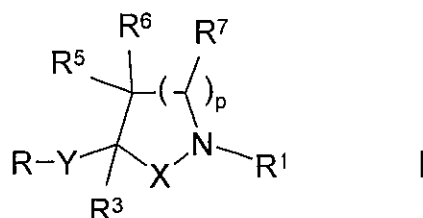


Cyclic amides as MetAP-2 inhibitors

The invention relates to compounds of the formula I

5



10 in which

R denotes NR^2R^4 , Alk, $\text{C}(\text{=CH}_2)[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, Het², $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$ or OA,

X denotes CO or CH_2 ,

Y denotes CO or CH_2 ,

15

R¹ denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $(\text{CH}_2)_n\text{Het}$, $(\text{CH}_2)_n\text{Cyc}$, $[\text{C}(\text{R}^4)_2]_n\text{COOH}$, $[\text{C}(\text{R}^4)_2]_n\text{CONHAr}^1$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}_2$, $[\text{C}(\text{R}^4)_2]_n\text{NHA}$, $[\text{C}(\text{R}^4)_2]_n\text{NA}_2$, $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{OR}^7$, $[\text{C}(\text{R}^4)_2]_n\text{COO}(\text{CH}_2)_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{-COOA}$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}[\text{C}(\text{R}^4)_2]_p\text{CON}(\text{R}^4)_2$ or $[\text{C}(\text{R}^4)_2]_n\text{CONHCR}^4\text{-}[(\text{CH}_2)_n\text{N}(\text{R}^4)_2]\text{CON}(\text{R}^4)_2$,

20

R² denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, $(\text{CH}_2)_n\text{COHet}^1$, $(\text{CH}_2)_n\text{COAr}^2$, $(\text{CH}_2)_m\text{NA}_2$ or $(\text{CH}_2)_n\text{Het}$,

R³ denotes OH or OCOA,

25

R⁴ denotes H or alkyl having 1, 2, 3 or 4 C atoms,

R² and R⁴ together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by $\text{N}(\text{CH}_2)_m\text{OH}$ or SO_2 ,

R⁵, R⁶ each, independently of one another, denote H, F or A,

30

R⁵ and R⁶ together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by NCOA or O,

R⁷ denotes H or A,

Ar¹ denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, OH, OA, CONH_2 , CONHA, CONA_2 , NHSO_2A , CONHCyc , NHSO_2Cyc , CONHAr^2 , COHet^1 and/or NASO_2A ,

35

- Ar² denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, CONH₂, and/or OAr³,
- Ar³ denotes phenyl which is unsubstituted or monosubstituted by NH₂,
- 5 Het denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, and/or O and/or S atoms which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OA, CN, NH₂, NHA, NA₂, NO₂, CN, COOH, COOA, (CH₂)_nCONH₂, (CH₂)_nCONHA, (CH₂)_nCONA₂, NHCOA, COA, CHO, Het¹, SO₂A, SO₂NH₂, SO₂NHA, SO₂NA₂, CONHNNH₂, CONHAr³, =O and/or Ar³,
- 10 Het¹ denotes a monocyclic saturated heterocycle having 1 to 4 N, and/or O and/or S atoms which is unsubstituted or mono-, di- or trisubstituted by =O and/or COOA,
- 15 Het² denotes isoindolyl,
- A denotes unbranched or branched alkyl having 1-10 C atoms, in which 1-7 H atoms may be replaced by F, Cl, Br, OH, CHO, COA, COOA, CN, CONA₂, CONHA and/or CONH₂, and/or in which one or two non-adjacent CH and/or CH₂ groups may be replaced by O,
- 20 or Cyc,
- Alk denotes alkenyl having 2, 3, 4, 5 or 6 C atoms
- Cyc denotes cyclic alkyl having 3-7 C atoms which is unsubstituted or
- 25 mono-, di- or trisubstituted by NHCOA, NHSO₂, OH, OA, A, NH₂, NHA, NA₂, COOA, COOH and/or CONHA,
- Hal denotes F, Cl, Br or I,
- m denotes 1, 2, 3 or 4,
- 30 n denotes 0, 1, 2, 3 or 4,
- p denotes 1, 2 or 3,
- and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

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

5 It has been found that the compounds of the formula I and salts thereof have very valuable pharmacological properties while being well tolerated.

10 In particular, they exhibit a regulatory, modulatory and/or inhibiting action on metal proteases, preferably on methionine aminopeptidase (MetAP), particularly on the sub-type MetAP-2.

15 They can be used as medicaments against cancer, but also as medicaments which positively influence fat metabolism, but also as medicaments against inflammation.

20 It has been found that the S enantiomer of the compounds according to the invention is significantly more active against MetAP-2 than the mirror image (R enantiomer).

Other hydroxyl-substituted pyrrolidinones are known from:
Zeitschrift für Naturforschung, B: Chemical Sciences (1994), 49(11), 1586-95;
Analytica Chimica Acta (1987), 202, 167-74;
25 Journal of Electroanalytical Chemistry and Interfacial Electrochemistry (1988), 239(1-2), 161-73;
Zeitschrift fuer Naturfor.Part B: Anorg. Chem. Org. Chem (1978), 33B(12), 1540-6;
J. Chem. Soc. (1965), (Oct.), 5556-62;
30 J. Chem. Soc. (1965), (Oct.), 5551-6.

