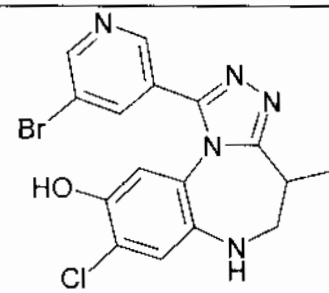
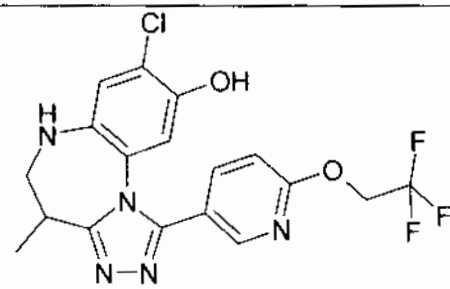
"A61"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A62"	 (R,S)-8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A63"	 (R,S)-8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A64"	 (R,S)-9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

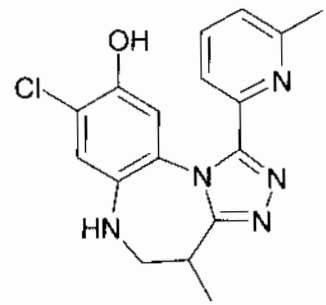
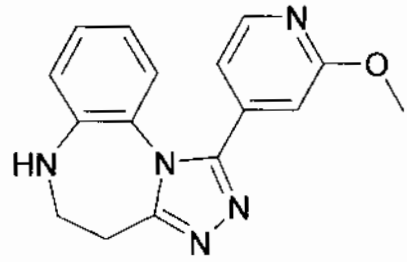
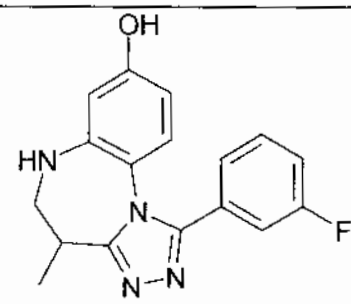
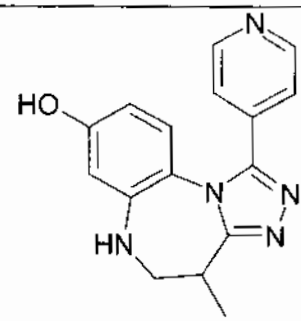
"A65"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A66"	 (R,S)-[4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)-phenyl]dimethylamine
"A67"	 (S)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A68"	 (R)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol

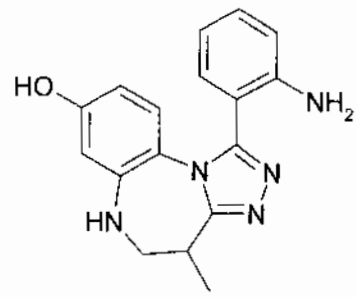
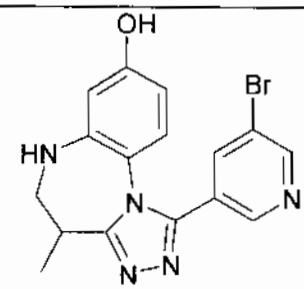
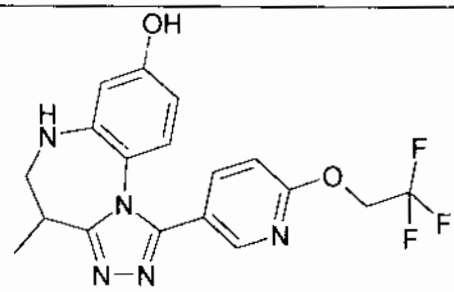
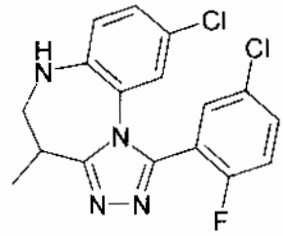
"A69"	 (R,S)-8-Methoxy-4-methyl-1-(5-methylpyridin-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A70"	 (R,S)-1-(3-Chloro-4-methylphenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A71"	 (R,S)-8-Chloro-4-methyl-1-(5-methylthiophen-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A72"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

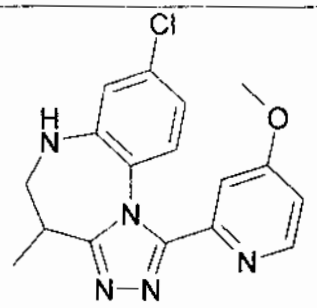
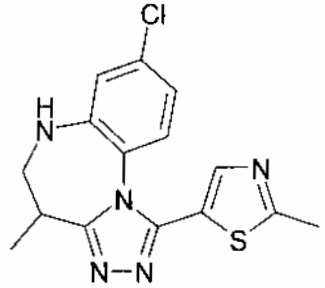
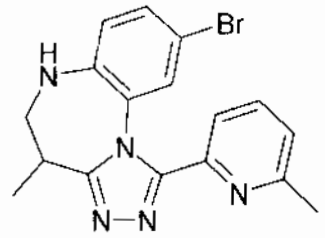
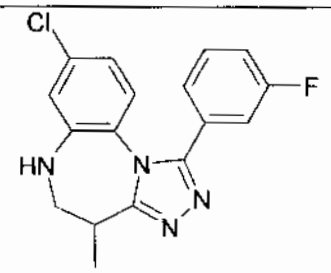
"A73"	 (R,S)-1-(3-Fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A74"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A75"	 (R,S)-2-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenylamine
"A76"	 (R,S)-9-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene bistrifluoroacetate

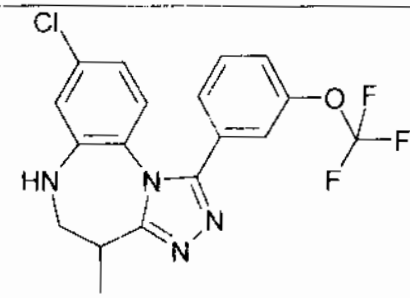
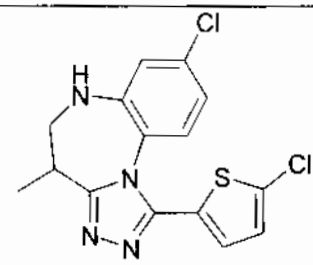
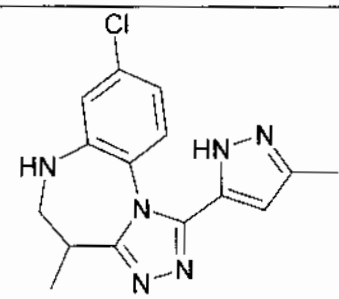
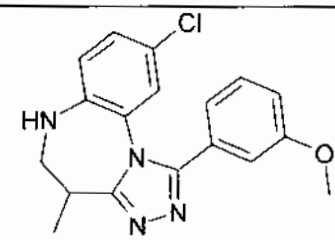
"A77"	 8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A78"	 5-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A79"	 8-Methoxy-1-(6-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A80"	 2,2-Dimethyl-N-[4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulen-9-yl]propion-amide

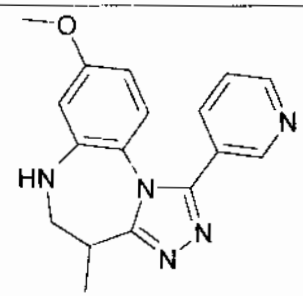
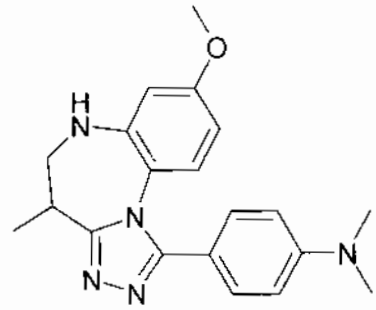
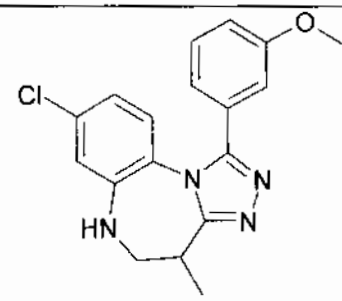
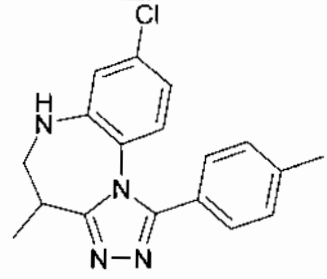
"A81"	 9-Methanesulfonyl-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A82"	 8-Methoxy-5-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A83"	 1-(5-Bromopyridin-3-yl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A84"	 8-Chloro-4-methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol

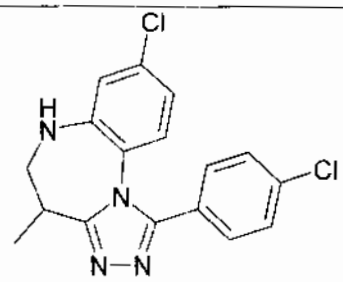
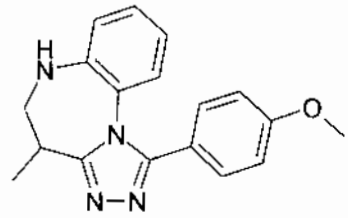
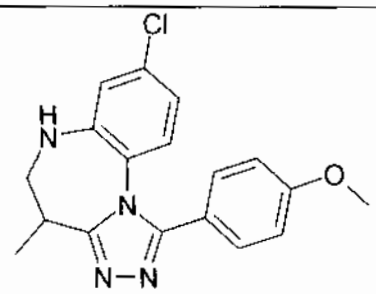
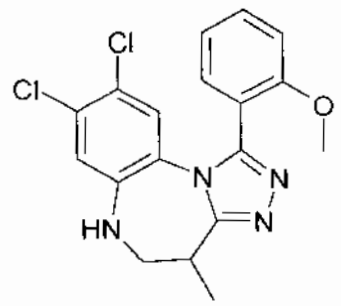
"A85"	 8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A86"	 1-(2-Methoxypyridin-4-yl)-5,6-dihydro-4*H*-2,3,6.10b-tetraaza-benzo[*e*]azulene
"A87"	 1-(3-Fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A88"	 4-Methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

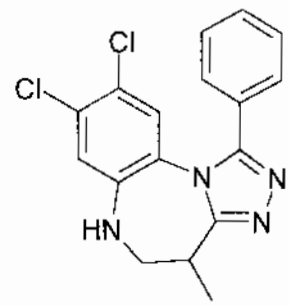
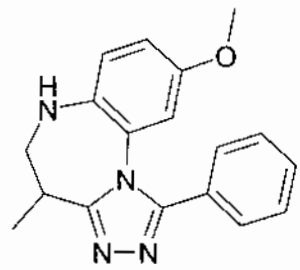
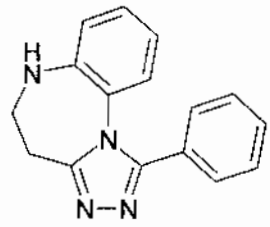
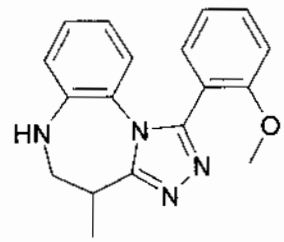
"A89"	 1-(2-Aminophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A90"	 1-(5-Bromopyridin-3-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A91"	 4-Methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A92"	 9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

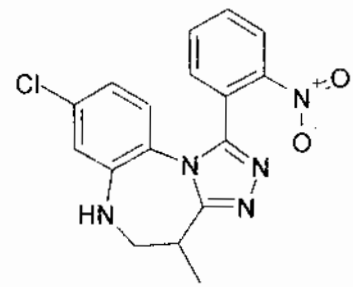
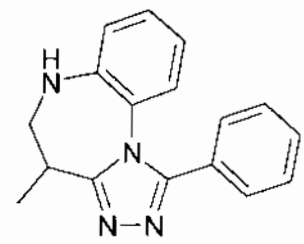
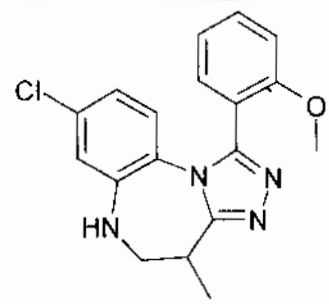
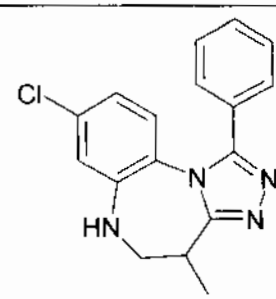
"A93"	 8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A94"	 8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A95"	 9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A96"	 8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

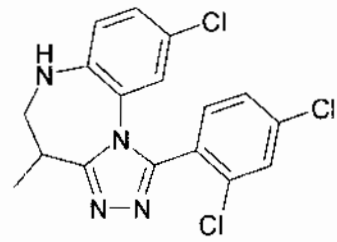
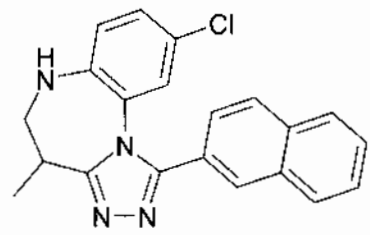
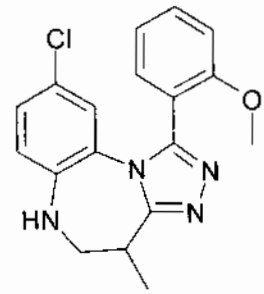
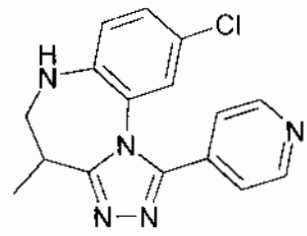
"A97"	 8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A98"	 8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A99"	 8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A100"	 9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

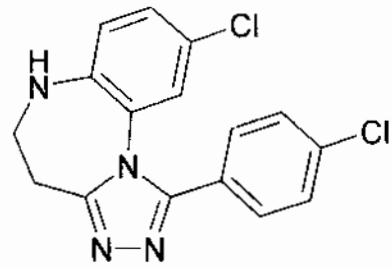
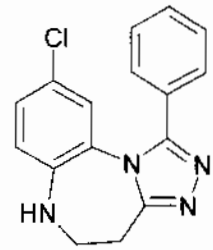
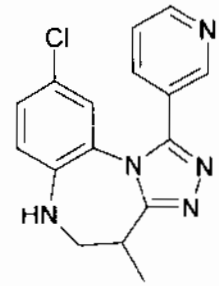
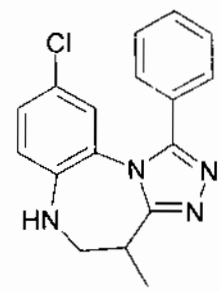
"A101"	 8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A102"	 [4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)-phenyl]dimethylamine
"B1"	 (R,S)-8-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B2"	 (R,S)-8-Chloro-4-methyl-1-*p*tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B3"	 (R,S)-8-Chloro-1-(4-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B4"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B5"	 (R,S)-8-Chloro-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B6"	 (R,S)-8,9-Dichloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B7"	 (R,S)-8,9-Dichloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B8"	 (R,S)-9-Methoxy-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B9"	 1-Phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B10"	 (R,S)-1-(2-Methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B11"	 (R,S)-8-Chloro-4-methyl-1-(2-nitrophenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B12"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"B13"	 (R,S)-8-Chloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B14"	 (R,S)-8-Chloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B15"	 (R,S)-9-Chloro-1-(2,4-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B16"	 (R,S)-9-Chloro-4-methyl-1-naphthalen-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B17"	 (R,S)-9-Chloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B18"	 (R,S)-9-Chloro-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B19"	 9-Chloro-1-(4-chlorophenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B20"	 9-Chloro-1-phenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"B21"	 (R,S)-9-Chloro-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B22"	 (R,S)-9-Chloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

and pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, are suitable as pharmaceutical active ingredients for mammals, in particular for humans, for the preparation of a medicament for the treatment and/or combating of cancer, tumour growth, metastatic growth, fibrosis, restenosis, HIV infection, Alzheimer's, atherosclerosis and/or for promoting wound healing.

Particular preference is given to the use for the treatment of a disease where the disease is a solid tumour.
The solid tumour is preferably selected from the group of tumours of the squamous epithelium, the bladder, the stomach, the kidneys, of head and neck, the oesophagus, the cervix, the thyroid, the intestine, the liver, the brain, the prostate, the urogenital tract, the lymphatic system, the stomach, the larynx and/or the lung.

The solid tumour is furthermore preferably selected from the group lung adenocarcinoma, smallcell lung carcinomas, pancreatic cancer, glioblastomas, colon carcinoma and breast carcinoma.

Preference is furthermore given to the use for the treatment of a tumour of the blood and immune system, preferably for the treatment of a tumour selected from the group of acute myeloid leukaemia, chronic myeloid leukaemia, acute lymphatic leukaemia and/or chronic lymphatic leukaemia.

The present compounds are also suitable for combination with known anticancer agents. These known anticancer agents include the following: oestrogen receptor modulators, androgen receptor modulators, retinoid receptor modulators, cytotoxic agents, antiproliferative agents, prenyl-protein transferase inhibitors, HMG-CoA reductase inhibitors, HIV protease inhibitors, reverse transcriptase inhibitors and further angiogenesis inhibitors.
The present compounds are particularly suitable for administration at the

same time as radiotherapy. The synergistic effects of inhibiting VEGF in combination with radiotherapy have been described in the art (see WO 00/61186).

"Oestrogen receptor modulators" refers to compounds which interfere with or inhibit the binding of oestrogen to the receptor, regardless of mechanism. Examples of oestrogen receptor modulators include, but are not limited to, tamoxifen, raloxifene, idoxifene, LY353381, LY 117081, toremifene, fulvestrant, 4-[7-(2,2-dimethyl-1-oxopropoxy-4-methyl-2-[4-[2-(1-piperidinyl)ethoxy]phenyl]-2H-1-benzopyran-3-yl]phenyl 2,2-dimethylpropanoate, 4,4'-dihydroxybenzophenone-2,4-dinitrophenylhydrazone and SH646.

"Androgen receptor modulators" refers to compounds which interfere with or inhibit the binding of androgens to the receptor, regardless of mechanism. Examples of androgen receptor modulators include finasteride and other 5α-reductase inhibitors, nilutamide, flutamide, bicalutamide, liarozole and abiraterone acetate.

"Retinoid receptor modulators" refers to compounds which interfere with or inhibit the binding of retinoids to the receptor, regardless of mechanism. Examples of such retinoid receptor modulators include bexarotene, tretinoin, 13-cisretinoic acid, 9-cisretinoic acid, α-difluoromethylornithine, ILX23-7553, trans-N-(4'-hydroxyphenyl)retinamide and N-4-carboxyphenylretinamide.

"Cytotoxic agents" refers to compounds which result in cell death primarily through direct action on the cellular function or inhibit or interfere with cell myosis, including alkylating agents, tumour necrosis factors, intercalators, microtubulin inhibitors and topoisomerase inhibitors.

Examples of cytotoxic agents include, but are not limited to, tirapazimine, sertenef, cachectin, ifosfamide, tasonermin, lonidamine, carboplatin, altretamine, prednimustine, dibromoodulcitol, ranimustine, fotemustine, nedaplatin, oxaliplatin, temozolomide, heptaplatin, estramustine, improsulfan tosylate, trofosfamide, nimustine, dibrospidium chloride, pumitepa,

lobaplatin, satraplatin, profiromycin, cisplatin, irofulven, dexifosfamide, cis-aminedichloro(2-methylpyridine)platinum, benzylguanine, glufosfamide, GPX100, (trans,trans,trans)bismu-(hexane-1,6-diamine)-mu-[diamine-platinum(II)]bis[diamine(chloro)platinum(II)] tetrachloride, diarizidinyl-spermine, arsenic trioxide, 1-(11-dodecylamino-10-hydroxyundecyl)-3,7-dimethylxanthine, zorubicin, idarubicin, daunorubicin, bisantrene, mitoxantrone, pirarubicin, pinafide, valrubicin, amrubicin, antineoplaston, 3'-deamino-3'-morpholino-13-deoxo-10-hydroxycarminomycin, annamycin, galarubicin, elinafide, MEN10755 and 4-demethoxy-3-deamino-3-aziridinyl-4-methylsulfonyldaunorubicin (see WO 00/50032).

Examples of microtubulin inhibitors include paclitaxel, vindesine sulfate, 3',4'-didehydro-4'-deoxy-8'-norvincaleukoblastine, docetaxol, rhizoxin, dolastatin, mivobulin isethionate, auristatin, cemadotin, RPR109881, BMS184476, vinflunine, cryptophycin, 2,3,4,5,6-pentafluoroo-N-(3-fluoroo-4-methoxyphenyl)benzenesulfonamide, anhydrovinblastine, N,N-dimethyl-L-valyl-L-valyl-N-methyl-L-valyl-L-prolyl-L-prolinet-butylamide, TDX258 and BMS188797.

Topoisomerase inhibitors are, for example, topotecan, hycaptamine, irinotecan, rubitecan, 6-ethoxypropionyl-3',4'-O-exobenzylidenechartreusin, 9-methoxy-N,N-dimethyl-5-nitropyrazolo[3,4,5-kl]acridine-2-(6H)propanamine, 1-amino-9-ethyl-5-fluoroo-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':b,7]indolizino[1,2b]quinoline-10,13(9H,15H)-dione, lurtotecan, 7-[2-(N-isopropylamino)ethyl]-(20S)camptothecin, BNP1350, BNPI1100, BN80915, BN80942, etoposide phosphate, teniposide, sobuzoxane, 2'-dimethylamino-2'-deoxyetoposide, GL331, N-[2-(dimethylamino)ethyl]-9-hydroxy-5,6-dimethyl-6H-pyrido[4,3-b]carbazole-1-carboxamide, asulacrine, (5a,5aB,8aa,9b)-9-[2-[N-[2-(dimethylamino)ethyl]-N-methylamino]ethyl]-5-[4-hydroxy-3,5-dimethoxyphenyl]-5,5a,6,8,8a,9-hexohydrofuro(3',4':6,7)naphtho(2,3-d)-1,3-dioxol-6-one, 2,3-(methylenedioxy)-5-methyl-7-hydroxy-8-methoxybenzo[c]phenanthridinium, 6,9-bis[(2-aminoethyl)amino]benzo[g]isoquinoline-5,10-dione, 5-(3-aminopropylamino)-7,10-dihydroxy-2-(2-hydroxyethylaminomethyl)-6H-pyrazolo[4,5,1-de]-

acridin-6-one, N-[1-[2(diethylamino)ethylamino]-7-methoxy-9-oxo-9H-thioxanthen-4-ylmethyl]formamide, N-(2-(dimethylamino)ethyl)acridine-4-carboxamide, 6-[[2-(dimethylamino)ethyl]amino]-3-hydroxy-7H-indeno[2,1-c]quinolin-7-one and dimesna.

"Antiproliferative agents" include antisense RNA and DNA oligonucleotides such as G3139, ODN698, RVASKRAS, GEM231 and INX3001 and antimetabolites such as enocitabine, carmofur, tegafur, pentostatin, doxifluridine, trimetrexate, fludarabine, capecitabine, galocitabine, cytarabine ocfosfate, fosteabine sodium hydrate, raltitrexed, paltitrexid, emitefur, tiazofurin, decitabine, nolatrexed, pemetrexed, nelzarabine, 2'-deoxy-2'-methylidenecytidine, 2'-fluoroomethylene-2'-deoxycytidine, N-[5-(2,3-dihydrobenzofuryl)sulfonyl]-N'-(3,4-dichlorophenyl)urea, N6-[4-deoxy-4-[N2-[2(E),4(E)-tetradecadienoyl]glycylamino]-L-glycero-B-L-mannoheptopyranosyl]adenine, aplidine, ecteinascidin, troxacitabine, 4-[2-amino-4-oxo-4,6,7,8-tetrahydro-3H-pyrimidino[5,4-b]-1,4-thiazin-6-yl-(S)-ethyl]-2,5-thienoyl-L-glutamic acid, aminopterin, 5-fluoroouracil, alanosine, 11-acetyl-8-(carbamoyloxymethyl)-4-formyl-6-methoxy-14-oxa-1,11-diazatetracyclo-(7.4.1.0.0)tetradeca-2,4,6-trien-9-ylacetic acid ester, swainsonine, lometrexol, dexrazoxane, methioninase, 2'-cyanoo-2'-deoxy-N4-palmitoyl-1-B-D-arabinofuranosyl cytosine and 3-aminopyridine-2-carboxaldehyde thiosemicarbazone. "Antiproliferative agents" also include monoclonal antibodies to growth factors other than those listed under "angiogenesis inhibitors", such as trastuzumab, and tumour suppressor genes, such as p53, which can be delivered via recombinant virusmediated gene transfer (see US Patent No. 6,069,134, for example).

In-vitro (enzyme) assay for determination of the efficacy of inhibitors of the inhibition of TGF-beta-mediated effects

As an example, the ability of the inhibitors to eliminate TGF-beta-mediated growth inhibition is tested.

Cells of the lung epithelial cell line Mv1Lu are sown in a defined cell density in a 96-well microtitre plate and cultivated overnight under stan-

dard conditions. Next day, the medium is replaced by medium which comprises 0.5% of FCS and 1 ng/ml of TGF-beta, and the test substances are added in defined concentrations, generally in the form of dilution series with 5-fold steps. The concentration of the solvent DMSO is constant at 0.5%. After a further two days, Crystal Violet staining of the cells is carried out. After extraction of the Crystal Violet from the fixed cells, the absorption is measured spectrophotometrically at 550 nm. It can be used as a quantitative measure of the adherent cells present and thus of the cell proliferation during the culture.

Table 1: Inhibition of TGF-beta

Compound No.	IC_{50} [mol/l]
"A1"	1.80 E-07
"A2"	9.70 E-07
"A3"	3.50 E-06
"A4"	3.80 E-06
"A5"	2.40 E-06
"A6"	3.90 E-06
"A7"	2.20 E-06
"A8"	6.60 E-06
"A9"	9.10 E-07
"A10"	5.70 E-06
"A78"	1.5 E-07
"A80"	3.3 E-06
"B1"	7.00 E-06

Cellular assay for testing
TGF-beta receptor I kinase inhibitors

The kinase assay is carried out as 384-well flashplate assay.

31.2 nM of GST-ALK5, 439 nM of GST-SMAD2 and 3 mM of ATP (with 0.3µCi of ^{33}P-ATP/well) are incubated in a total volume of 35µl (20 mM of HEPES, 10 mM of MgCl, 5 mM of MnCl, 1 mM of DTT, 0.1% of BSA, pH 7.4) without or with test substance (5-10 concentrations) at 30°C for 45 min. The reaction is stopped using 25µl of 200 mM EDTA solution, filtered with suction at room temperature after 30 min, and the wells are washed with 3 times 100 µl of 0.9% NaCl solution. Radioactivity is measured in the TopCount. The IC_{50} values are calculated using RS1.

Above and below, all temperatures are indicated in °C. In the following examples, "conventional workup" means: water is added if necessary, the pH is adjusted, if necessary, to a value of between 2 and 10, depending on the constitution of the end product, the mixture is extracted with ethyl acetate or dichloromethane, the phases are separated, the organic phase is dried over sodium sulfate and evaporated, and the product is purified by chromatography on silica gel and/or by crystallisation. Rf values on silica gel; eluent: ethyl acetate/methanol 9:1.

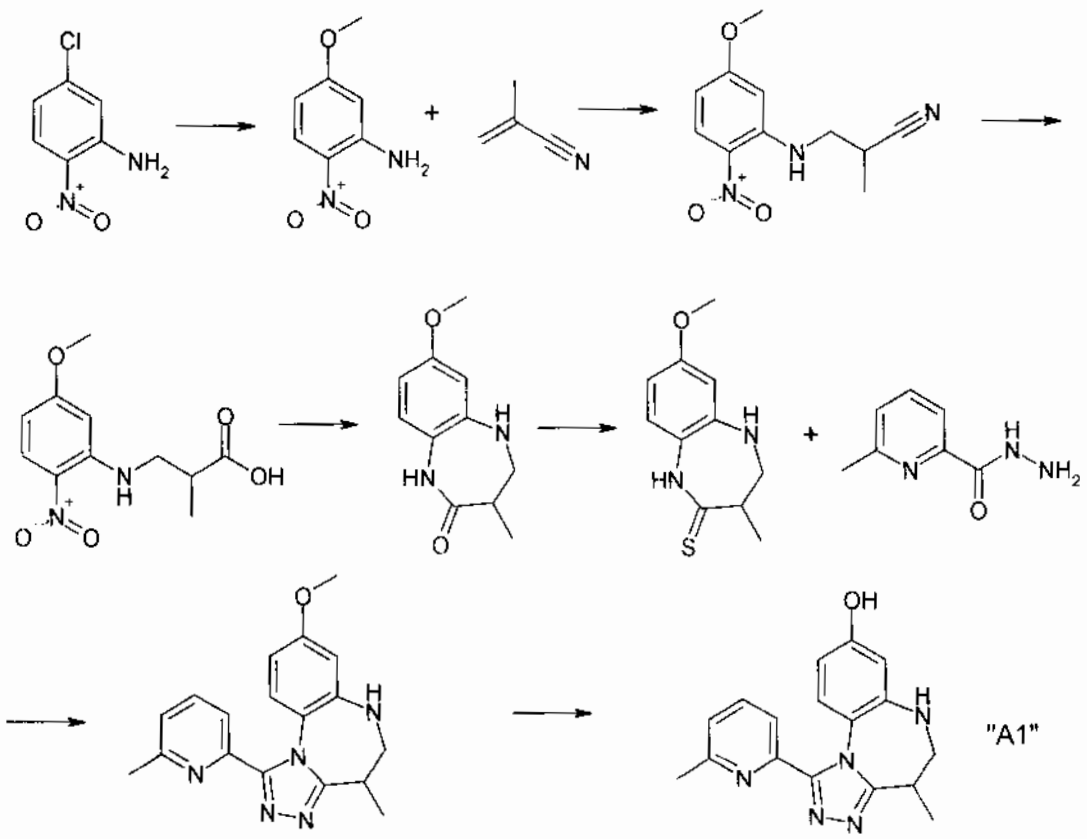
Mass spectrometry (MS): EI (electron impact ionisation) M^+
FAB (fast atom bombardment) $(M+H)^+$
ESI (electrospray ionisation) $(M+H)^+$
APCI-MS (atmospheric pressure chemical ionisation - mass spectrometry) $(M+H)^+$.

Retention time R_t [min]: Determination is carried out by HPLC

Column: Chromolith SpeedROD, 50 x 4.6 mm^2 (Order No. 1.51450.0001) from Merck
Gradient: 5.0 min, t = 0 min, A:B = 95:5, t = 4.4 min: A:B = 25:75, t = 4.5 min to t = 5.0 min: A:B = 0:100
Flow rate: 3.00 ml/min
Eluent A: water + 0.1% of TFA (trifluorooacetic acid),
Eluent B: acetonitrile + 0.08% of TFA
Wavelength: 220 nm

Example 1

The preparation of (*R*,*S*)-8-hydroxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10btetraazabenzo[*e*]azulene ("A1") is carried out analogously to the following scheme:



1.1 Preparation of 5-methoxy-2-nitroaniline

10 g of 5-chloro-2-nitroaniline are dissolved in 100 ml of methanol, and 32.3 g of sodium methoxide are added. The reaction mixture is heated at the boil under reflux for 18 hours. After cooling, the mixture is evaporated to dryness, 500 ml of water are added, and the crude product is isolated by filtration. Drying gives 9.15 g of 5-methoxy-2-nitroaniline.

1.2 Preparation of (*R*,*S*)-3-(5-methoxy-2-nitrophenylamino)-2-methylpropionic acid

9.15 g of 5-methoxy-2-nitroaniline are dissolved in 60 ml of THF, and 6.5 ml of 2-methacrylonitrile and 1.35 ml of a 40% solution of benzyltrimethylammonium hydroxide in methanol are added. The reaction mixture is heated at the boil for about 20 hours and, after cooling, evaporated to give an oily residue. The crude product is dissolved in 400 ml of methanol and 150 ml of water, and 150 ml of 32% sodium hydroxide solution are added. The mixture is heated at the boil for 3 hours, cooled, evaporated and worked up, giving 8.9 g of (*R*,*S*)-3-(5-methoxy-2-nitrophenylamino)-2-methylpropionic acid as crude product.

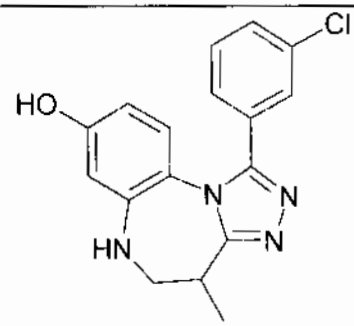
1.3 Preparation of (*R*,*S*)-8-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10btetraazabenzo[*e*]azulene

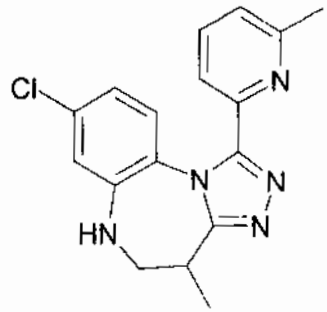
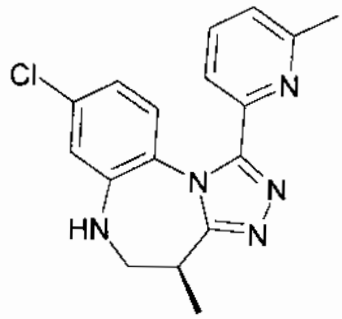
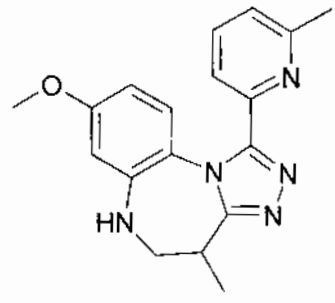
8.9 g of the (*R*,*S*)-3-(5-methoxy-2-nitrophenylamino)-2-methylpropionic acid obtained are dissolved in 40 ml of water and 40 ml of acetic acid, 8.4 g of zinc (coarsely powdered) are added, and the mixture is heated at the boil for 18 hours. Aqueous work-up gives 2.35 g of (*R*,*S*)-7-methoxy-3-methyl-1,3,4,5-tetrahydrobenzo[*b*]-1,4-diazepin-2-one, which is reacted further without purification. To this end, the crude product is dissolved in 25 ml of pyridine, 5.1 g of 2,4-bis(4-methoxyphenyl)-2,4-dithioxo-1,3,2,4-dithiadiphosphetane are added, and the mixture is heated at 110°C for 3 hours. After cooling, the mixture is subjected to aqueous work-up, and the crude product is precipitated by addition of diethyl ether. Drying gives 2.34 g of (*R*,*S*)-7-methoxy-3-methyl-1,3,4,5-tetrahydrobenzo[*b*]-1,4-diazepine-2-thione. This is heated at 110°C for 17 hours together with 6-methylpyridine-2-carbohydrazide in 5 ml of 1-butanol. After cooling and aqueous work-up, the oily crude product is purified by means of prepara-

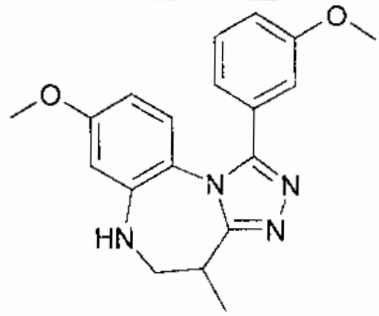
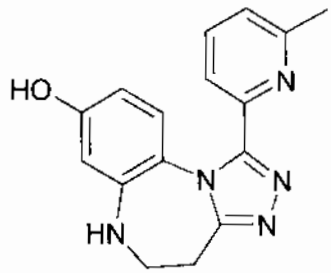
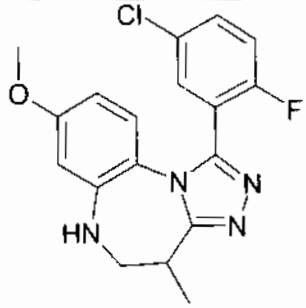
tive HPLC, giving 78 mg of (*R,S*)-8-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10btetraazabenzo[*e*]azulene.

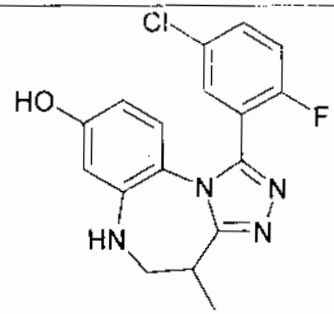
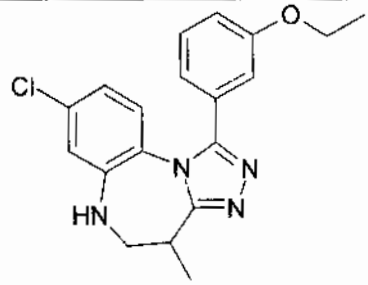
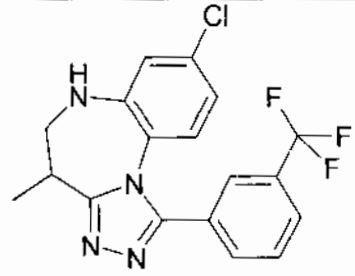
1.4 60 mg of (*R,S*)-8-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10btetraazabenzo[*e*]azulene are dissolved in 2.5 ml of dichloromethane, and 162 µl of boron tribromide are added dropwise. After 6 hours at room temperature, the mixture was evaporated to dryness, and the crude product was purified by means of preparative HPLC, giving 40 mg of "A1",

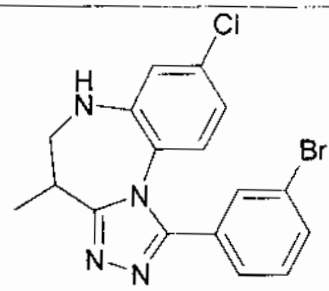
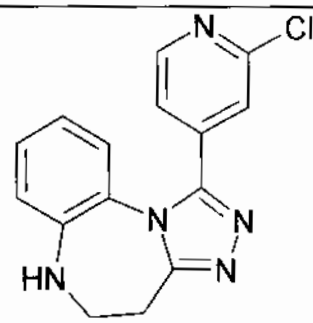
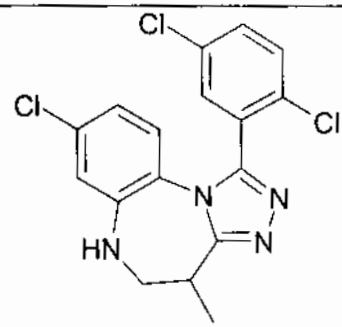
The following compounds are obtained analogously

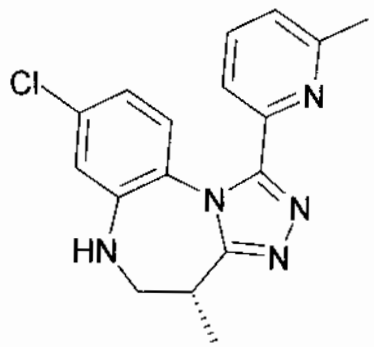
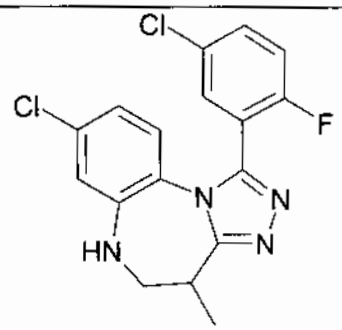
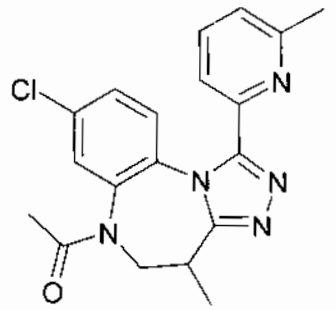
Compound No.	Structure / name	Analytical data
"A2"	 (R,S)-1-(3-Chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	