The development of MetAP-2 inhibitors in the treatment of cancer is described by S.-Q. Yin et al. in Current Medicinal Chemistry, 2012, 19, 1021-1035.

35 WO 01/79157 describes substituted hydrazides and N-alkoxyamides which have MetAP-2 inhibitory activity and can be used for the inhibition of angio-

genesis, in particular for the treatment of diseases, such as, for example, cancer, whose development is dependent on angiogenesis.

WO 02/081415 describes MetAP-2 inhibitors which can be used for the treatment of cancer, haemangioma, proliferative retinopathy, rheumatoid arthritis, atherosclerotic neovascularisation, psoriasis, ocular neovascularisation and obesity.

WO 2008/011114 describes compounds as angiogenesis inhibitors and MetAP-2 inhibitors which can be used for the treatment of lymphoid leukaemia and lymphoma.

The action of the compounds according to the invention against cancer lies in particular in their action against angiogenesis. Angiogenesis inhibition has proven helpful in more than 70 diseases, such as, for example, ovarian cancer (F. Spinella et al. J. Cardiovasc. Pharmacol. 2004, 44, S140), breast cancer (A. Morabito et al. Crit. Rev. Oncol./Hematol. 2004, 49, 91), prostate cancer (B. Nicholson et al. Cancer Metastas. Rev. 2001, 20, 297), diabetic blindness, psoriasis and macular degeneration (E. Ng et al. Can. J. Ophthalmol. 2005, 23, 3706).

Proteases regulate many different cell processes, particularly the modulation of peptides and proteins, particularly protein conversion, protein ripening and signal peptide processing, the breakdown of abnormal proteins and the deactivation/activation of regulatory proteins. In particular, the amino-terminal modification of nascent polypeptides represents the most frequent modulation.

Aminoproteases are metalloproteases which cleave off amino acids from the unprotected N terminus of peptides or proteins, which can be carried out in either a co- or post-translatory manner.

Methionine aminopeptidase (MetAP) cleaves terminal methionine of nascent peptides in particular if the penultimate amino acid is small and uncharged (for example Gly, Ala, Ser, Thr, Val, Pro or Cys).

In many disease processes, angiogenesis is either causally at the centre of the disease or has a worsening effect on the progression of the disease. In cancer events, for example, angiogenesis results in the tumour increasing in size and being able to enter other organs. Other diseases in which angiogenesis plays an important role are psoriasis, arthrosis, arteriosclerosis and eye diseases, such as diabetic retinopathy, age-induced macular degeneration, rubeosis iridis or neovascular glaucoma, furthermore in inflammations. The compounds of the formula I on which this invention is based, compositions which comprise these compounds, and the processes described can thus be employed for the treatment of these diseases.

Accordingly, the compounds according to the invention or a pharmaceutically acceptable salt thereof are administered for the treatment of cancer, including solid carcinomas, such as, for example, carcinomas (of the lungs, pancreas, thyroid, bladder or colon), myeloid diseases (for example myeloid leukaemia) or adenomas (for example villous colon adenoma).

The tumours furthermore include monocytic leukaemia, brain, urogenital, lymphatic system, stomach, laryngeal and lung carcinoma, including lung adenocarcinoma and small-cell lung carcinoma, pancreatic and/or breast carcinoma.

The present invention therefore relates to compounds according to the invention as medicaments and/or medicament active compounds 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 and to a process 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.

It can be shown that the compounds according to the invention have an anti-carcinogenic action. The compounds according to the invention are administered to a patient having a disease, for example to inhibit tumour growth, to reduce inflammation associated with a lymphoproliferative disease, to inhibit

transplant rejection or neurological damage due to tissue repair, etc. The present compounds are suitable for prophylactic or therapeutic purposes. As used herein, the term "treatment" is used to refer to both the prevention of diseases and the treatment of pre-existing conditions. The prevention of proliferation/vitality is achieved by administration of the compounds according to the invention prior to the development of overt disease, for example for preventing tumour growth. Alternatively, the compounds are used for the treatment of ongoing diseases by stabilising or improving the clinical symptoms of the patient.

5

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 a human disease.

10

The susceptibility of a particular cell to treatment with the compounds according to the invention can be determined by in vitro testing. Typically, a culture of the cell is incubated 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 cell proliferation, cell vitality or migration, usually between about one hour and one week. In vitro testing can be carried out using cultivated cells from a biopsy sample. The amount of cells remaining after the treatment are then determined.

20

25

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.

30

35

5 It has been found that the compounds according to the invention cause specific inhibition of MetAP-2. The compounds according to the invention preferably exhibit an advantageous biological activity which can be detected in the tests described, for example, herein. In such tests, the compounds according to the invention exhibit and cause an inhibiting effect, which is usually documented by IC₅₀ values in a suitable range, preferably in the micromolar range and more preferably in the nanomolar range.

10 In addition, the compounds according to the invention can be used to achieve additive or synergistic effects in certain existing cancer chemotherapies and radiotherapies and/or to restore the efficacy of certain existing cancer chemotherapies and radiotherapies.

15 The compounds according to the invention can also be used for the treatment of obesity. Henri R. Lijnen et al. in Obesity, Vol.18 no.12, 2241-2246 (2010) describes the use of fumagillin, an Met-AP2 inhibitor, in the reduction of adipose tissue.

20 The use of Met-AP2 inhibitors (compounds of the fumagillin type) for the treatment of obesity is also described in WO 2011/085201 A1.