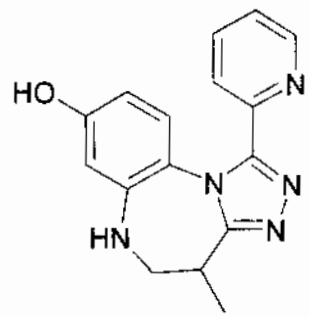
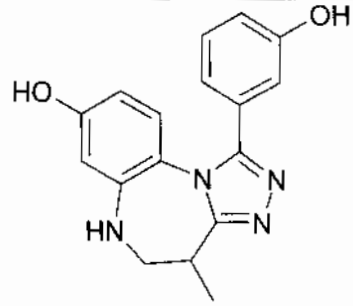
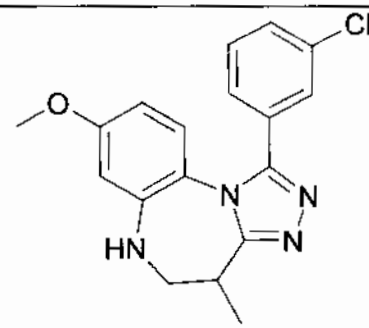
"A3"	 (R,S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	^{1}H-NMR (250MHz, d_6-DMSO): δ 1.40 (*d*, 3H, *J* = 6.4 Hz, CH_3), 2.27 (*s*, 3H, CH_3), 3.1-3.3 (*m*, 2H), 3.58-3.68 (*m*, 1H), 5.90 (*d*, 1H, *J* = 5 Hz, NH), 6.65-6.79 (*m*, 2H), 7.09 (*s*, 1H), 7.30 (*d*, *J* = 7.6 Hz, 1H), 7.69 (*d*, *J* = 7.6 Hz, 1H), 7.83 (*t*, *J* = 7.6 Hz, 1H)
"A4"	 (+)-(S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A5"	 (R,S)-8-Methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

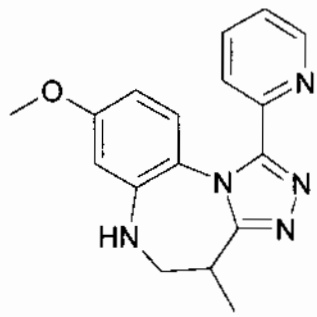
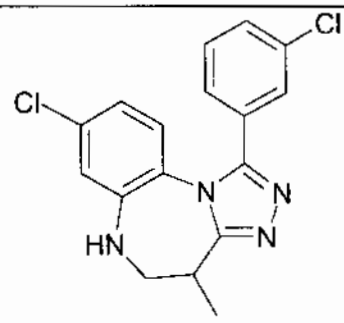
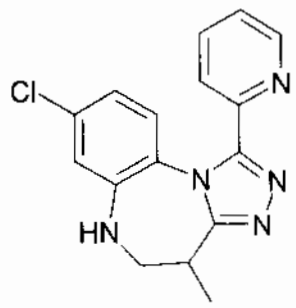
"A6"	 (R,S)-8-Methoxy-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A7"	 1-(6-Methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A8"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

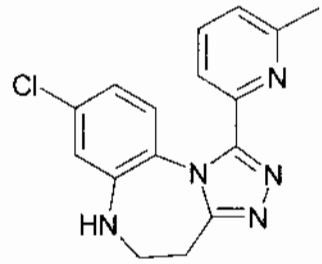
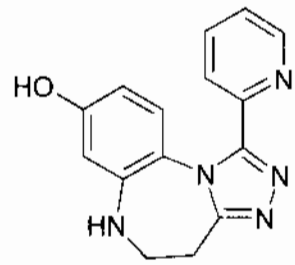
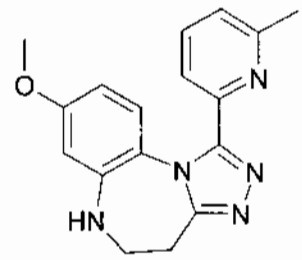
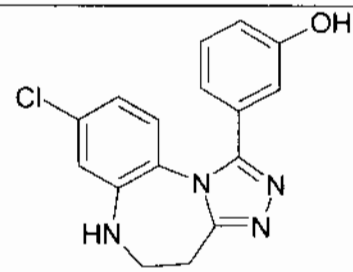
"A9"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	^{1}H-NMR (500MHz, d_6-DMSO): δ 1.40 (*d*, 3H, *J* = 6.8 Hz, CH_3), 3.16-3.21 (*m*, 1H), 3.31 (*t*, 1H, *J* = 10.9 Hz), 3.69 (*dd*, 1H, *J* = 10.7 Hz, 5.1 Hz), 6.22 (*d*, 1H, *J* = 8.6 Hz), 6.54 (*d*, 1H, *J* = 8.8 Hz), 6.61 (*s*, 1H), 7.35 (*t*, 1H, *J* = 9.1 Hz), 7.62-7.69 (*m*, 2H)
"A10"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A11"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethyl-phenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

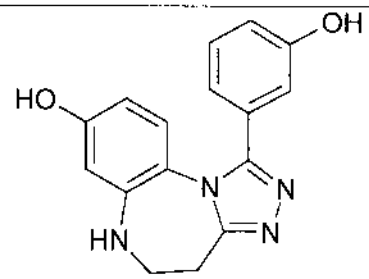
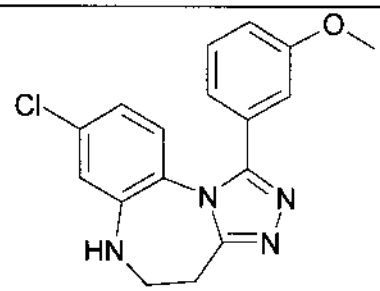
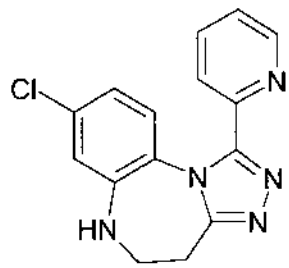
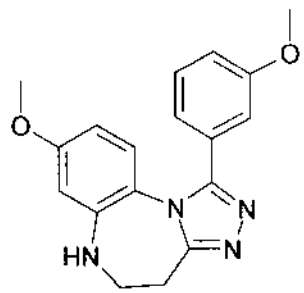
"A12"	 (R,S)-1-(3-Bromophenyl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[e]azulene	
"A13"	 1-(2-Chloropyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A14"	 (R,S)-8-Chloro-1-(2,5-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[e]azulene	

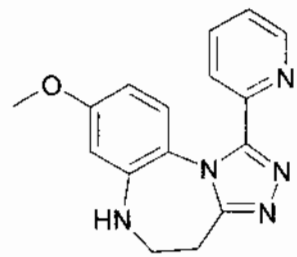
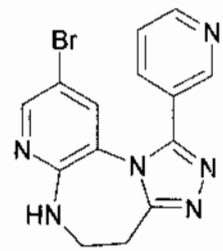
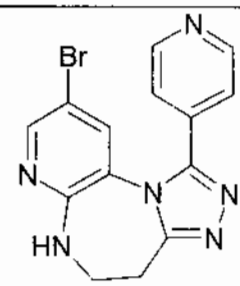
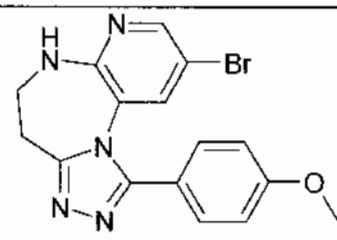
"A15"	 (-)-(R)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A16"	 (R,S)-8-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A17"	 (R,S)-1-[8-Chloro-4-methyl-1-(6-methyl-pyridin-2-yl)-4,5-dihydro-2,3,6,10b-tetraaza-benzo[*e*]azulen-6-yl]ethanone	

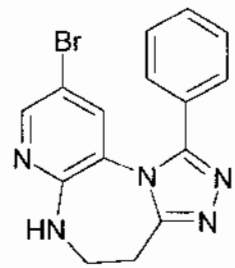
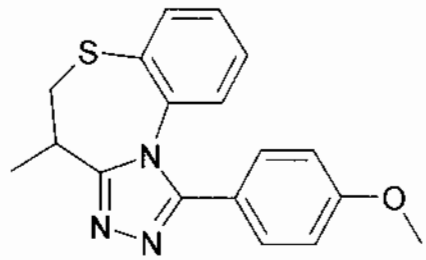
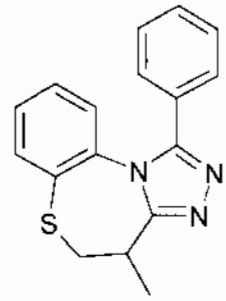
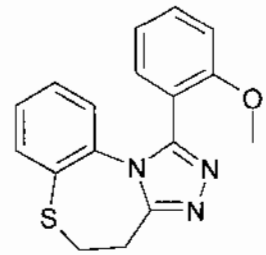
"A18"	 (R,S)-4-Methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	^{1}H-NMR (500MHz, d_6-DMSO): δ 1.46 (*d*, 3H, *J* = 6.1 Hz, CH_3), 3.40 (*t*, 1H, *J* = 10.7 Hz), 3.50-3.62 (*m*, 1H), 3.70 (*dd*, 1H, *J* = 11.5 Hz, 3.9 Hz), 6.25-6.44 (*bs*, 1H, NH), 6.46-6.52 (*m*, 1H), 6.56 (*s*, 1H), 7.71 (*d*, 1H, *J* = 8.7 Hz), 8.20 (*d*, 1H, *J* = 8.0 Hz), 8.32 (*t*, 1H, *J* = 6.8 Hz), 8.76 (*t*, 1H, *J* = 7.8 Hz), 9.58 (*d*, 1H, *J* = 5.2 Hz), 10.1-10.3 (*bs*, 1Hz, OH)
"A19"	 (R,S)-1-(3-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	
"A20"	 (R,S)-1-(3-Chlorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

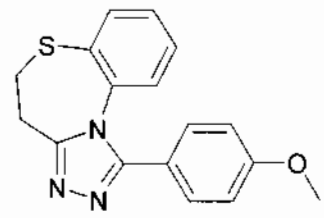
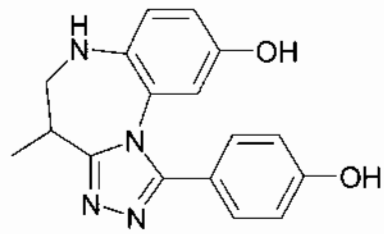
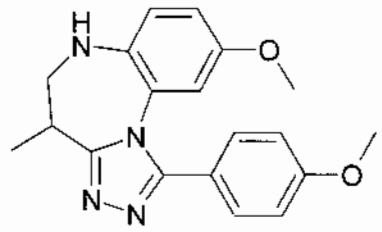
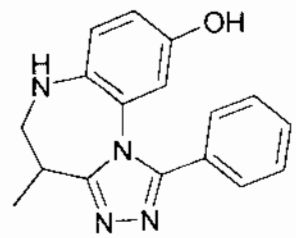
"A21"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A22"	 (R,S)-8-Chloro-1-(3-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A23"	 (R,S)-8-Chloro-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

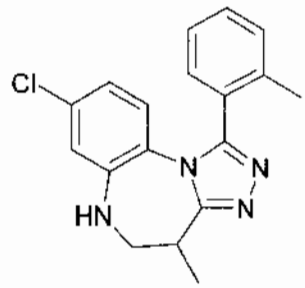
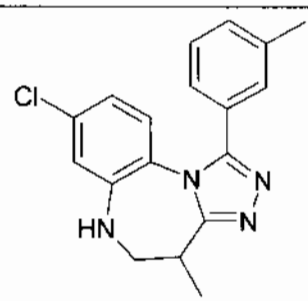
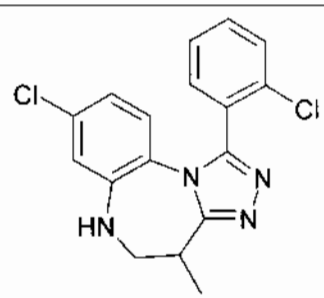
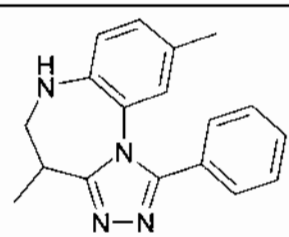
"A24"	 8-Chloro-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A25"	 1-Pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A26"	 8-Methoxy-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A27"	 3-(8-Chloro-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenol	

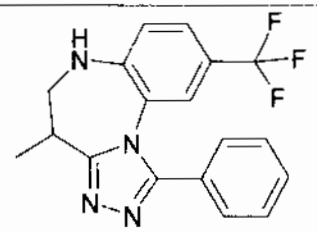
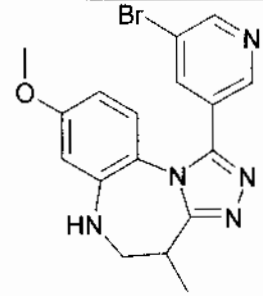
"A28"	 1-(3-Hydroxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A29"	 8-Chloro-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A30"	 8-Chloro-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A31"	 8-Methoxy-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	

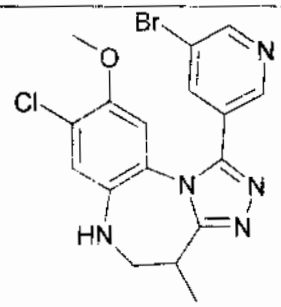
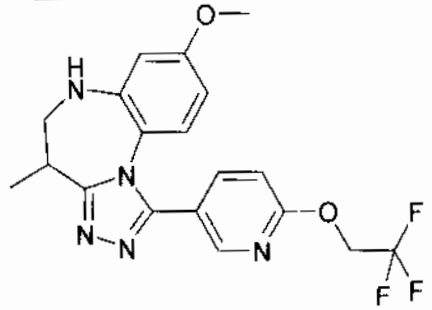
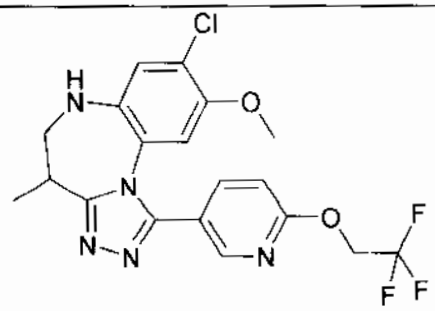
"A32"	 8-Methoxy-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A33"	 9-Bromo-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene	
"A34"	 9-Bromo-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene	
"A35"	 9-Bromo-1-(4-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene	

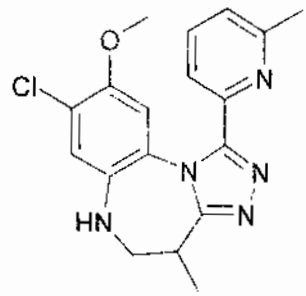
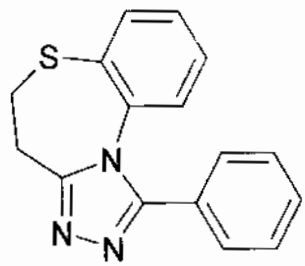
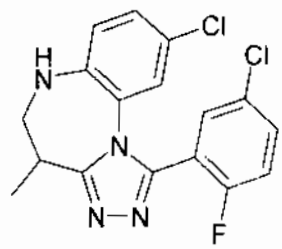
"A36"	 9-Bromo-1-phenyl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene	
"A37"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene	
"A38"	 (R,S)-4-Methyl-1-phenyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene	
"A39"	 1-(2-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene	

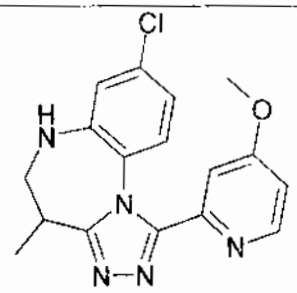
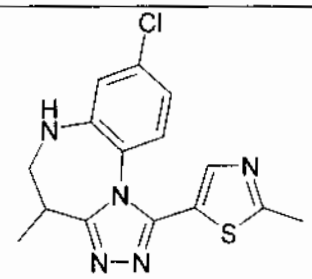
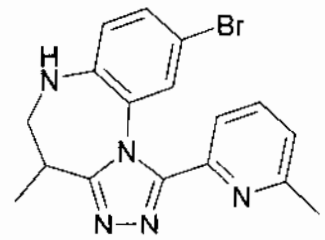
"A40"	 1-(4-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene	
"A41"	 (R,S)-1-(4-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol	
"A42"	 (R,S)-9-Methoxy-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A43"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol	

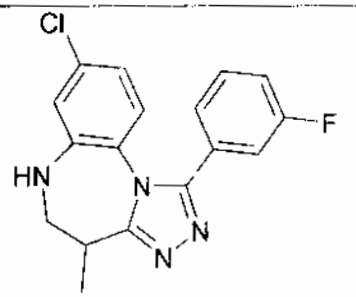
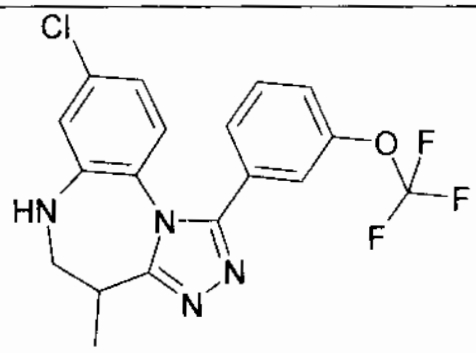
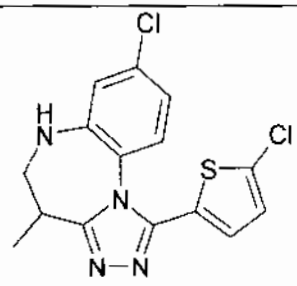
"A44"	 (R,S)-8-Chloro-4-methyl-1-*o*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A45"	 (R,S)-8-Chloro-4-methyl-1-*m*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A46"	 (R,S)-8-Chloro-1-(2-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A47"	 (R,S)-4,9-Dimethyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	

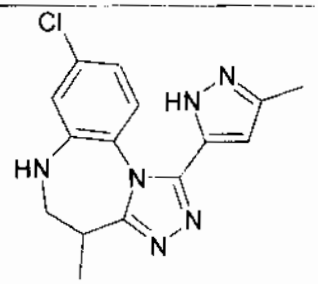
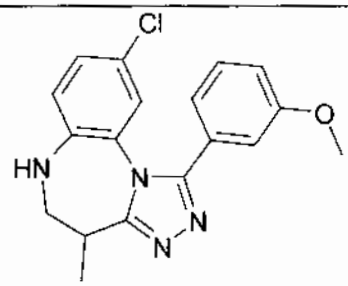
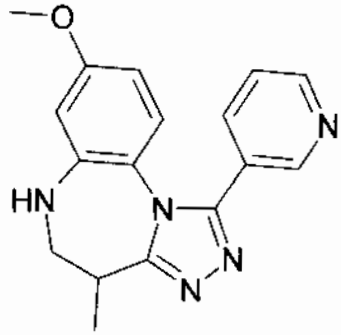
"A48"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A49"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulene-6-carbaldehyde	
"A50"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

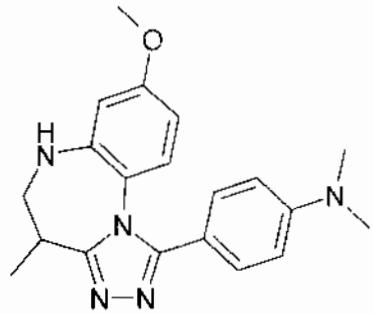
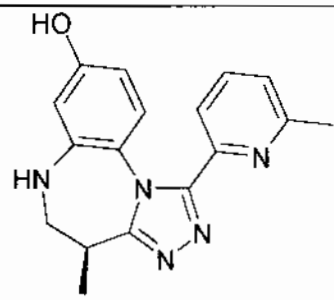
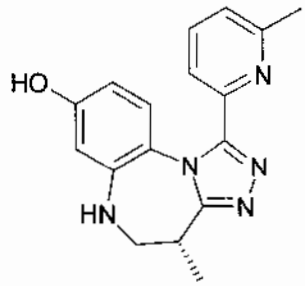
"A51"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-chloro-9-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A52"	 (R,S)-8-Methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A53"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

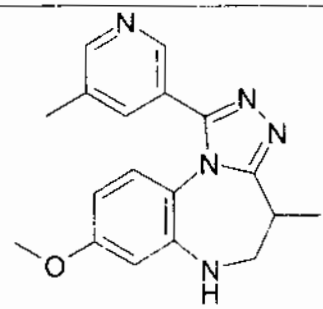
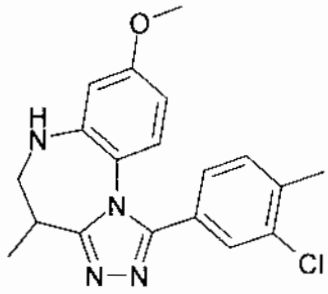
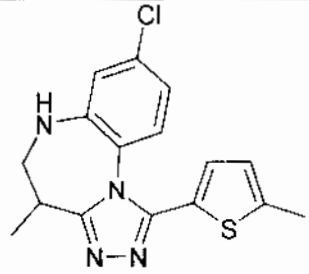
"A54"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A55"	 1-Phenyl-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene	
"A56"	 (R,S)-9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene trifluoroacetate	

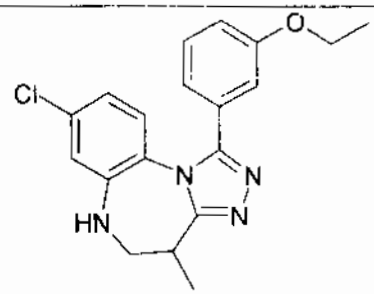
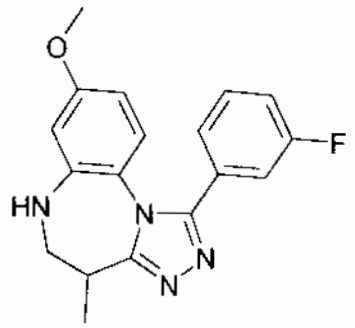
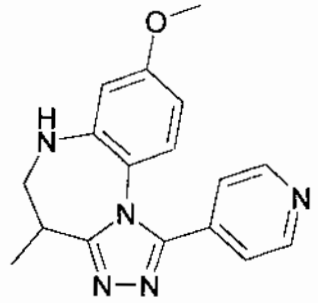
"A57"	 (R,S)-8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A58"	 (R,S)-8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A59"	 (R,S)-9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

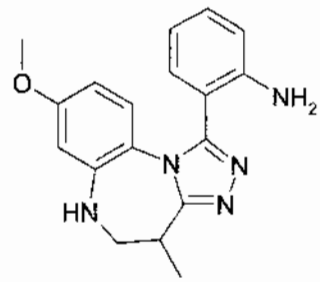
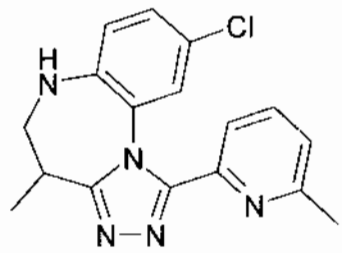
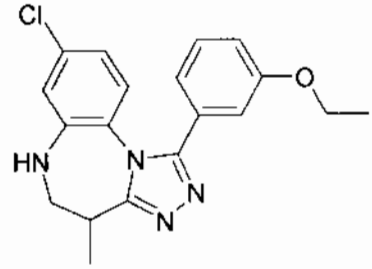
"A60"	 (R,S)-8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A61"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoro-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A62"	 (R,S)-8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

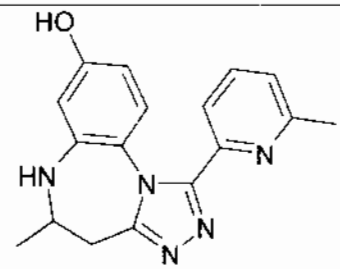
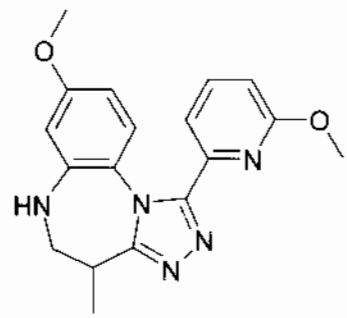
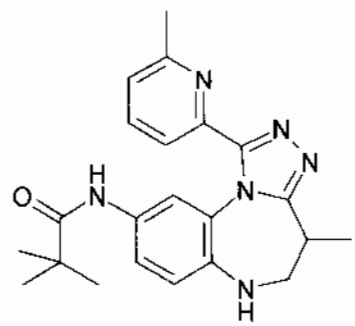
"A63"	 (R,S)-8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A64"	 (R,S)-9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene trifluoroacetate	
"A65"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

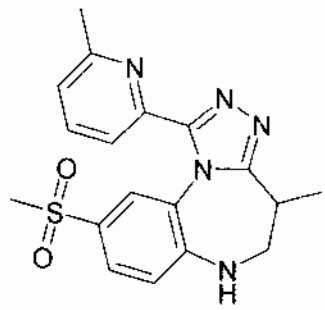
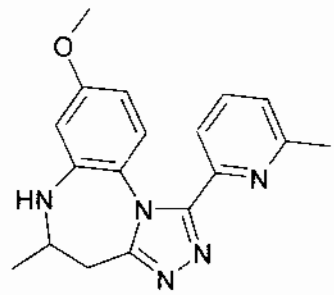
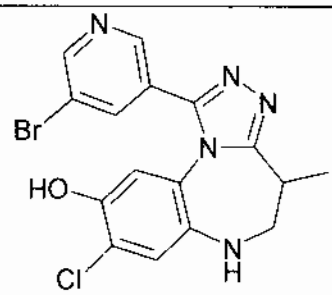
"A66"	 (R,S)-[4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)-phenyl]dimethylamine	
"A67"	 (S)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	
"A68"	 (R)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	

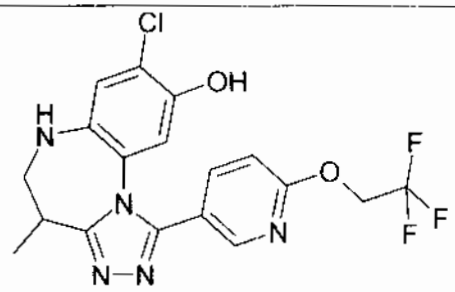
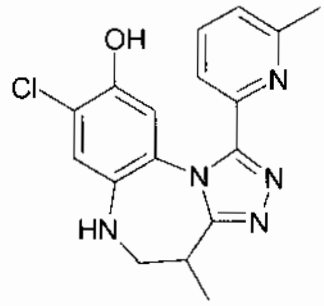
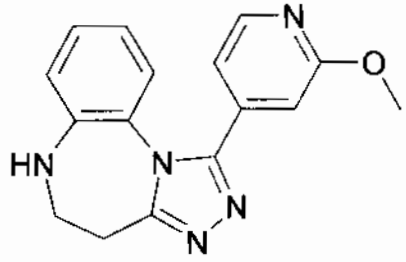
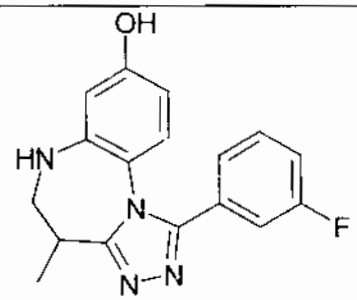
"A69"	 (R,S)-8-Methoxy-4-methyl-1-(5-methylpyridin-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A70"	 (R,S)-1-(3-Chloro-4-methylphenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A71"	 (R,S)-8-Chloro-4-methyl-1-(5-methylthiophen-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	

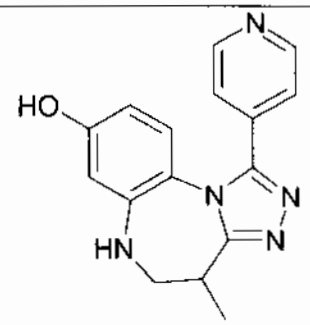
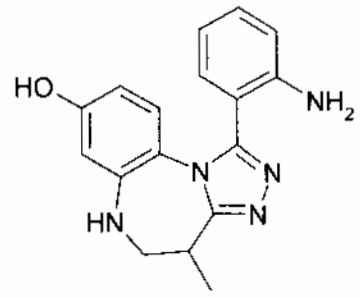
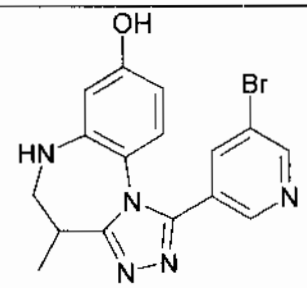
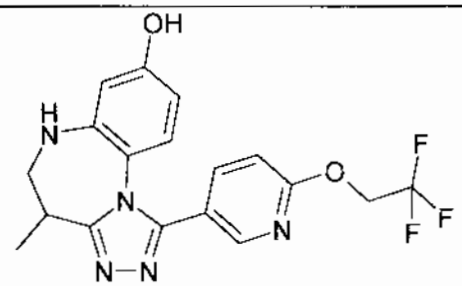
"A72"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A73"	 (R,S)-1-(3-Fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A74"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

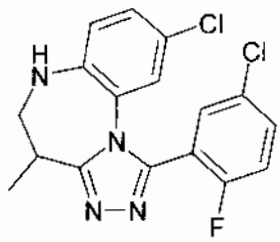
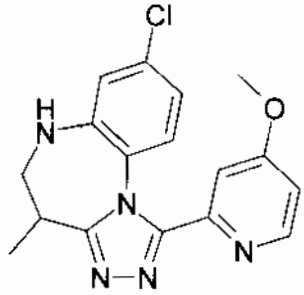
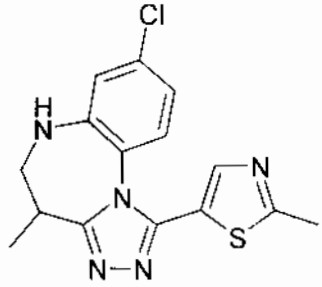
"A75"	 (R,S)-2-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)-phenylamine	
"A76"	 (R,S)-9-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene bistrifluoroacetate	
"A77"	 8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

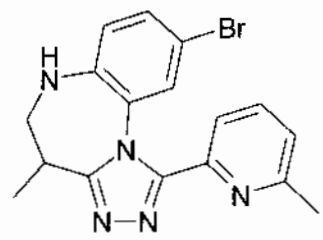
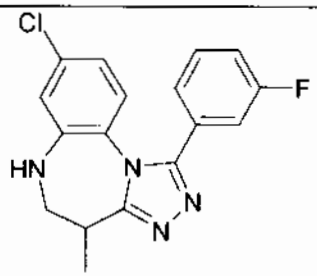
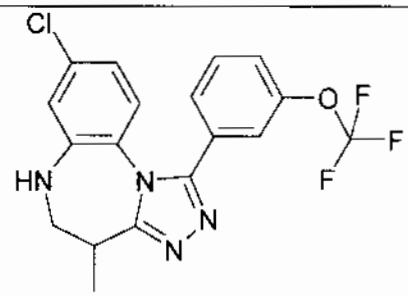
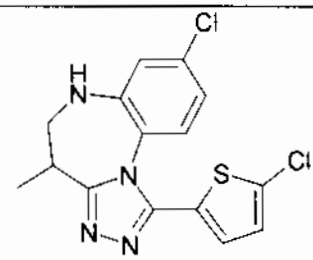
"A78"	 5-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A79"	 8-Methoxy-1-(6-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A80"	 2,2-Dimethyl-N-[4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-yl]propionamide	

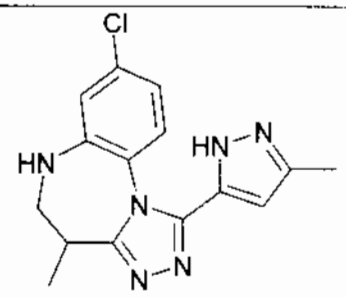
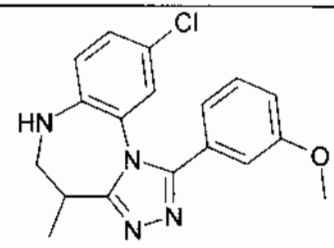
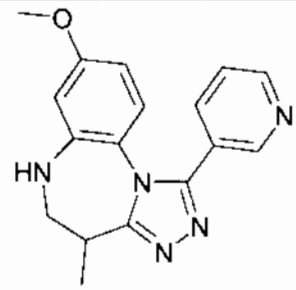
"A81"	 9-Methanesulfonyl-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A82"	 8-Methoxy-5-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A83"	 1-(5-Bromopyridin-3-yl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol	

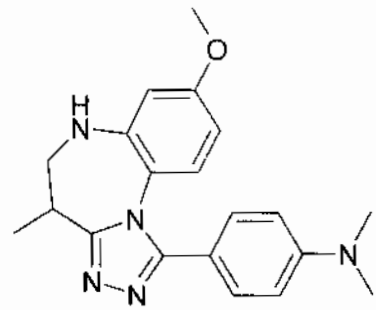
"A84"	 8-Chloro-4-methyl-1-[6-(2,2,2-trifluoro-ethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol	
"A85"	 8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol	
"A86"	 1-(2-Methoxypyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene	
"A87"	 1-(3-Fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	

"A88"	 4-Methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A89"	 1-(2-Aminophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A90"	 1-(5-Bromopyridin-3-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol	
"A91"	 4-Methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol	

"A92"	 9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A93"	 8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A94"	 8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

"A95"	 9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A96"	 8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A97"	 8-Chloro-4-methyl-1-(3-trifluoromethoxy-phenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A98"	 8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

"A99"	 8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A100"	 9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	
"A101"	 8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene	

"A102"	 [4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)-phenyl]dimethylamine	

The following examples relate to medicaments:

Example A: Injection vials

A solution of 100 g of an active ingredient of the formula I and 5 g of disodium hydrogenphosphate in 3 l of bidistilled water is adjusted to pH 6.5 using 2 N hydrochloric acid, sterile filtered, transferred into injection vials, lyophilised under sterile conditions and sealed under sterile conditions. Each injection vial contains 5 mg of active ingredient.

Example B: Suppositories

A mixture of 20 g of an active ingredient of the formula I with 100 g of soya lecithin and 1400 g of cocoa butter is melted, poured into moulds and allowed to cool. Each suppository contains 20 mg of active ingredient.

Example C: Solution

A solution is prepared from 1 g of an active ingredient of the formula I, 9.38 g of $NaH_2PO_4 \cdot 2\ H_2O$, 28.48 g of $Na_2HPO_4 \cdot 12\ H_2O$ and 0.1 g of benzalkonium chloride in 940 ml of bidistilled water. The pH is adjusted to 6.8, and the solution is made up to 1 l and sterilised by irradiation. This solution can be used in the form of eye drops.

Example D: Ointment

500 mg of an active ingredient of the formula I are mixed with 99.5 g of Vaseline under aseptic conditions.

Example E: Tablets

A mixture of 1 kg of active ingredient of the formula I, 4 kg of lactose, 1.2 kg of potato starch, 0.2 kg of talc and 0.1 kg of magnesium stearate is pressed in a conventional manner to give tablets in such a way that each tablet contains 10 mg of active ingredient.

Example F: Dragees

Tablets are pressed analogously to Example E and subsequently coated in a conventional manner with a coating of sucrose, potato starch, talc, tragacanth and dye.

Example G: Capsules

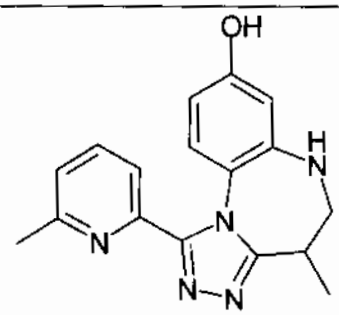
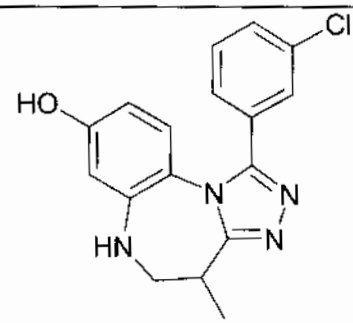
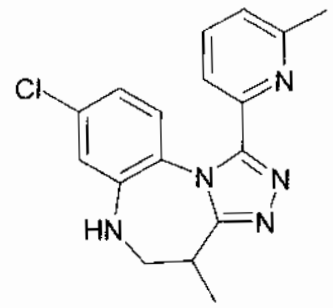
2 kg of active ingredient of the formula I are introduced into hard gelatine capsules in a conventional manner in such a way that each capsule contains 20 mg of the active ingredient.

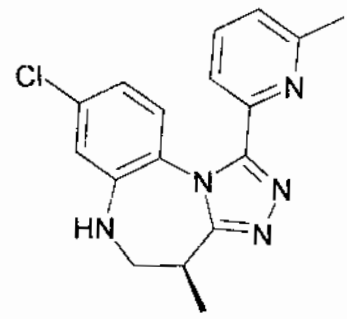
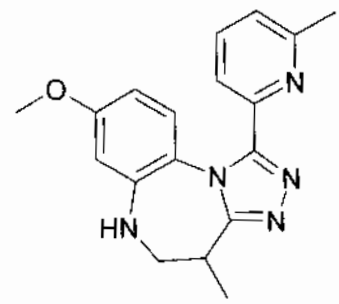
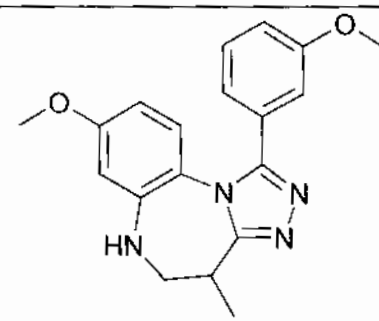
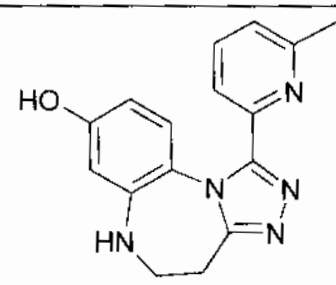
Example H: Ampoules

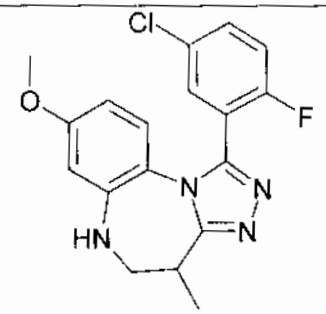
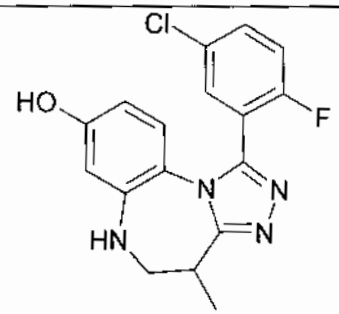
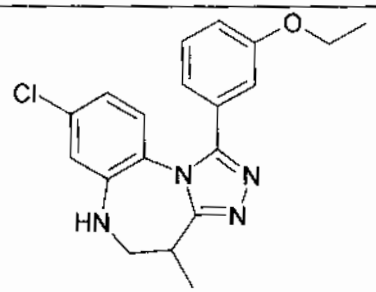
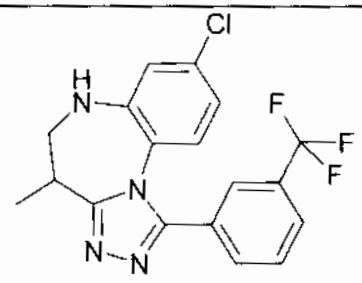
A solution of 1 kg of active ingredient of the formula I in 60 l of bidistilled water is sterile filtered, transferred into ampoules, lyophilised under sterile conditions and sealed under sterile conditions. Each ampoule contains 10 mg of active ingredient.