25 The compounds according to the invention can also be used for the treatment of malaria. X. Chem et al. in Chemistry & Biology, Vol.16, 193-202 (2009) describes the use of fumagillin, an Met-AP2 inhibitor, for the treatment of malaria.

30 The compounds according to the invention can also be used for the treatment of benign prostate hypertrophy.

The use of Met-AP2 inhibitors (compounds of the fumagillin type) for the treatment of benign prostate hypertrophy is described in WO 2011/085198 A1.

35 Compounds of the formula I are also taken to mean the hydrates and solvates of these compounds, furthermore pharmaceutically usable derivatives.

5 The invention also relates to the optically active forms (stereoisomers), salts, 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.

10 The invention naturally also encompasses the solvates of the salts of the compounds of the formula I, such as, for example, the hydrochloride hydrate Pharmaceutically usable derivatives are taken to mean, for example, the salts of the compounds according to the invention and also so-called prodrug compounds.

15 Prodrug derivatives are taken to mean compounds of the formula I 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.

20 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).

25 The expression "effective amount" denotes the amount of a medicament or of a pharmaceutical active compound 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.

30 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, condition or disorder.

35 The expression "therapeutically effective amount" also encompasses the amounts which are effective for increasing normal physiological function.

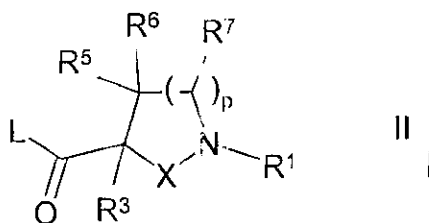
The invention also relates to the use of mixtures of the compounds of the formula I, for example mixtures of two diastereomers, for example in the ratio 1:1, 1:2, 1:3, 1:4, 1:5, 1:10, 1:100 or 1:1000.

These are particularly preferably mixtures of stereoisomeric compounds.

The invention relates to the compounds of the formula I and salts thereof and to a process for the preparation of compounds of the formula I and pharmaceutically usable salts, tautomers and stereoisomers thereof, characterised in that

a) for the preparation of compounds of the formula I in which Y denotes CO and R denotes NR^2R^4 ,

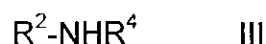
a compound of the formula II



in which X, R^1 , R^3 , R^5 , R^6 , R^7 and p have the meanings indicated in Claim 1,

and L denotes Cl, Br, I or a free or reactively functionally modified OH group,

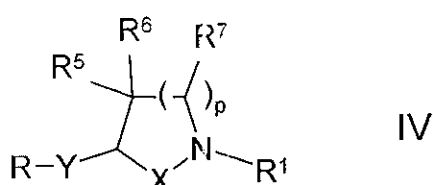
is reacted with a compound of the formula III



in which R^2 and R^4 have the meanings indicated in Claim 1,

or

b) a compound of the formula IV



10 in which R¹, R⁵, R⁶, R⁷, R, X, Y and p have the meanings indicated in Claim 1,

15 is oxidised,

or

20 c) for the preparation of compounds of the formula I in which X and Y denote CH₂,

a compound of the formula I in which X and Y denote CO,

25 is reduced,

and/or a base or acid of the formula I is converted into one of its salts.

30 Above and below, the radicals R¹, R³, R⁵, R⁶, R⁷, R, X, Y and p have the meanings indicated in the case of the formula I, unless expressly indicated otherwise.

A denotes alkyl, is unbranched (linear) or branched, and has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 C atoms. A preferably denotes methyl, furthermore ethyl, propyl, iso-
 35 propyl, butyl, isobutyl, sec-butyl or tert-butyl, furthermore also pentyl, 1-, 2- or 3-methylbutyl, 1,1-, 1,2- or 2,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1-, 2-, 3- or

- 4-methylpentyl, 1,1-, 1,2-, 1,3-,
2,2-, 2,3- or 3,3-dimethylbutyl, 1- or 2-ethylbutyl, 1-ethyl-1-methylpropyl, 1-ethyl-
2-methylpropyl, 1,1,2- or 1,2,2-trimethylpropyl, further preferably, for example,
trifluoromethyl.
- 5 A preferably denotes unbranched or branched alkyl having 1-6 C atoms, in
which 1-7 H atoms may be replaced by F and/or Cl,
and/or in which one or two non-adjacent CH and/or CH₂ groups may be
replaced by O.
- 10 A very particularly preferably denotes alkyl having 1, 2, 3, 4, 5 or 6 C atoms,
preferably methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl,
pentyl, hexyl, trifluoromethyl, pentafluoroethyl or 1,1,1-trifluoroethyl.
- 15 Cyclic alkyl preferably denotes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or
cycloheptyl.
- R preferably denotes NR²R⁴, furthermore Alk, C(=CH₂)[C(R⁴)₂]_nAr² or Het².
R particularly preferably denotes NR²R⁴, very particularly preferably
20 NHCH₂Ar².
- X preferably denotes CO, furthermore CH₂.
Y preferably denotes CO, furthermore CH₂.
- 25 R¹ preferably denotes [C(R⁴)₂]_nAr¹, (CH₂)_nHet or (CH₂)_nCyc, furthermore
[C(R⁴)₂]_nCOOH, [C(R⁴)₂]_nCONHAr¹, [C(R⁴)₂]_nCONH₂, [C(R⁴)₂]_nNHA or
[C(R⁴)₂]_nNA₂.
- 30 R⁴ preferably denotes H, methyl, ethyl or propyl, very particularly preferably H
or methyl.
- 35 Ar¹ denotes, for example, phenyl, o-, m- or p-fluorophenyl, o-, m- or p-bromo-
phenyl, o-, m- or p-chlorophenyl, o-, m- or p-hydroxyphenyl, o-, m- or p-
methoxyphenyl, o-, m- or p-aminocarbonylphenyl, further preferably 2,3-, 2,4-,
2,5-, 2,6-, 3,4- or 3,5-difluorophenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dichloro-

phenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dibromophenyl, 2,3,4-, 2,3,5-, 2,3,6-, 2,4,6- or 3,4,5-trichlorophenyl, p-iodophenyl, 4-fluoro-3-chlorophenyl, 2-fluoro-4-bromophenyl or 2,5-difluoro-4-bromophenyl.

5 Ar² denotes, for example, phenyl, o-, m- or p-tolyl, o-, m- or p-ethylphenyl, o-, m- or p-propylphenyl, o-, m- or p-isopropylphenyl, o-, m- or p-tert-butylphenyl, o-, m- or p-trifluoromethylphenyl, o-, m- or p-fluorophenyl, o-, m- or p-bromophenyl, o-, m- or p-chlorophenyl, o-, m- or p-aminocarbonylphenyl,
 10 further preferably 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-difluorophenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dichlorophenyl, 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dibromophenyl, 2,3,4-, 2,3,5-, 2,3,6-, 2,4,6- or 3,4,5-trichlorophenyl, p-iodophenyl, 4-fluoro-3-chlorophenyl, 2-fluoro-4-bromophenyl, 2,5-difluoro-4-bromophenyl or 2,5-dimethyl-4-chlorophenyl.

15 Ar² furthermore particularly preferably denotes phenyl which is mono- or disubstituted by Hal.

20 Irrespective of further substitutions, Het denotes, for example, 2- or 3-furyl, 2- or 3-thienyl, 1-, 2- or 3-pyrrolyl, 1-, 2, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, furthermore preferably 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -3- or 5-yl, 1- or 5-tetrazolyl, 1,2,3-oxadiazol-4- or
 25 -5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 3- or 4-pyridazinyl, pyrazinyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 4- or 5-isoindolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indazolyl, 1-, 3-, 4-, 5-, 6- or 7-benzopyrazolyl, 2-, 4-, 5-, 6- or 7-benzoxazolyl, 3-, 4-, 5-, 6- or 7- benzisoxazolyl, 2-, 4-, 5-, 6- or 7-benzothiazolyl, 2-, 4-, 5-, 6- or 7-benzisothiazolyl, 4-, 5-, 6- or 7-benz-2,1,3-oxadiazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 5- or 6-quinoxaliny, 2-, 3-, 5-, 6-, 7- or 8-2H-benzo-1,4-oxazinyl, further preferably 1,3-benzodioxol-5-yl, 1,4-benzodioxan-6-yl, 2,1,3-benzothiadiazol-4- or -5-yl or 2,1,3-benzoxadiazol-5-yl.

35 The heterocyclic radicals may also be partially or fully hydrogenated.

Unsubstituted Het can thus also denote, for example, 2,3-dihydro-2-, -3-, -4- or
 -5-furyl, 2,5-dihydro-2-, -3-, -4- or 5-furyl, tetrahydro-2- or -3-furyl, 1,3-dioxolan-4-
 yl, tetrahydro-2- or -3-thienyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 2,5-di-
 hydro-1-, -2-, -3-, -4- or -5-pyrrolyl, 1-, 2- or 3-pyrrolidinyl, tetrahydro-1-, -2- or -4-
 5 imidazolyl, 2,3-dihydro-1-, -2-, -3-, -4- or -5-pyrazolyl, tetrahydro-1-, -3- or -4-
 pyrazolyl, 1,4-dihydro-1-, -2-, -3- or -4-pyridyl, 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-,
 -5- or -6-pyridyl, 1-, 2-, 3- or 4-piperidinyl, 2-, 3- or 4-morpholinyl, tetrahydro-2-,
 -3- or -4-pyranyl, 1,4-dioxanyl, 1,3-dioxan-2-, -4- or -5-yl, hexahydro-1-, -3- or -4-
 10 pyridazinyl, hexahydro-1-, -2-, -4- or -5-pyrimidinyl, 1-, 2- or 3-piperazinyl,
 1,2,3,4-tetrahydro-1-, -2-, -3-, -4-, -5-, -6-, -7- or -8-quinolyl, 1,2,3,4-tetrahydro-1-,
 -2-, -3-, -4-, -5-, -6-, -7- or -8-isoquinolyl, 2-, 3-, 5-, 6-, 7- or 8- 3,4-dihydro-2H-
 benzo-1,4-oxazinyl, further preferably 2,3-methylenedioxyphenyl, 3,4-methylene-
 15 dioxypheyl, 2,3-ethylenedioxyphenyl, 3,4-ethylenedioxyphenyl, 3,4-(difluoro-
 methylenedioxy)phenyl, 2,3-dihydrobenzofuran-5- or 6-yl, 2,3-(2-oxomethylene-
 dioxy)phenyl or also 3,4-dihydro-2H-1,5-benzodioxepin-6- or -7-yl, furthermore
 preferably 2,3-dihydrobenzofuranyl or 2,3-dihydro-2-oxofuranyl.