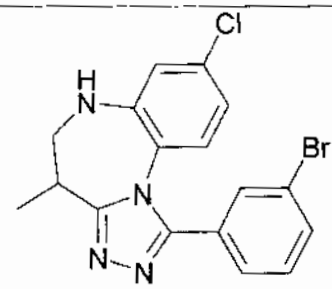
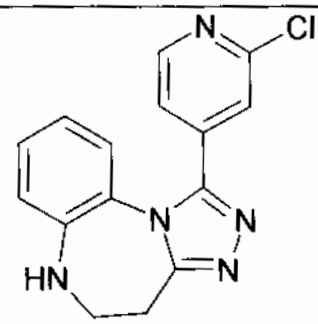
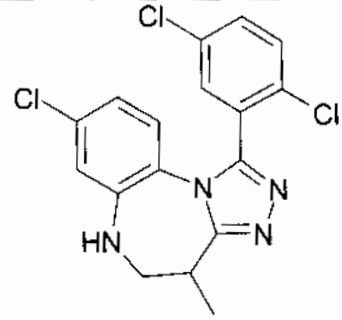
Patent Claims

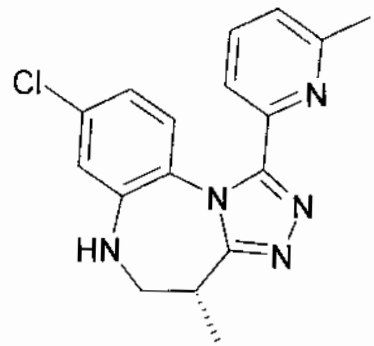
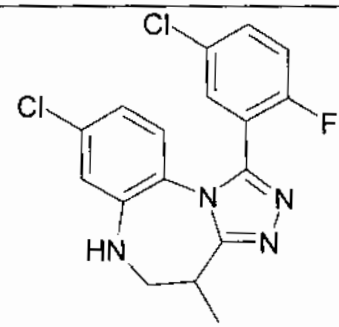
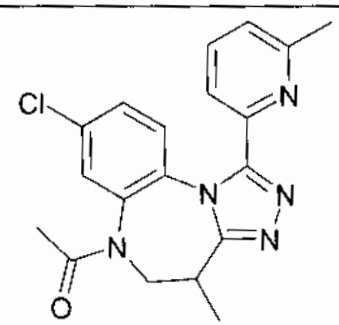
1. Compounds selected from the group

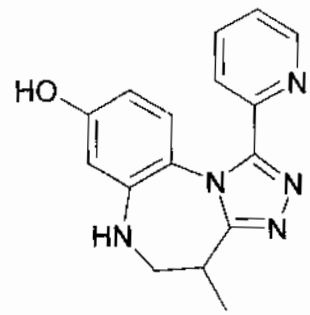
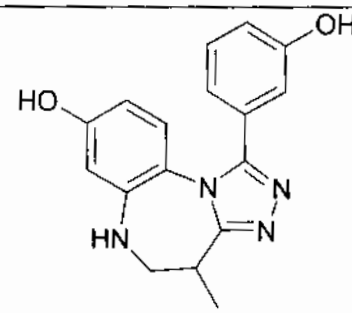
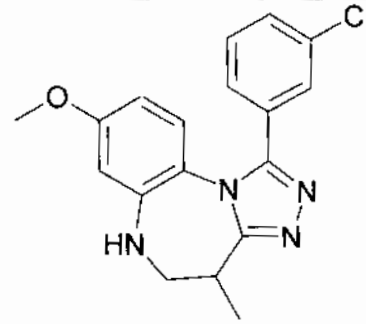
Compound No.	Structure / name
"A1"	 (*R,S*)-8-Hydroxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A2"	 (R,S)-1-(3-Chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A3"	 (R,S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

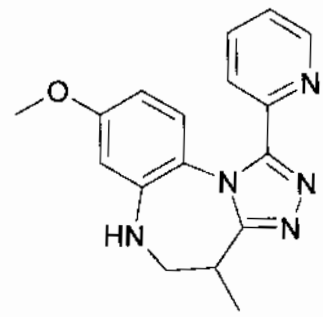
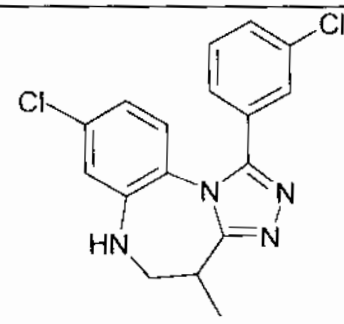
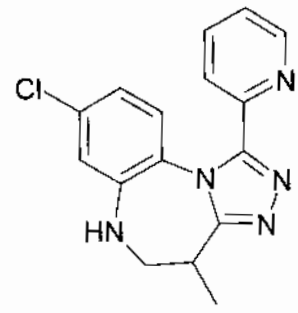
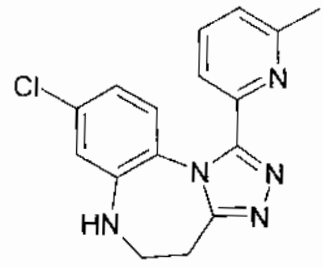
"A4"	 (+)-(S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A5"	 (R,S)-8-Methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A6"	 (R,S)-8-Methoxy-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A7"	 1-(6-Methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

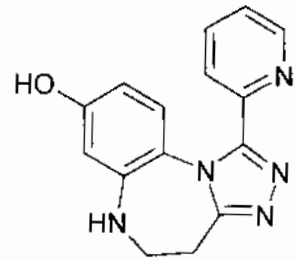
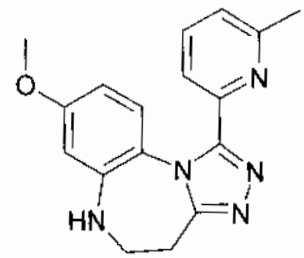
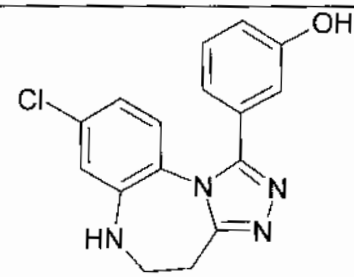
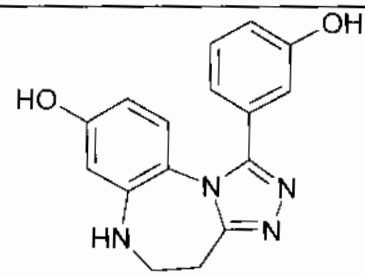
"A8"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A9"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A10"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A11"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethylphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

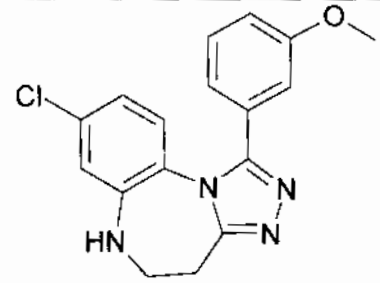
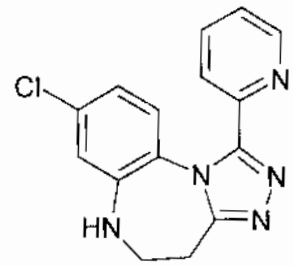
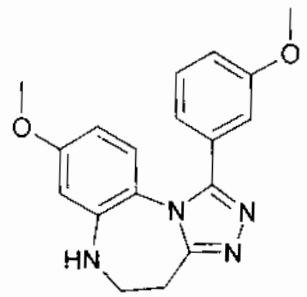
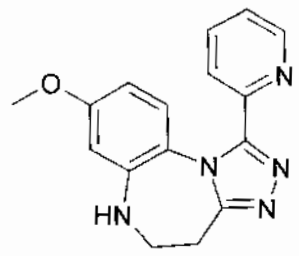
"A12"	 (R,S)-1-(3-Bromophenyl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulene
"A13"	 1-(2-Chloropyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A14"	 (R,S)-8-Chloro-1-(2,5-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

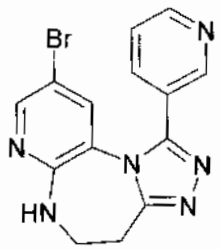
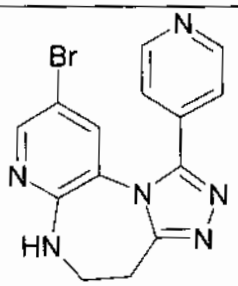
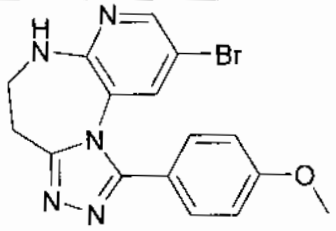
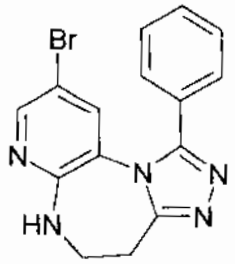
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"A16"	 (R,S)-8-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A17"	 (R,S)-1-[8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulen-6-yl]ethanone

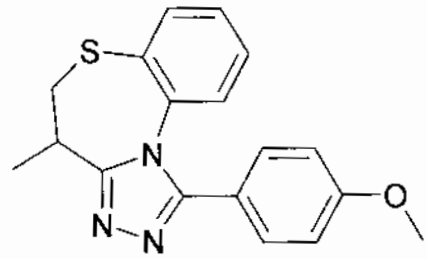
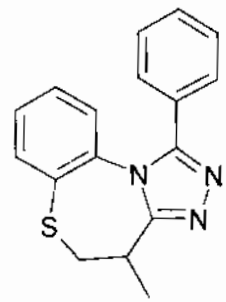
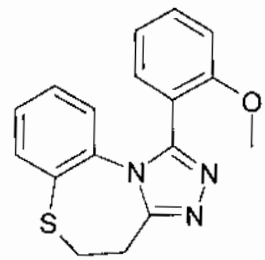
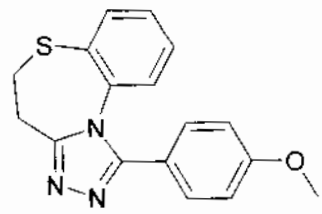
"A18"	 (R,S)-4-Methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A19"	 (R,S)-1-(3-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A20"	 (R,S)-1-(3-Chlorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

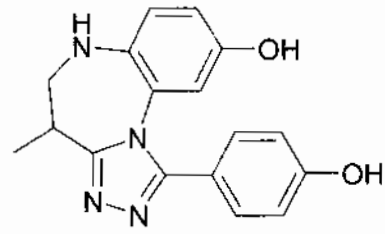
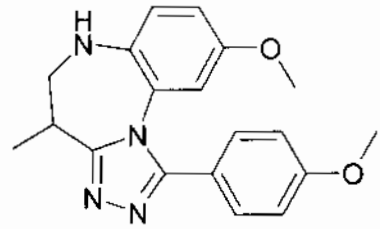
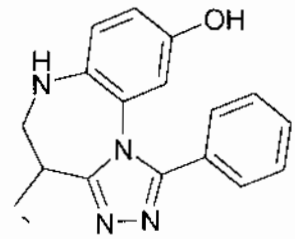
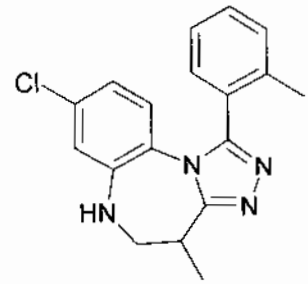
"A21"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A22"	 (R,S)-8-Chloro-1-(3-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A23"	 (R,S)-8-Chloro-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A24"	 8-Chloro-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

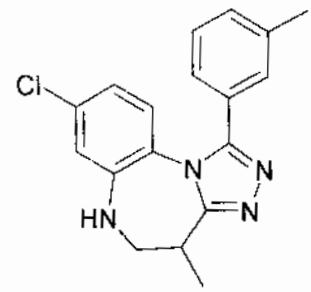
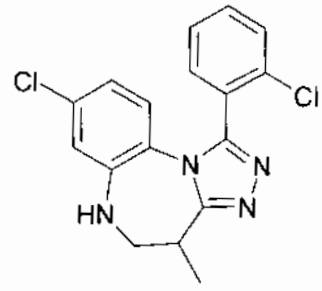
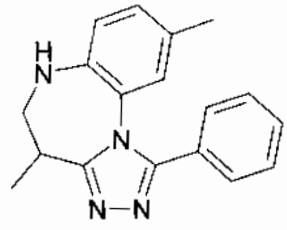
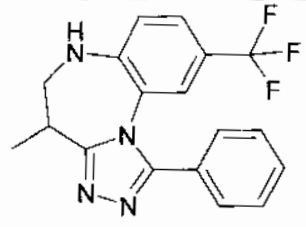
"A25"	 1-Pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol
"A26"	 8-Methoxy-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A27"	 3-(8-Chloro-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)phenol
"A28"	 1-(3-Hydroxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

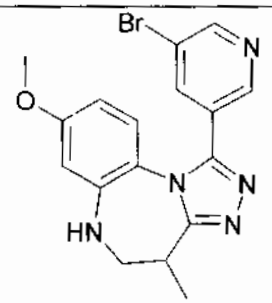
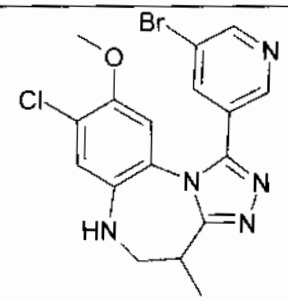
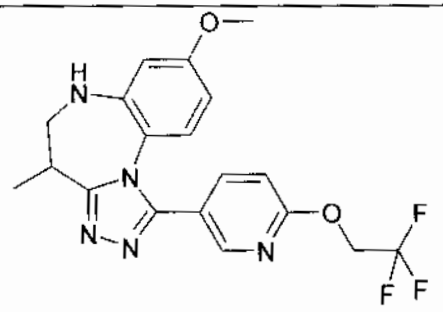
"A29"	 8-Chloro-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A30"	 8-Chloro-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A31"	 8-Methoxy-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A32"	 8-Methoxy-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene

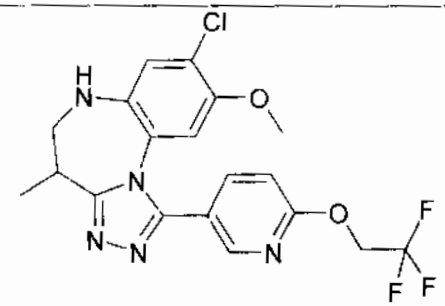
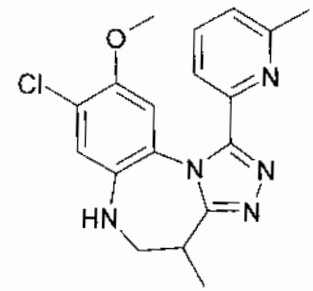
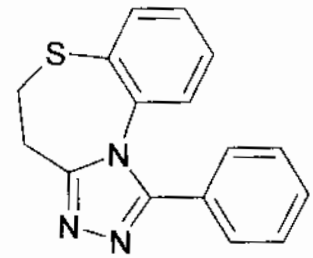
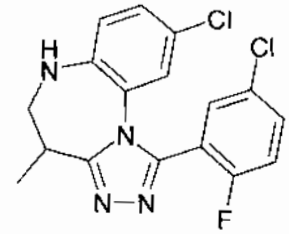
"A33"	 9-Bromo-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A34"	 9-Bromo-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A35"	 9-Bromo-1-(4-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene
"A36"	 9-Bromo-1-phenyl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene

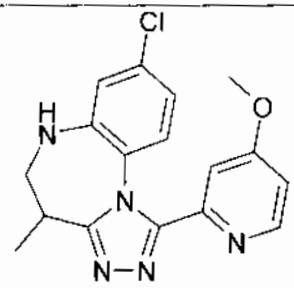
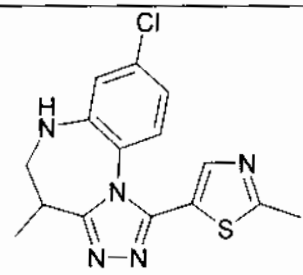
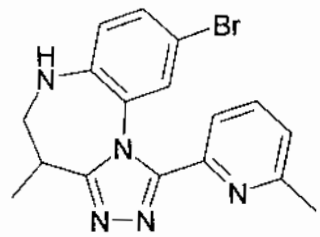
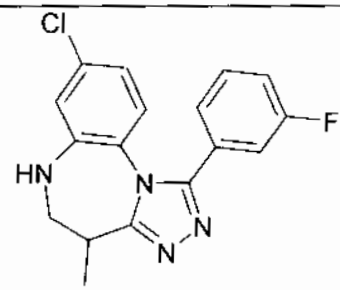
"A37"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A38"	 (R,S)-4-Methyl-1-phenyl-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A39"	 1-(2-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A40"	 1-(4-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene

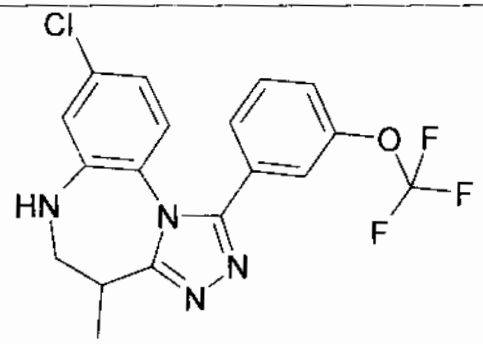
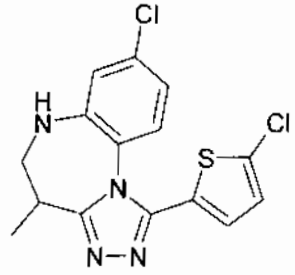
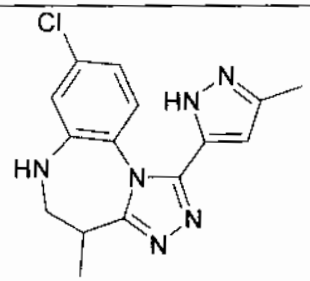
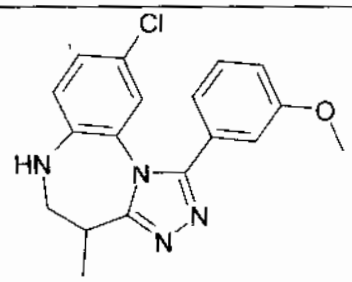
"A41"	 (R,S)-1-(4-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A42"	 (R,S)-9-Methoxy-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A43"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol
"A44"	 (R,S)-8-Chloro-4-methyl-1-*o*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

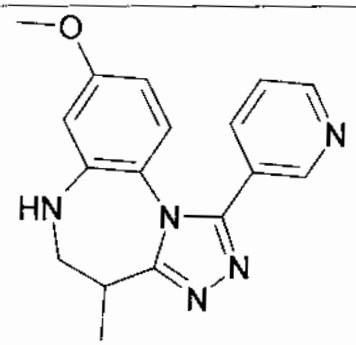
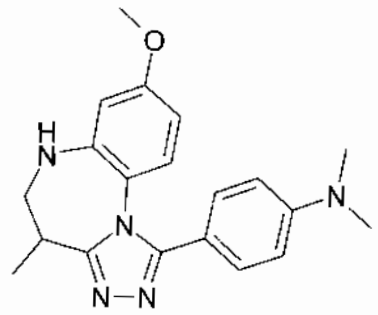
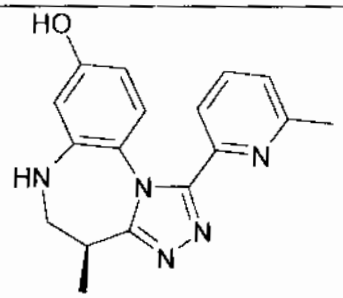
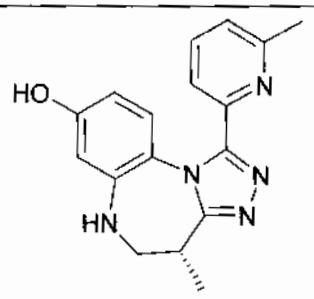
"A45"	 (R,S)-8-Chloro-4-methyl-1-*m*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A46"	 (R,S)-8-Chloro-1-(2-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A47"	 (R,S)-4,9-Dimethyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A48"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

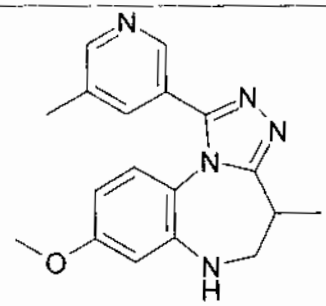
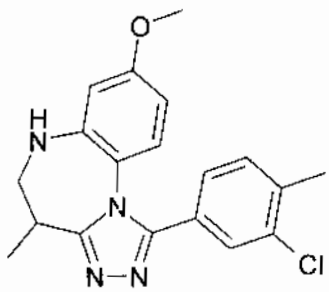
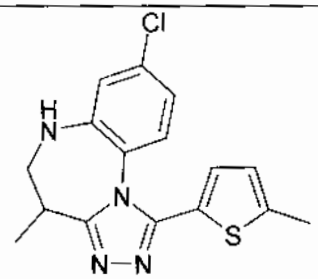
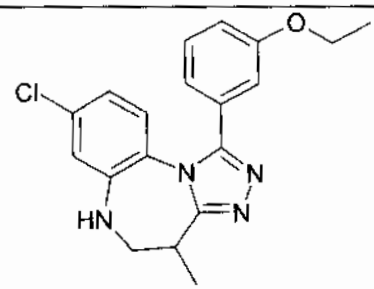
"A49"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulene-6-carbaldehyde
"A50"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A51"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-chloro-9-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A52"	 (R,S)-8-Methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