20 Het furthermore preferably denotes pyrazinyl, pyrazolyl, benzimidazolyl,
 pyridyl, indolyl, dihydroindolyl, benzofuranyl, tetrahydropyranyl, dihydro-
 quinolyl, dihydroisoquinolyl, tetrahydroquinolyl, tetrahydroisoquinolyl,
 indazolyl, imidazolyl, pyrrolyl, oxazolyl, oxadiazolyl, isoxazolyl, benzothiazolyl,
 25 piperidin-1-yl, pyrrolidin-1-yl, 3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl, 3,4-
 dihydro-2H-benzo-1,4-oxazinyl, benzofuranyl, azetidyl, 3-azabicyclo[3.2.0]-
 hexyl, pyrrolo[2,3-b]pyridinyl, tetrahydrofuranyl, tetrahydro-1,8-naphthyridinyl,
 2,3-dihydrobenzothiazolyl, 1,2,3,4-tetrahydrobenzothiazinyl or hexahydro-
 30 benzo-1,3-dioxolyl, each of which is unsubstituted or mono-, di- or trisubsti-
 tuted by Hal, A, OA, CN, NH₂, NHA, NA₂, NO₂, CN, COOH, COOA, (CH₂)_n-
 CONH₂, (CH₂)_nCONHA, (CH₂)_nCONA₂, NHCOA, COA, CHO, Het¹, SO₂A,
 SO₂NH₂, SO₂NHA, SO₂NA₂, CONHNH₂, CONHAr³, =O and/or Ar³.

35 Het¹ preferably denotes pyridazinyl, pyrazolyl, pyridyl, piperazinyl, morpholinyl,
 pyrimidinyl, furyl, thienyl, imidazolyl, pyrrolyl, oxazolyl, oxadiazolyl, isoxazolyl,

thiazolyl, triazolyl, tetrazolyl, thiadiazol, piperidin-1-yl, pyrrolidin-1-yl, tetra-
hydropyranyl, 1,2-oxazinan-2-yl, 1,2,5-oxadiazinan-2-yl, -1,3-oxazinan-3-yl or
hexahydropyrimidinyl, each of which is unsubstituted or mono-, di- or trisubsti-
tuted by A and/or OA.

5

Hal preferably denotes F, Cl or Br, but also I, particularly preferably F or Cl.

10

Throughout the invention, all radicals which occur more than once may be
identical or different, i.e. are independent of one another.

The compounds of the formula I may have one or more chiral centres and can
therefore occur in various stereoisomeric forms. The formula I encompasses
all these forms.

15

Accordingly, the invention relates, in particular, to the compounds of the for-
mula I in which at least one of the said radicals has one of the preferred
meanings indicated above. Some preferred groups of compounds may be
expressed by the following sub-formulae Ia to Ic, which conform to the formula
I and in which the radicals not designated in greater detail have the meaning
indicated for the formula I, but in which

20

25

in Ia Het denotes pyrazinyl, pyrazolyl, benzimidazolyl, pyridyl, indolyl,
dihydroindolyl, benzofuranyl, tetrahydropyranyl, dihydro-
quinolinyl, dihydroisoquinolinyl, tetrahydroquinolinyl, tetra-
hydroisoquinolinyl, indazolyl, imidazolyl, pyrrolyl, oxazolyl,
oxadiazolyl, isoxazolyl, benzothiazolyl, piperidin-1-yl,
pyrrolidin-1-yl, 3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl,
3,4-dihydro-2H-benzo-1,4-oxazinyl, benzofuranyl, azetid-
inyl, 3-azabicyclo[3.2.0]hexyl, pyrrolo[2,3-b]pyridinyl, tetra-
hydrofuranyl, tetrahydro-1,8-naphthyridinyl, 2,3-dihydro-
benzothiazolyl, 1,2,3,4-tetrahydrobenzothiazinyl or
hexahydrobenzo-1,3-dioxolyl, each of which is unsubsti-
tuted or mono-, di- or trisubstituted by Hal, A, OA, CN, NH₂,

35

30

NHA, NA_2 , NO_2 , CN, COOH, COOA, $(\text{CH}_2)_n\text{CONH}_2$, $(\text{CH}_2)_n\text{CONHA}$, $(\text{CH}_2)_n\text{CONA}_2$, NHCOA , COA , CHO , Het^1 , SO_2A , SO_2NH_2 , SO_2NHA , SO_2NA_2 , CONHNH_2 , CONHAr^3 , $=\text{O}$ and/or Ar^3 .

5

in lb Het¹ denotes pyridazinyl, pyrazolyl, pyridyl, piperazinyl, morpho-
linyl, pyrimidinyl, furyl, thienyl, imidazolyl, pyrrolyl, oxazolyl,
10 oxadiazolyl, isoxazolyl, thiazolyl, triazolyl, tetrazolyl, thia-
diazole, piperidin-1-yl, pyrrolidin-1-yl, tetrahydropyranyl, 1,2-
oxazinan-2-yl, 1,2,5-oxadiazinan-2-yl, 1,3-oxazinan-3-yl or
15 hexahydropyrimidinyl, each of which is unsubstituted or
mono-, di- or trisubstituted by A and/or OA;

in Ic R denotes NR^2R^4 , Alk, $\text{C}(=\text{CH}_2)[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, Het^2 , $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$ or OA,

X denotes CO or CH₂.

20 Y denotes CO or CH₂.

25 R^1 denotes H, $[C(R^4)_2]_nAr^1$, $(CH_2)_nHet$, $(CH_2)_nCyc$, $[C(R^4)_2]_nCOOH$, $[C(R^4)_2]_nCONHAr^1$, $[C(R^4)_2]_nCONH_2$, $[C(R^4)_2]_nNHA$, $[C(R^4)_2]_nNA_2$, $O[C(R^4)_2]_nAr^1$, $[C(R^4)_2]_nOR^7$, $[C(R^4)_2]_nCOO-(CH_2)_nAr^1$, $[C(R^4)_2]_nCOOA$, $[C(R^4)_2]_nCONH[C(R^4)_2]_pCON(R^4)_2$ or $[C(R^4)_2]_nCONHCR^4[(CH_2)_nN(R^4)_2]CON(R^4)_2$,

R^2 denotes H, $[C(R^4)_2]_nAr^2$, $(CH_2)_nCOHet^1$, $(CH_2)_nCOAr^2$, $(CH_2)_mNA_2$ or $(CH_2)_mHet$,

30 R^3 denotes OH or OCOA.

R⁴ denotes H or alkyl having 1, 2, 3 or 4 C atoms,

R² and R⁴ together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH₂ group may also be replaced by N(CH₂)_mOH or SO₂.

35 R^5, R^6 each, independently of one another, denote H or A,

- R^5 and R^6 together also denote alkylene having 2, 3, 4 or 5 C atoms,
 where a CH_2 group may also be replaced by NCOA or O,
- R^7 denotes H or A,
- 5 Ar^1 denotes phenyl which is unsubstituted or mono-, di-, tri-,
 tetra- or pentasubstituted by Hal, OH, OA, $CONH_2$,
 $CONHA$, $CONA_2$, $NHSO_2A$, $CONHCyc$, $NHSO_2Cyc$,
 $CONHAr^2$, $COHet^1$ and/or $NASO_2A$,
- 10 Ar^2 denotes phenyl which is unsubstituted or mono-, di-, tri-,
 tetra- or pentasubstituted by Hal, A, $CONH_2$, and/or OAr^3 ,
- Ar^3 denotes phenyl which is unsubstituted or monosubstituted
 by NH_2 ,
- 15 Het denotes pyrazinyl, pyrazolyl, benzimidazolyl, pyridyl, indolyl,
 dihydroindolyl, benzofuranyl, tetrahydropyranyl, dihydro-
 quinoliny, dihydroisoquinoliny, tetrahydroquinoliny, tetra-
 hydroisoquinoliny, indazolyl, imidazolyl, pyrrolyl, oxazolyl,
 oxadiazolyl, isoxazolyl, benzothiazolyl, piperidin-1-yl,
 20 pyrrolidin-1-yl, 3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl,
 3,4-dihydro-2H-benzo-1,4-oxazinyl, benzofuranyl, azetid-
 inyl, 3-azabicyclo[3.2.0]hexyl, pyrrolo[2,3-b]pyridinyl, tetra-
 hydrofuranyl, tetrahydro-1,8-naphthyridinyl, 2,3-dihydro-
 benzoisothiazolyl, 1,2,3,4-tetrahydrobenzothiazinyl or hexa-
 25 hydrobenzo-1,3-dioxolyl, each of which is unsubstituted or
 mono-, di- or trisubstituted by Hal, A, OA, CN, NH_2 , NHA,
 NA_2 , NO_2 , CN, COOH, COOA, $(CH_2)_nCONH_2$, $(CH_2)_n$ -
 $CONHA$, $(CH_2)_nCONA_2$, $NHCOA$, COA, CHO, Het^1 , SO_2A ,
 30 SO_2NH_2 , SO_2NHA , SO_2NA_2 , $CONHNNH_2$, $CONHAr^3$, =O
 and/or Ar^3 ,
- Het^1 denotes pyridazinyl, pyrazolyl, pyridyl, piperazinyl, morpho-
 liny, pyrimidinyl, furyl, thienyl, imidazolyl, pyrrolyl, oxazolyl,
 35 oxadiazolyl, isoxazolyl, thiazolyl, triazolyl, tetrazolyl, thia-
 diazole, piperidin-1-yl, pyrrolidin-1-yl, tetrahydropyranyl, 1,2-
 oxazinan-2-yl, 1,2,5-oxadiazinan-2-yl, 1,3-oxazinan-3-yl or

		hexahydropyrimidinyl, each of which is unsubstituted or mono-, di- or trisubstituted by A and/or OA,
	Het ²	denotes isoindolyl,
5	A	denotes unbranched or branched alkyl having 1-10 C atoms, in which 1-7 H atoms may be replaced by F, Cl, Br, OH, CHO, COA, COOA, CN, CONA ₂ , CONHA and/or CONH ₂ ,
10		and/or in which one or two non-adjacent CH and/or CH ₂ groups may be replaced by O, or Cyc,
	Alk	denotes alkenyl having 2, 3, 4, 5 or 6 C atoms
15	Cyc	denotes cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by NHCOA, NHSO ₂ , OH, OA, A, NH ₂ , NHA, NA ₂ , COOA, COOH and/or CONHA,
	Hal	denotes F, Cl, Br or I,
	m	denotes 1, 2, 3 or 4,
20	n	denotes 0, 1, 2, 3 or 4,
	p	denotes 1, 2 or 3;

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

25

The compounds of the formula I 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.