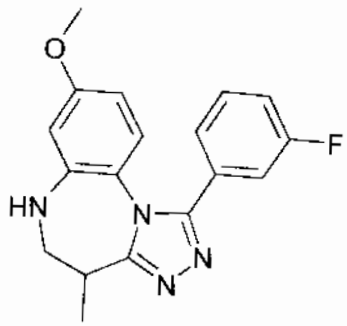
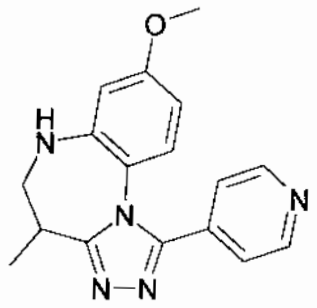
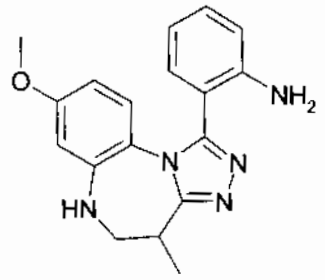
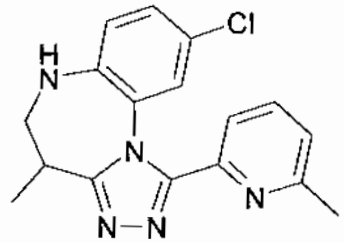
"A53"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-[6-(2,2,2-trifluoro-ethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A54"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A55"	 1-Phenyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A56"	 (R,S)-9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

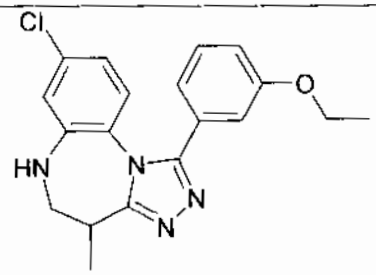
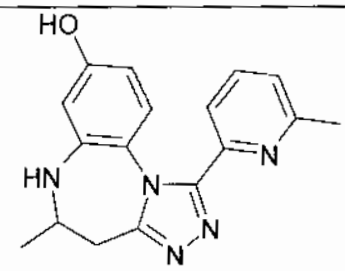
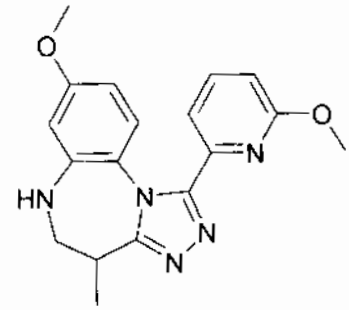
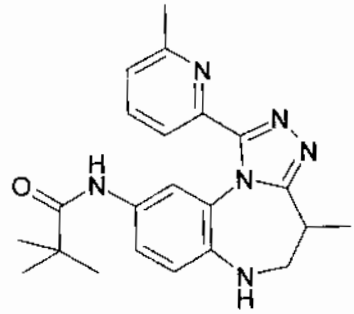
"A57"	 (R,S)-8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A58"	 (R,S)-8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A59"	 (R,S)-9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A60"	 (R,S)-8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

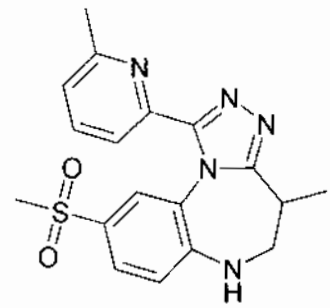
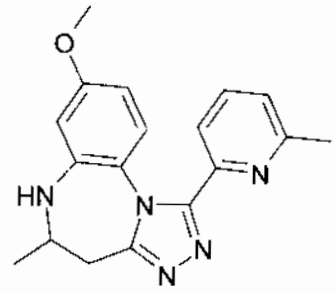
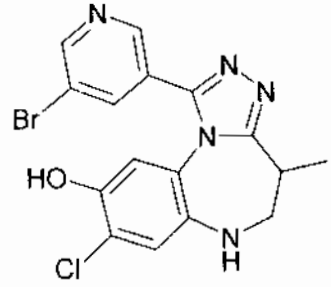
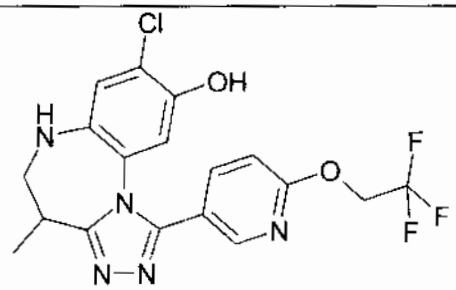
"A61"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A62"	 (R,S)-8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A63"	 (R,S)-8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A64"	 (R,S)-9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

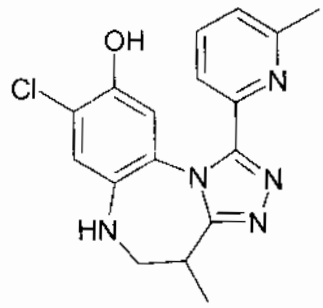
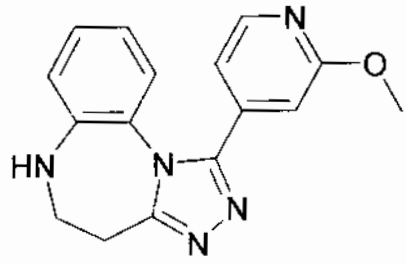
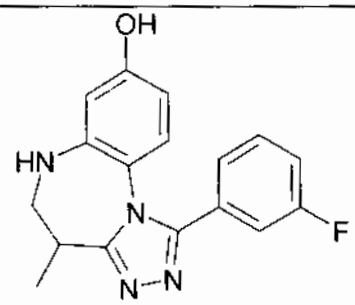
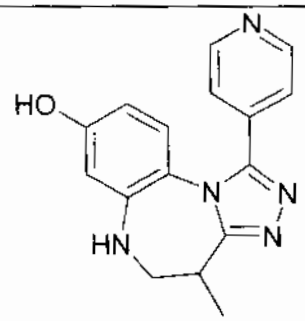
"A65"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A66"	 (R,S)-[4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenyl]dimethylamine
"A67"	 (S)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A68"	 (R)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol

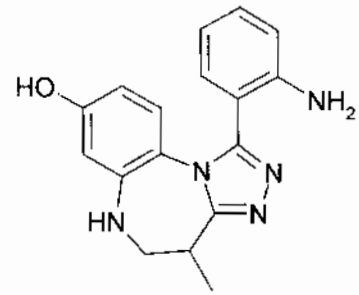
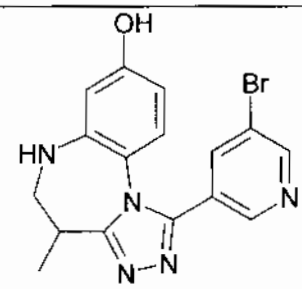
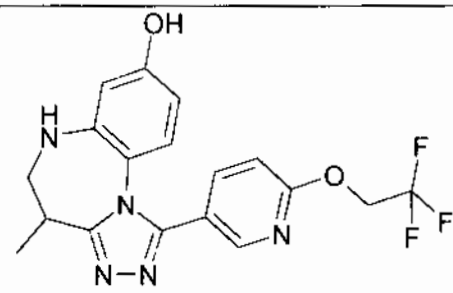
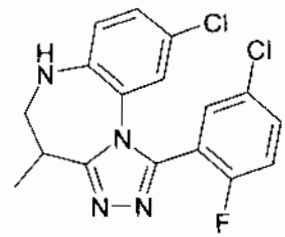
"A69"	 (R,S)-8-Methoxy-4-methyl-1-(5-methylpyridin-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A70"	 (R,S)-1-(3-Chloro-4-methylphenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A71"	 (R,S)-8-Chloro-4-methyl-1-(5-methylthiophen-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A72"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

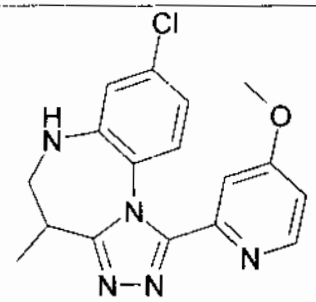
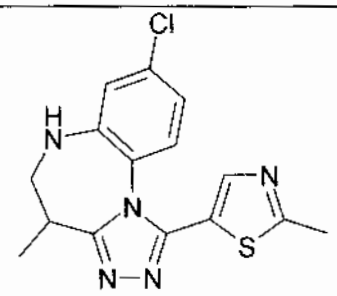
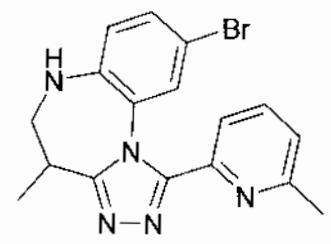
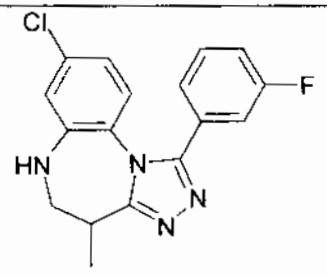
"A73"	 (R,S)-1-(3-Fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A74"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A75"	 (R,S)-2-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenylamine
"A76"	 (R,S)-9-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene bistrifluoroacetate

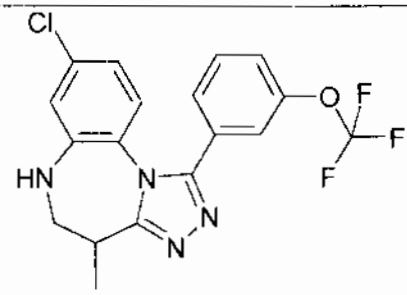
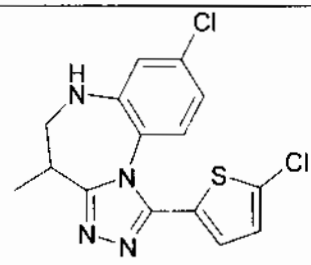
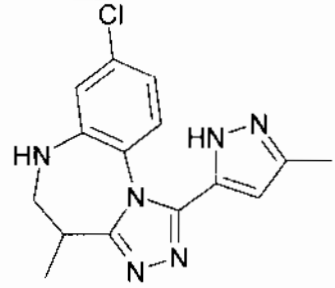
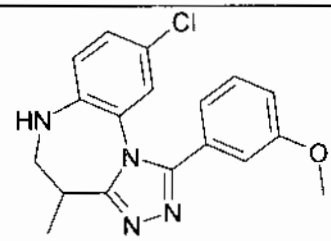
"A77"	 8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A78"	 5-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A79"	 8-Methoxy-1-(6-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A80"	 2,2-Dimethyl-N-[4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-yl]propion-amide

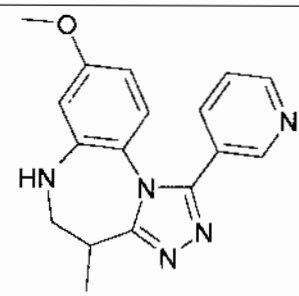
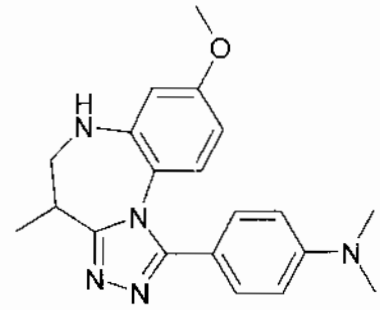
"A81"	 9-Methanesulfonyl-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A82"	 8-Methoxy-5-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A83"	 1-(5-Bromopyridin-3-yl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A84"	 8-Chloro-4-methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol

"A85"	 8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A86"	 1-(2-Methoxypyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A87"	 1-(3-Fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A88"	 4-Methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

"A89"	 1-(2-Aminophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A90"	 1-(5-Bromopyridin-3-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A91"	 4-Methyl-1-[6-(2,2,2-trifluoroethoxy)pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A92"	 9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"A93"	 8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A94"	 8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A95"	 9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A96"	 8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

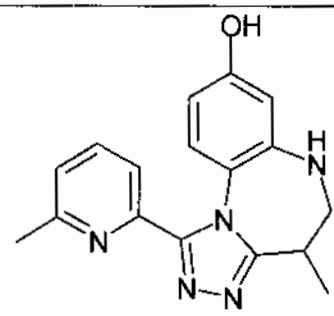
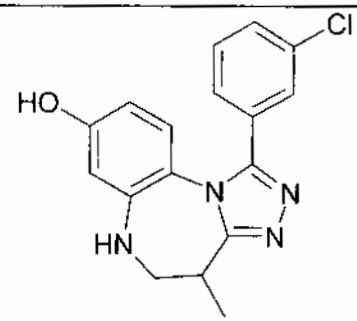
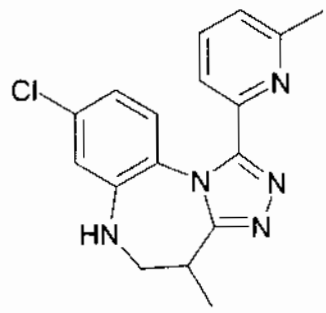
"A97"	 8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A98"	 8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A99"	 8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A100"	 9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

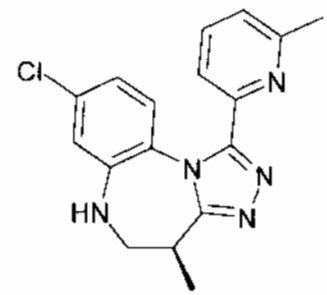
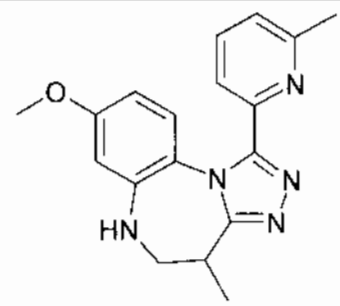
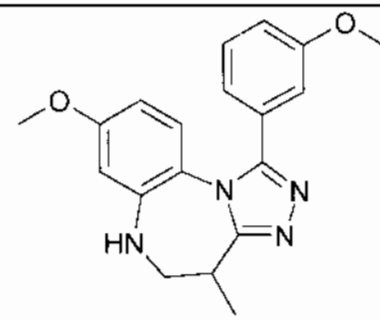
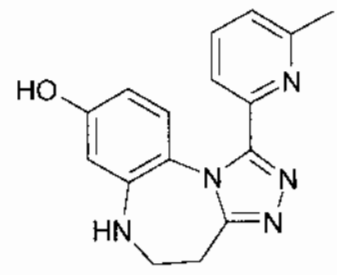
"A101"	 8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A102"	 [4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)phenyl]dimethylamine

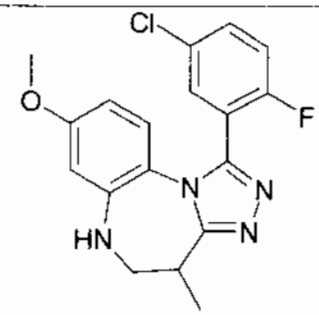
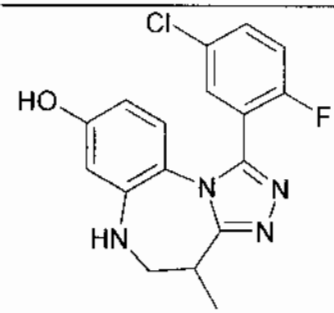
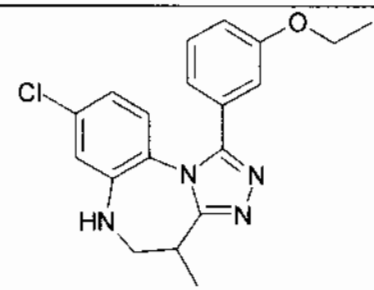
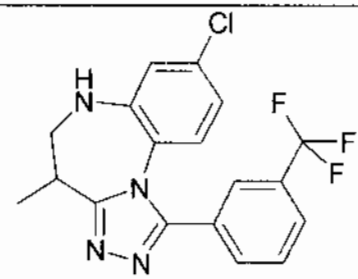
and pharmaceutically usable derivatives, solvates, salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

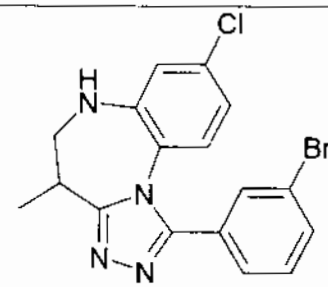
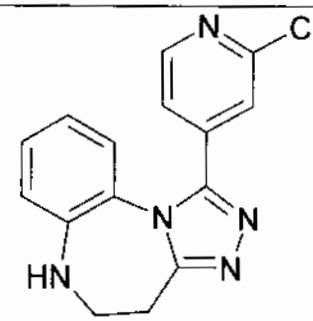
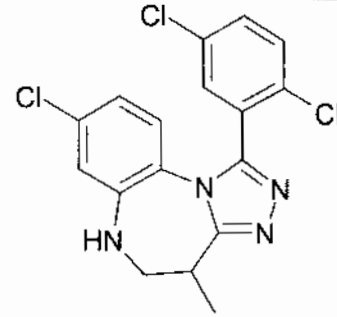
2. Medicaments comprising at least one compound according to Claim 1 and/or pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

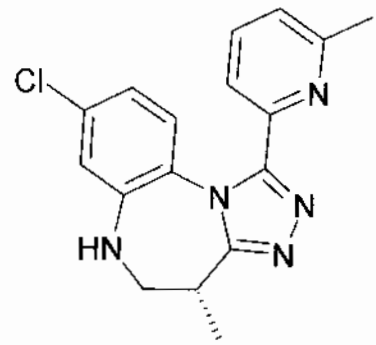
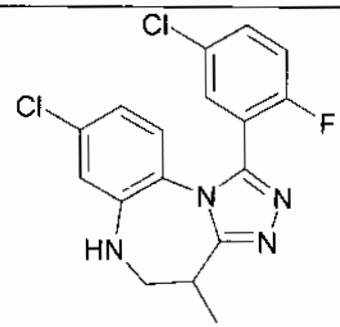
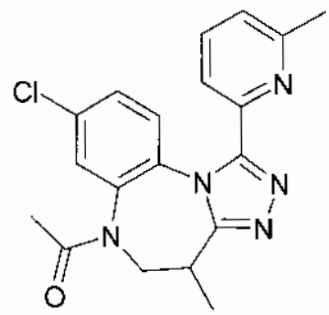
3. Use of compounds selected from the group

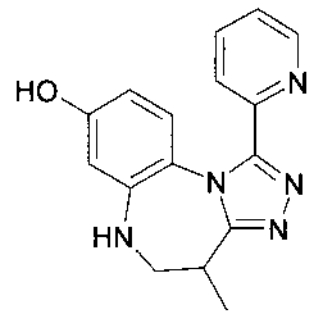
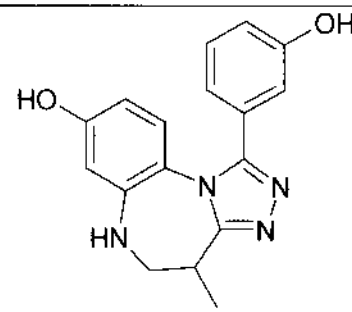
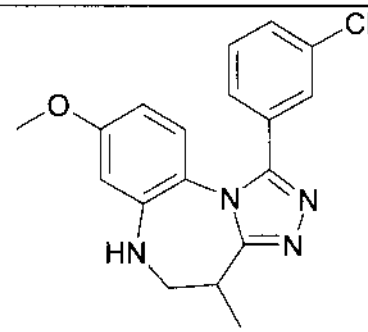
Compound No.	Structure / name
"A1"	 (*R,S*)-8-Hydroxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A2"	 (R,S)-1-(3-Chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A3"	 (R,S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

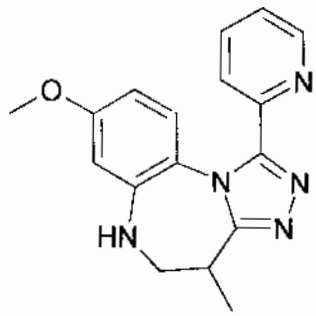
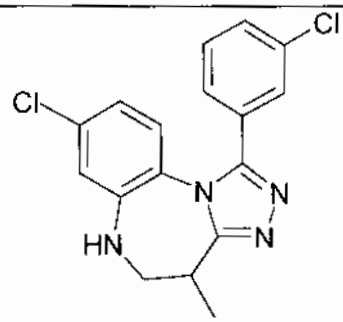
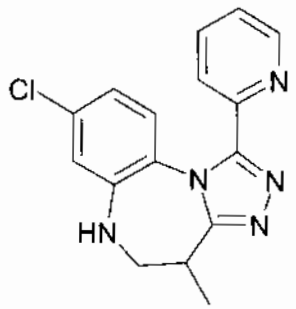
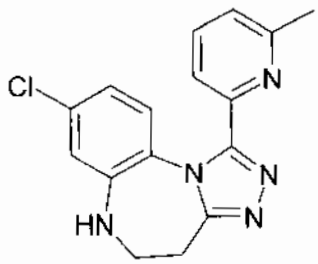
"A4"	 (+)-(S)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A5"	 (R,S)-8-Methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A6"	 (R,S)-8-Methoxy-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A7"	 1-(6-Methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

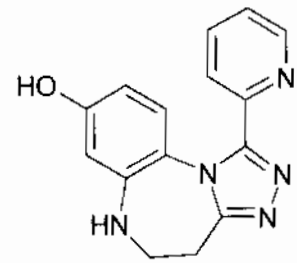
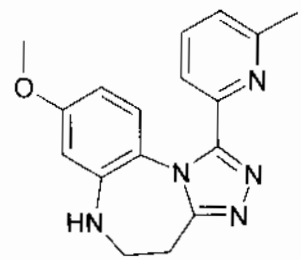
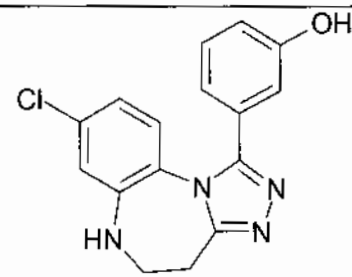
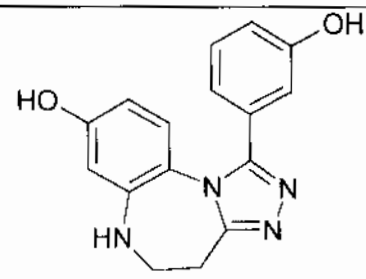
"A8"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A9"	 (R,S)-1-(5-Chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A10"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A11"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethylphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

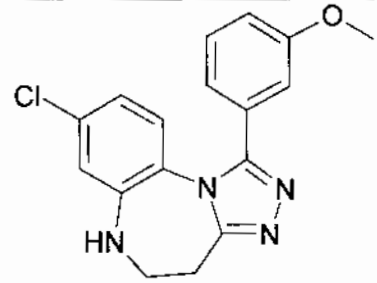
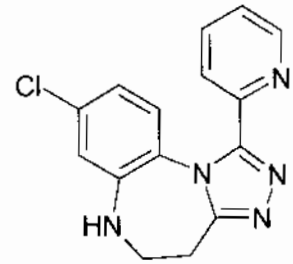
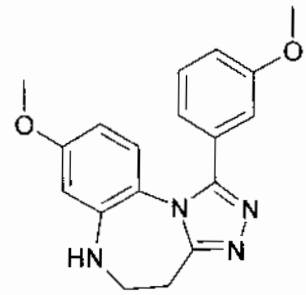
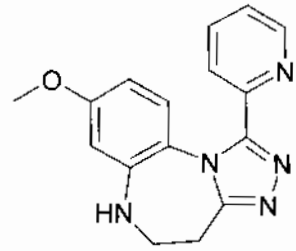
"A12"	 (R,S)-1-(3-Bromophenyl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[e]azulene
"A13"	 1-(2-Chloropyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A14"	 (R,S)-8-Chloro-1-(2,5-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

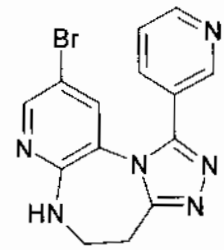
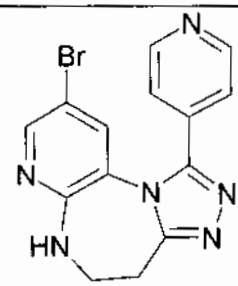
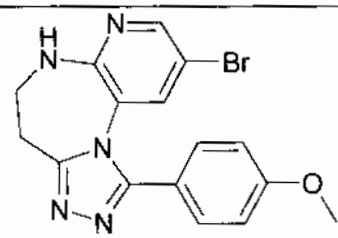
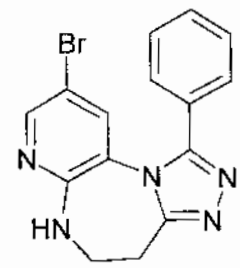
"A15"	 (-)-(R)-8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A16"	 (R,S)-8-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A17"	 (R,S)-1-[8-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulen-6-yl]ethanon

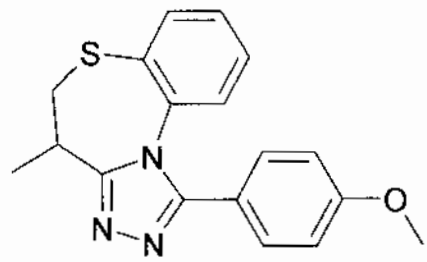
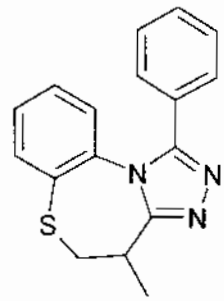
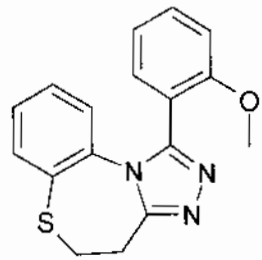
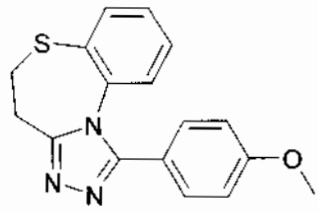
"A18"	 (R,S)-4-Methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A19"	 (R,S)-1-(3-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A20"	 (R,S)-1-(3-Chlorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

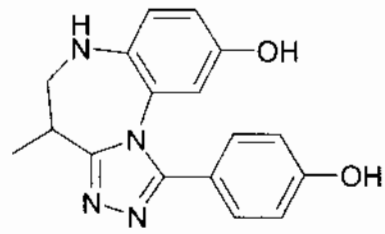
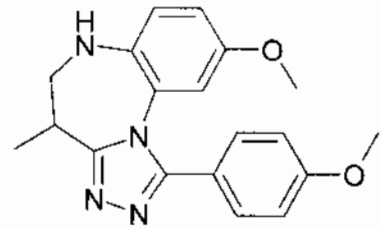
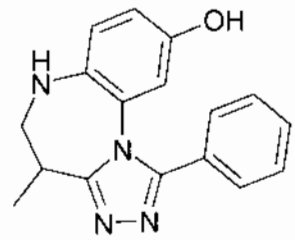
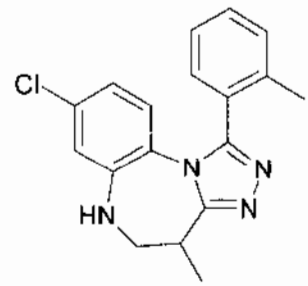
"A21"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A22"	 (R,S)-8-Chloro-1-(3-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A23"	 (R,S)-8-Chloro-4-methyl-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A24"	 8-Chloro-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

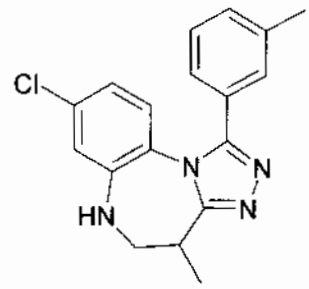
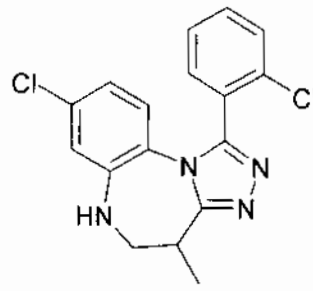
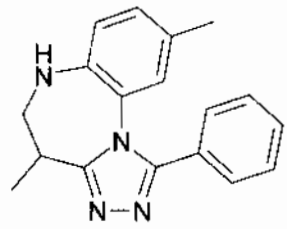
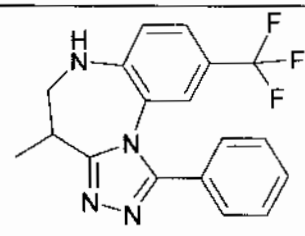
"A25"	 1-Pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol
"A26"	 8-Methoxy-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A27"	 3-(8-Chloro-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)-phenol
"A28"	 1-(3-Hydroxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

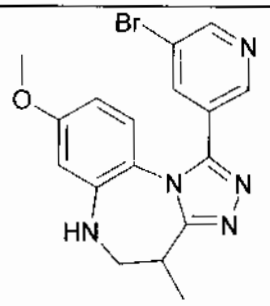
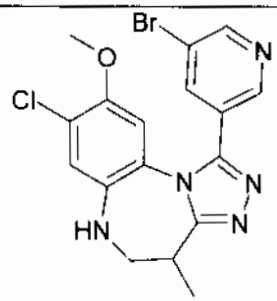
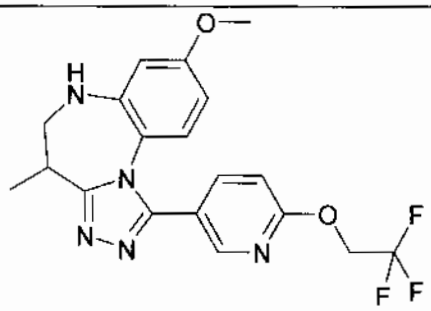
"A29"	 8-Chloro-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A30"	 8-Chloro-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A31"	 8-Methoxy-1-(3-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A32"	 8-Methoxy-1-pyridin-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene

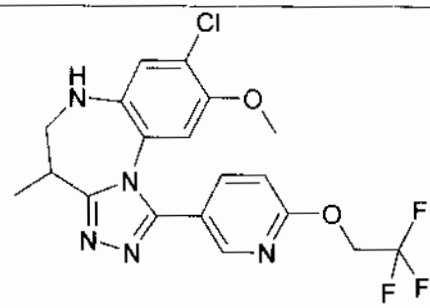
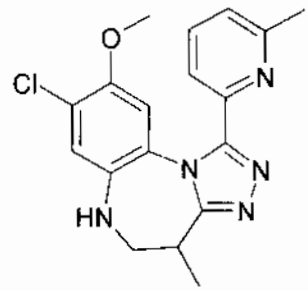
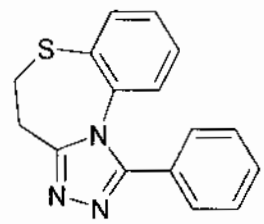
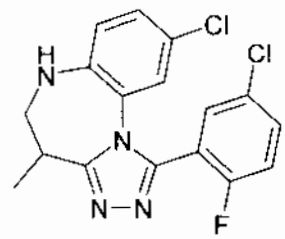
"A33"	 9-Bromo-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A34"	 9-Bromo-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene
"A35"	 9-Bromo-1-(4-methoxyphenyl)-5,6-dihydro-4*H*-2,3,6,7,10b-pentaazabenzo[*e*]azulene
"A36"	 9-Bromo-1-phenyl-5,6-dihydro-4*H*-2,3,6,7,10b-pentaaza-benzo[*e*]azulene

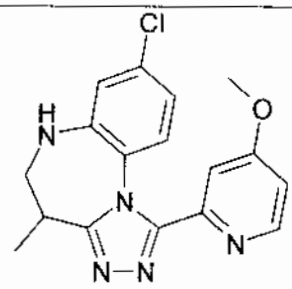
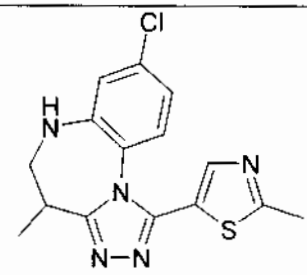
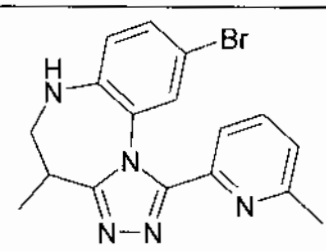
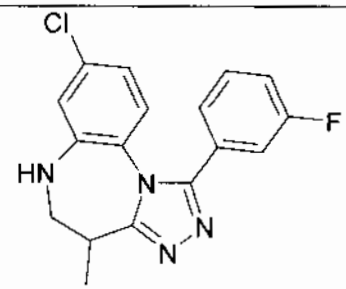
"A37"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A38"	 (R,S)-4-Methyl-1-phenyl-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A39"	 1-(2-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene
"A40"	 1-(4-Methoxyphenyl)-4,5-dihydro-6-thia-2,3,10b-triaza-benzo[*e*]azulene

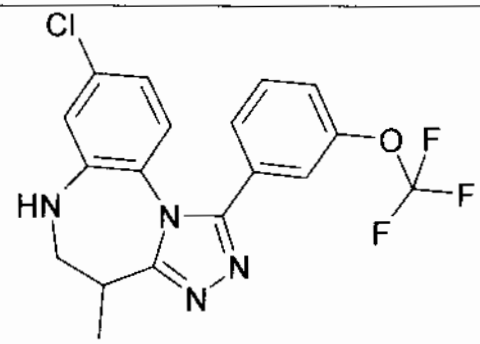
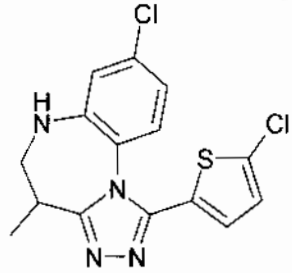
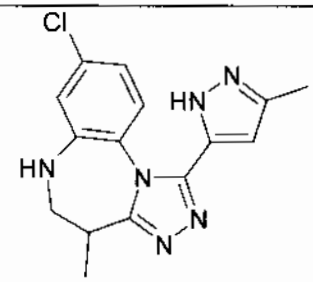
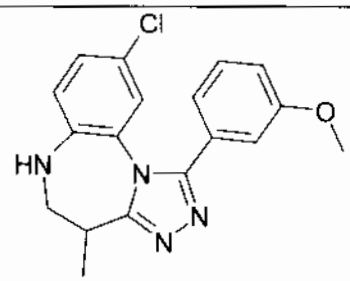
"A41"	 (R,S)-1-(4-Hydroxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A42"	 (R,S)-9-Methoxy-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A43"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-9-ol
"A44"	 (R,S)-8-Chloro-4-methyl-1-*o*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

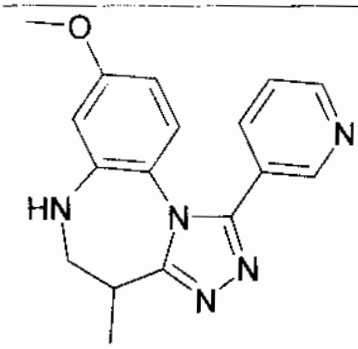
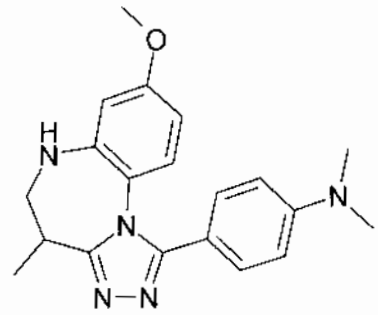
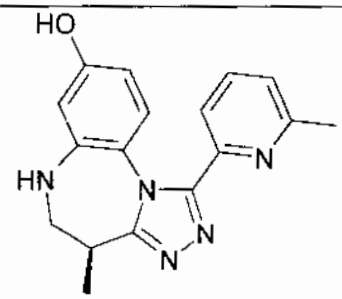
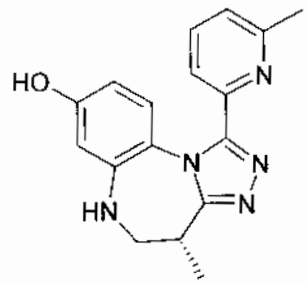
"A45"	 (R,S)-8-Chloro-4-methyl-1-*m*-tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A46"	 (R,S)-8-Chloro-1-(2-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A47"	 (R,S)-4,9-Dimethyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A48"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

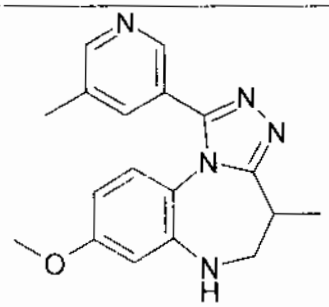
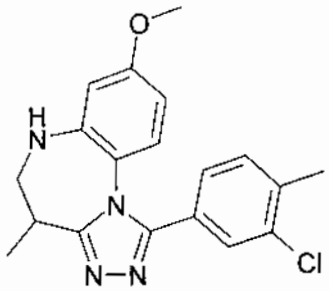
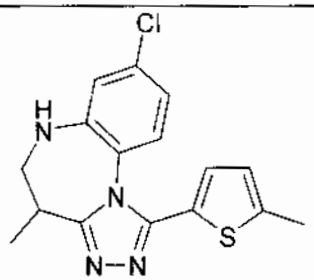
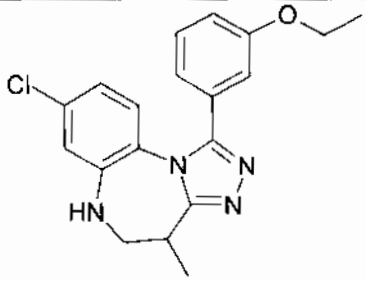
"A49"	 (R,S)-4-Methyl-1-phenyl-9-trifluoromethyl-4,5-dihydro-2,3,6,10b-tetraazabenzo[*e*]azulene-6-carbaldehyde
"A50"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A51"	 (R,S)-1-(5-Bromopyridin-3-yl)-8-chloro-9-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A52"	 (R,S)-8-Methoxy-4-methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3.6,10b-tetraazabenzo[*e*]azulene

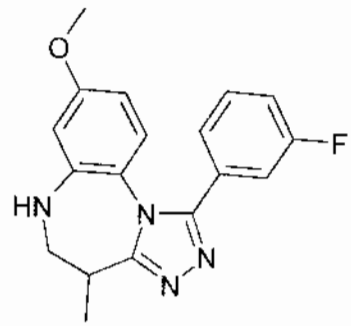
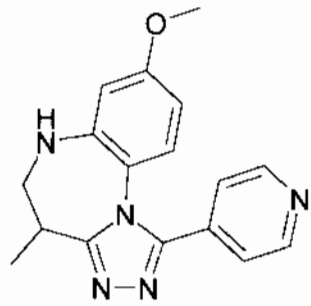
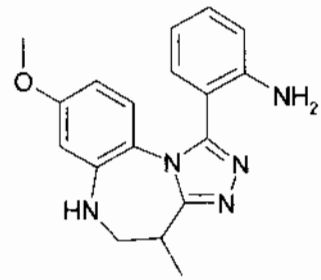
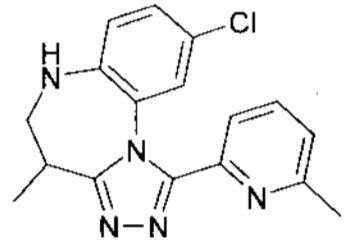
"A53"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-[6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A54"	 (R,S)-8-Chloro-9-methoxy-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A55"	 1-Phenyl-4,5-dihydro-6-thia-2,3,10b-triazabenzo[*e*]azulene
"A56"	 (R,S)-9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