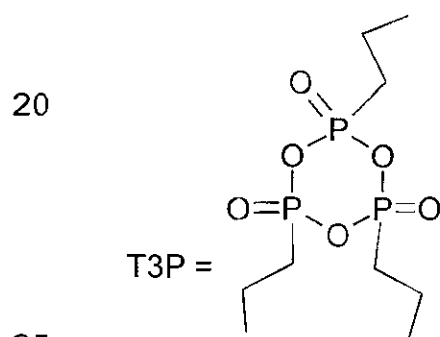
30

Compounds of the formula I can preferably be obtained by reacting compounds of the formula II with a compound of the formula III.

The compounds of the formula II and of the formula III are generally known. If they are novel, however, they can be prepared by methods known per se.

5 In the compounds of the formula II, L preferably denotes Cl, Br, I or a free or a reactively modified OH group, such as, for example, an activated ester, an imidazolidine or alkylsulfonyloxy having 1-6 C atoms (preferably methylsulfonyloxy or trifluoromethylsulfonyloxy) or arylsulfonyloxy having 6-10 C atoms (preferably phenyl- or p-tolylsulfonyloxy).

10 The reaction preferably succeeds in the presence of a dehydrating agent, such as, for example, a carbodiimide, such as N,N'-dicyclohexylcarbodiimide ("DCCI"), 1,1'-carbonyldiimidazole or N-3-dimethylaminopropyl-N'-ethylcarbodiimide ("DAPECI"), furthermore propanephosphonic anhydride T3P (cf. 15 Angew. Chem. 92, 129 (1980)), diphenylphosphoryl azide or 2-ethoxy-N-ethoxycarbonyl-1,2-dihydroquinoline, optionally in the presence of N-hydroxybenzotriazole;



The reaction is carried out in an inert solvent and is generally carried out in the presence of an acid-binding agent, preferably an organic base, such as DIPEA, triethylamine, dimethylaniline, pyridine or quinoline.

30 The addition of an alkali or alkaline-earth metal hydroxide, carbonate or bicarbonate or another salt of a weak acid of the alkali or alkaline-earth metals, preferably of potassium, sodium, calcium or caesium, may also be favourable.

35 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 40° and 130°, particularly preferably between 60° and 110°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 glycol ethers, such as ethylene glycol monomethyl ether, THF, dichloromethane and/or DMF.

Compounds of the formula I can furthermore preferably be obtained by oxidising compounds of the formula IV.

The oxidation is preferably carried out using tert-butyl hydroperoxide.

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 40° and 130°, particularly preferably between 60° and 110°C.

The solvent is preferably water, where the addition of an alkali or alkaline-earth metal hydroxide, carbonate or bicarbonate or another salt of a weak acid of the alkali or alkaline-earth metals, preferably of potassium, sodium, calcium or caesium, is also favourable.

Pharmaceutical salts and other forms

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 of the formula I are for the most part prepared by conventional methods. If the compound of the formula I contains a carboxyl group, one of its suitable salts can be formed by reacting the compound with a suitable base to
5 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, diethanol-
10 amine and N-methylglutamine. The aluminium salts of the compounds of the formula I are likewise included. In the case of certain compounds of the formula I, acid-addition salts can be formed by treating these compounds with
15 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 ethane-
20 sulfonate, 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 of the formula I include the following: acetate, adipate, alginate, arginate,
25 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, glycerophos-
30 phate, hemisuccinate, hemisulfate, heptanoate, hexanoate, hippurate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, iodide, isethionate, isobutyrate, lactate, lactobionate, malate, maleate, malonate, mandelate, metaphosphate, methanesulfonate, methylbenzoate, monohydrogenphos-
35 phate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, oleate, palmoate, pectinate, persulfate, phenylacetate, 3-phenylpropionate, phosphate, phos-

phonate, 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 of the formula I 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, chlorprocaine, 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 (C₁-C₄)alkyl halides, for example methyl, ethyl, isopropyl and tert-butyl chloride, bromide and iodide; di(C₁-C₄)alkyl sulfates, for example dimethyl, diethyl and diamyl sulfate; (C₁₀-C₁₈)alkyl halides, for example decyl, dodecyl, lauryl, myristyl and stearyl chloride, bromide and iodide; and aryl(C₁-C₄)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.

5 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.

10 The acid-addition salts of basic compounds of the formula I 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 cer-
15 tain 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.

20 As mentioned, the pharmaceutically acceptable base-addition salts of the compounds of the formula I 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
25 N,N'-dibenzylethylenediamine, chlorprocaine, choline, diethanolamine, ethylenediamine, N-methyl-D-glucamine and procaine.

30 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
35 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.

5 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.

10 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 compound which comprises a compound of the formula I in the form of one of its salts, in particular if this salt form imparts improved pharmacokinetic properties on the active compound compared with the free form of the active compound or any other salt form of the active compound used earlier. The pharmaceutically acceptable salt form of the active compound can also provide this active compound 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 compound with respect to its therapeutic efficacy in the body.