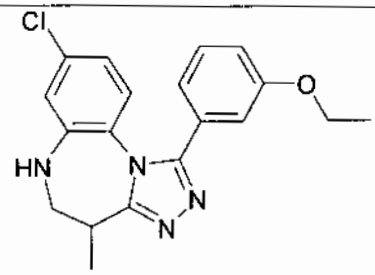
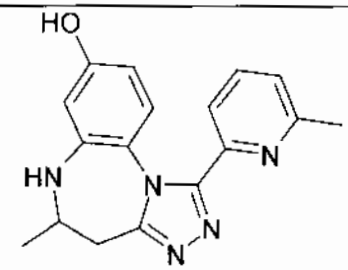
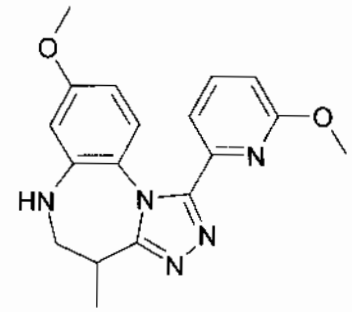
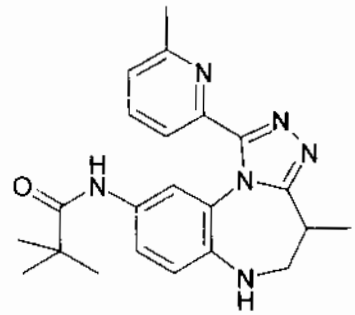
"A57"	 (R,S)-8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulenee
"A58"	 (R,S)-8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A59"	 (R,S)-9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A60"	 (R,S)-8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

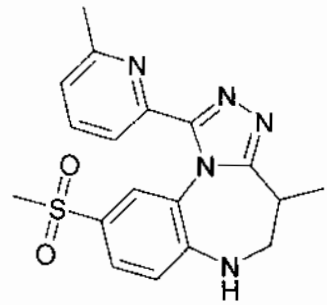
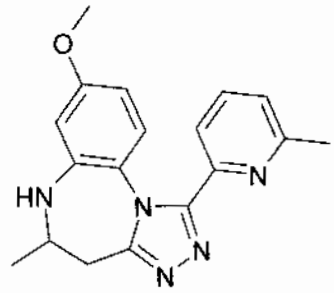
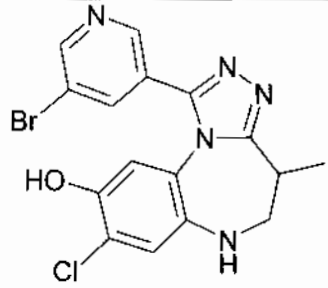
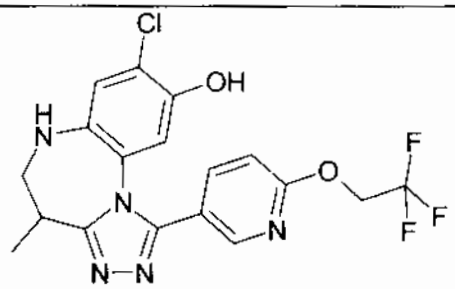
"A61"	 (R,S)-8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A62"	 (R,S)-8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A63"	 (R,S)-8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A64"	 (R,S)-9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene trifluoroacetate

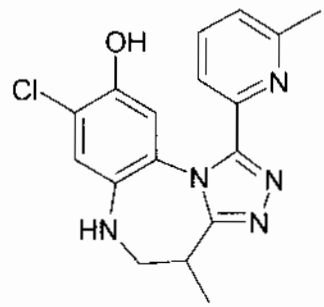
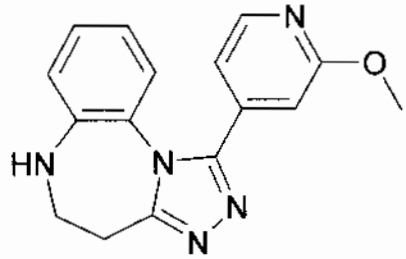
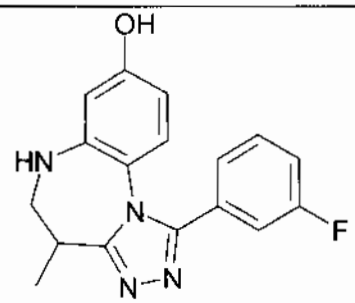
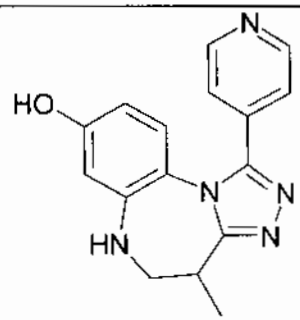
"A65"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A66"	 (R,S)-[4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)-phenyl]dimethylamine
"A67"	 (S)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A68"	 (R)-4-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol

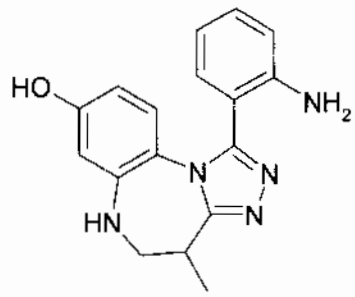
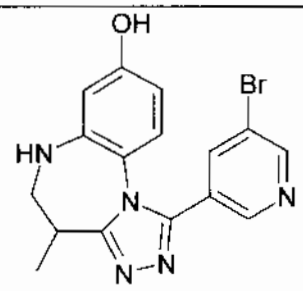
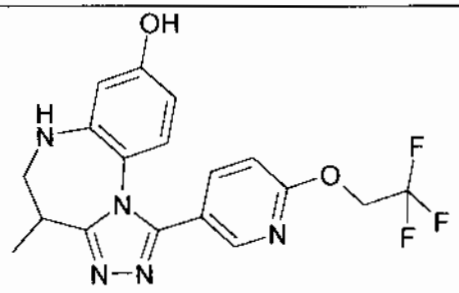
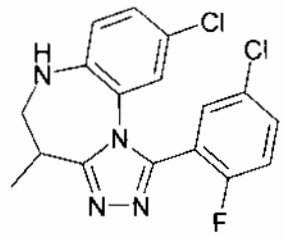
"A69"	 (R,S)-8-Methoxy-4-methyl-1-(5-methylpyridin-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A70"	 (R,S)-1-(3-Chloro-4-methylphenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A71"	 (R,S)-8-Chloro-4-methyl-1-(5-methylthiophen-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A72"	 (R,S)-8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

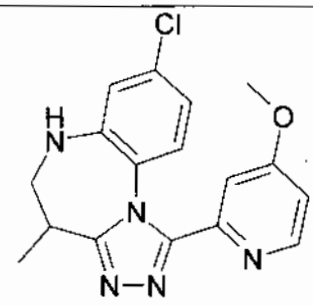
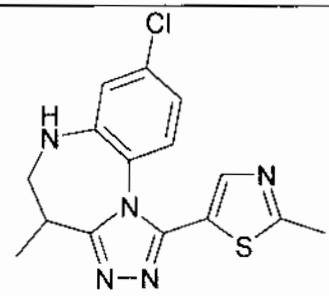
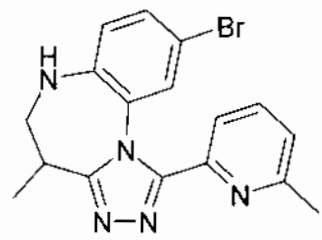
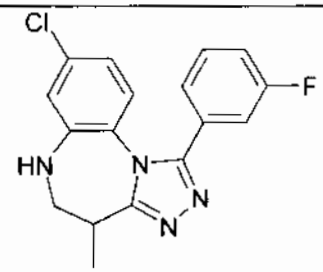
"A73"	 (R,S)-1-(3-Fluorophenyl)-8-methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A74"	 (R,S)-8-Methoxy-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A75"	 (R,S)-2-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-1-yl)phenylamine
"A76"	 (R,S)-9-Chloro-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene bistrifluoroacetate

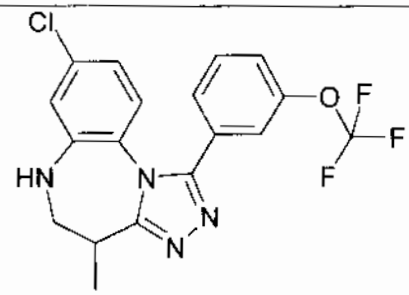
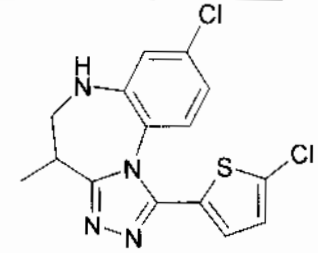
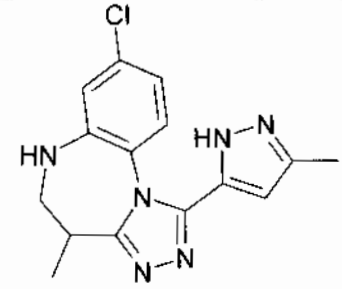
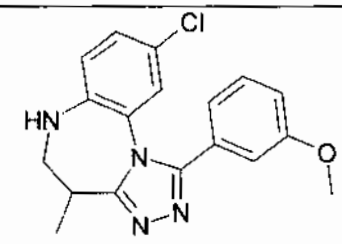
"A77"	 8-Chloro-1-(3-ethoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A78"	 5-Methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A79"	 8-Methoxy-1-(6-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A80"	 2,2-Dimethyl-N-[4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-yl]propion-amide

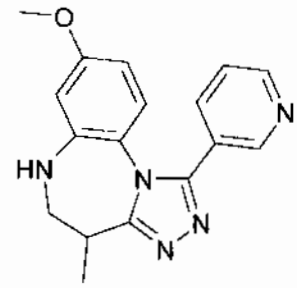
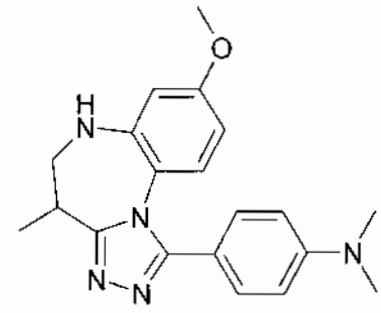
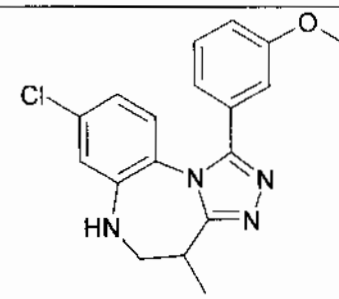
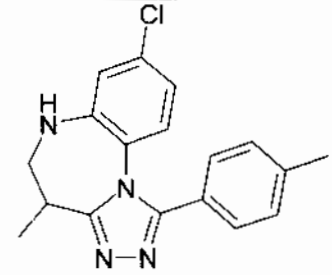
"A81"	 9-Methanesulfonyl-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A82"	 8-Methoxy-5-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A83"	 1-(5-Bromopyridin-3-yl)-8-chloro-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol
"A84"	 8-Chloro-4-methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-9-ol

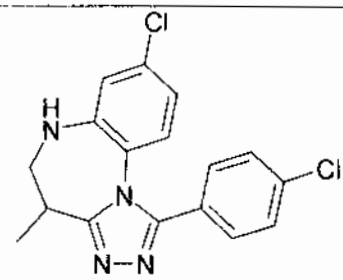
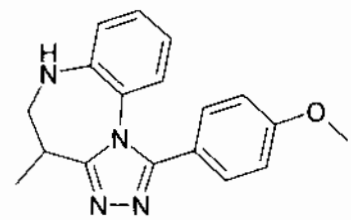
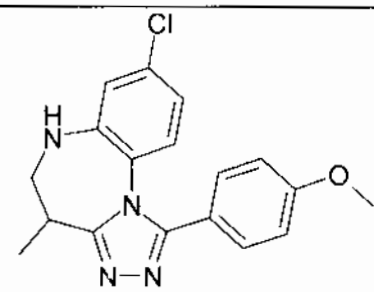
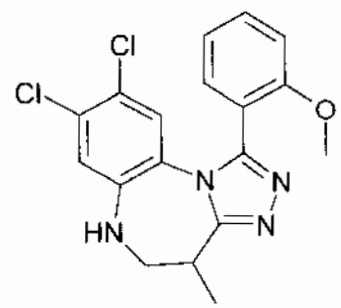
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"A86"	 1-(2-Methoxypyridin-4-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"A87"	 1-(3-Fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A88"	 4-Methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-8-ol

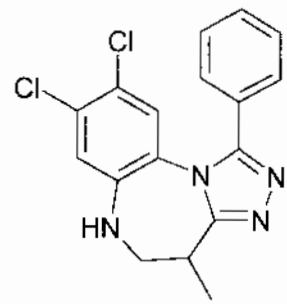
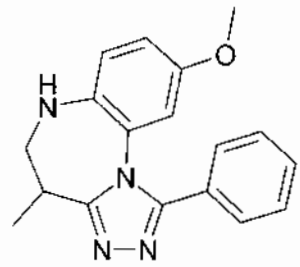
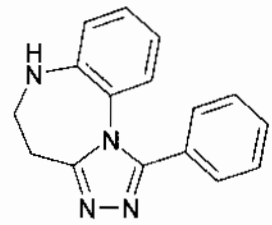
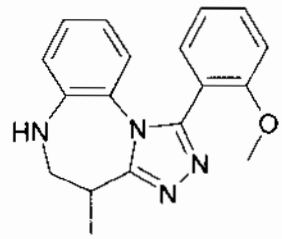
"A89"	 1-(2-Aminophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A90"	 1-(5-Bromopyridin-3-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A91"	 4-Methyl-1-[6-(2,2,2-trifluoroethoxy)-pyridin-3-yl]-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulen-8-ol
"A92"	 9-Chloro-1-(5-chloro-2-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

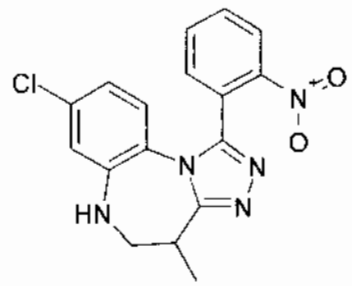
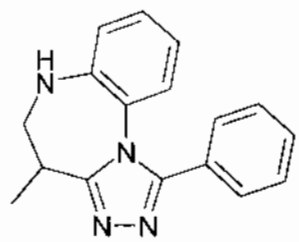
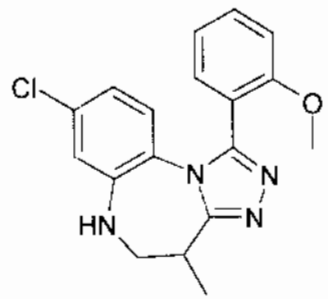
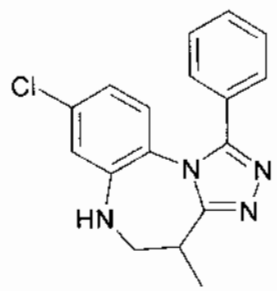
"A93"	 8-Chloro-1-(4-methoxypyridin-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A94"	 8-Chloro-4-methyl-1-(2-methylthiazol-5-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A95"	 9-Bromo-4-methyl-1-(6-methylpyridin-2-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A96"	 8-Chloro-1-(3-fluorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

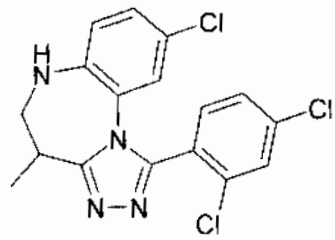
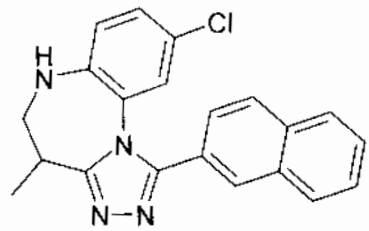
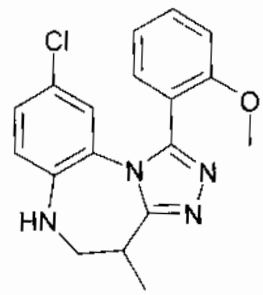
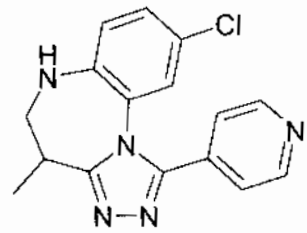
"A97"	 8-Chloro-4-methyl-1-(3-trifluoromethoxyphenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A98"	 8-Chloro-1-(5-chlorothiophen-2-yl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A99"	 8-Chloro-4-methyl-1-(5-methyl-2H-pyrazol-3-yl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A100"	 9-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

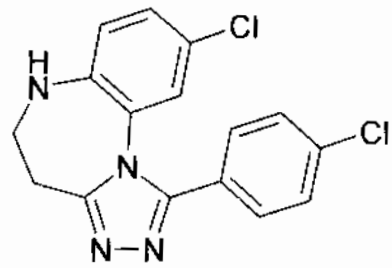
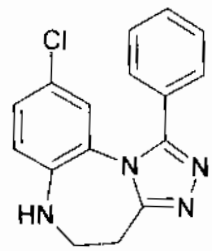
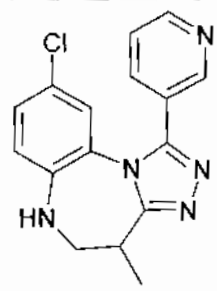
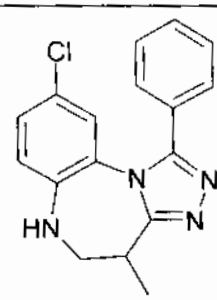
"A101"	 8-Methoxy-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"A102"	 [4-(8-Methoxy-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulen-1-yl)-phenyl]dimethylamine
"B1"	 (R,S)-8-Chloro-1-(3-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B2"	 (R,S)-8-Chloro-4-methyl-1-*p*tolyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B3"	 (R,S)-8-Chloro-1-(4-chlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B4"	 (R,S)-1-(4-Methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B5"	 (R,S)-8-Chloro-1-(4-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B6"	 (R,S)-8,9-Dichloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B7"	 (R,S)-8,9-Dichloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B8"	 (R,S)-9-Methoxy-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B9"	 1-Phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B10"	 (R,S)-1-(2-Methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B11"	 (R,S)-8-Chloro-4-methyl-1-(2-nitrophenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B12"	 (R,S)-4-Methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"B13"	 (R,S)-8-Chloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B14"	 (R,S)-8-Chloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B15"	 (R,S)-9-Chloro-1-(2,4-dichlorophenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B16"	 (R,S)-9-Chloro-4-methyl-1-naphthalen-2-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B17"	 (R,S)-9-Chloro-1-(2-methoxyphenyl)-4-methyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B18"	 (R,S)-9-Chloro-4-methyl-1-pyridin-4-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

"B19"	 9-Chloro-1-(4-chlorophenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B20"	 9-Chloro-1-phenyl)-5,6-dihydro-4*H*-2,3,6,10b-tetraaza-benzo[*e*]azulene
"B21"	 (R,S)-9-Chloro-4-methyl-1-pyridin-3-yl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene
"B22"	 (R,S)-9-Chloro-4-methyl-1-phenyl-5,6-dihydro-4*H*-2,3,6,10b-tetraazabenzo[*e*]azulene

and pharmaceutically usable derivatives, salts, solvates, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or combating of cancer, tumour growth, metastatic growth, fibrosis, restenosis, HIV infection, Alzheimer's, atherosclerosis, and/or for promoting wound healing.

4. Use according to Claim 3, where the tumour is selected from the group of tumours of the squamous epithelium, the bladder, the stomach, the kidneys, of head and neck, the oesophagus, the cervix, the thyroid, the intestine, the liver, the brain, the prostate, the urogenital tract, the lymphatic system, the stomach, the larynx, the lung, lung adenocarcinoma, small-cell lung carcinoma, pancreatic cancer, glioblastoma, colon carcinoma, breast carcinoma, tumour of the blood and immune system, acute myeloid leukaemia, chronic myeloid leukaemia, acute lymphatic leukaemia, chronic lymphatic leukaemia.

5. Use of compounds according to Claim 3 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of solid tumours, where a therapeutically effective amount of a compound according to Claim 3 is administered in combination with a compound from the group 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitor, 7) HMG-CoA reductase inhibitor, 8) HIV protease inhibitor, 9) reverse transcriptase inhibitor and 10) further angiogenesis inhibitor.

6. Use of compounds according to Claim 3 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of solid tumours, where a therapeutically effective amount of a compound according to Claim 3 is administered

in combination with radiotherapy and a compound from the group 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitor, 7) HMG-CoA reductase inhibitor, 8) HIV protease inhibitor, 9) reverse transcriptase inhibitor and 10) further angiogenesis inhibitor.