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

30 Pharmaceutical formulations can be administered in the form of dosage units which comprise a predetermined amount of active compound 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 35 the invention, depending on the condition treated, the method of administration and the age, weight and condition of the patient, or pharmaceutical formula-

tions can be administered in the form of dosage units which comprise a pre-determined amount of active compound 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 compound. 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 compound 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, can 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 absorbent, 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, acacia 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

5 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.

10 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 pre-specified 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
15 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
20 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
25 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 of the formula I and salts, solvates and physiologically functional derivatives thereof can also be administered in the form of liposome
30 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.
35

The compounds of the formula I 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.

5 The compounds can also be coupled to soluble polymers as targeted medication carriers. Such polymers may encompass polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidophenol, polyhydroxyethyl-aspartamidophenol 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 medication, for example polylactic acid, poly-epsilon-caprolactone, polyhydroxybutyric acid, polyorthoesters, polyacetals, polydihydroxypyranes, polycyanoacrylates and crosslinked or amphipathic block copolymers of hydrogels.

15 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 compound can be delivered from the plaster by iontophoresis, as described in general terms in
20 Pharmaceutical Research, 3(6), 318 (1986).

Pharmaceutical compounds adapted for topical administration can be formulated as ointments, creams, suspensions, lotions, powders, solutions, pastes,
25 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
30 the case of formulation to give an ointment, the active compound can be employed either with a paraffinic or a water-miscible cream base. Alternatively, the active compound can be formulated to give a cream with an oil-in-water cream base or a water-in-oil base.

35

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

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

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

15 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.

20 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.

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

30 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
35 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
5 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
10 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 of the formula I depends on
15 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
20 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
25 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 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
30 are suitable for the treatment of other conditions mentioned above.

The invention furthermore relates to medicaments comprising at least one
35 compound of the formula I and/or pharmaceutically usable salts and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active compound.

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

- (a) an effective amount of a compound of the formula I and/or pharmaceuti-
cally usable salts and stereoisomers thereof, including mixtures thereof in
all ratios,
and
(b) an effective amount of a further medicament active compound.

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 of the formula I and/or pharma-
ceutically usable salts and stereoisomers thereof, including mixtures thereof in
all ratios,
and an effective amount of a further medicament active compound in dissolved
or lyophilised form.

The invention relates to the compounds of the formula I according to Claim
1-5, and pharmaceutically usable salts, tautomers and stereoisomers thereof,
including mixtures thereof in all ratios, for use for the treatment of tumours,
tumour metastases, proliferative diseases of the mesangial cells, haemangi-
oma, proliferative retinopathy, rheumatoid arthritis, atherosclerotic neovascu-
larisation, psoriasis, ocular neovascularisation, osteoporosis, diabetes and
obesity, lymphoid leukaemia, lymphoma, malaria and prostate hypertrophy

Isotopes

It is furthermore intended that a compound of the formula I includes isotope-
labelled forms thereof. An isotope-labelled form of a compound of the formula I
is identical to this compound apart from the fact that one or more atoms of the
compound have been replaced by an atom or atoms having an atomic mass or
mass number which differs from the atomic mass or mass number of the atom
which usually occurs naturally. Examples of isotopes which are readily com-

mercially available and which can be incorporated into a compound of the formula I by well-known methods include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and chlorine, for example ^2H , ^3H , ^{13}C , ^{14}C , ^{15}N , ^{18}O , ^{17}O , ^{31}P , ^{32}P , ^{35}S , ^{18}F and ^{36}Cl , respectively. A compound of the formula I, a prodrug thereof or a pharmaceutically acceptable salt of either which contains one or more of the above-mentioned isotopes and/or other isotopes of other atoms is intended to be part of the present invention. An isotope-labelled compound of the formula I can be used in a number of beneficial ways. For example, an isotope-labelled compound of the formula I into which, for example, a radioisotope, such as ^3H or ^{14}C , has been incorporated is suitable for medicament and/or substrate tissue distribution assays. These radioisotopes, i.e. tritium (^3H) and carbon-14 (^{14}C), are particularly preferred owing to their simple preparation and excellent detectability. Incorporation of heavier isotopes, for example deuterium (^2H), into a compound of the formula I has therapeutic advantages owing to the higher metabolic stability of this isotope-labelled compound. Higher metabolic stability translates directly into an increased in-vivo half-life or lower dosages, which under most circumstances would represent a preferred embodiment of the present invention. An isotope-labelled compound of the formula I can usually be prepared by carrying out the procedures disclosed in the synthesis schemes and the related description, in the example part and in the preparation part in the present text, replacing a non-isotope-labelled reactant with a readily available isotope-labelled reactant.

In order to manipulate the oxidative metabolism of the compound by way of the primary kinetic isotope effect, deuterium (^2H) can also be incorporated into a compound of the formula I. The primary kinetic isotope effect is a change in the rate of a chemical reaction that results from exchange of isotopic nuclei, which in turn is caused by the change in ground state energies necessary for covalent bond formation after this isotopic exchange. Exchange of a heavier isotope usually results in a lowering of the ground state energy for a chemical bond and thus causes a reduction in the rate in rate-limiting bond breakage. If the bond breakage occurs in or in the vicinity of a saddle-point region along the

coordinate of a multi-product reaction, the product distribution ratios can be altered substantially. For explanation: if deuterium is bonded to a carbon atom in a non-exchangeable position, rate differences of $k_M/k_D = 2-7$ are typical. If this rate difference is successfully applied to a compound of the formula I that is susceptible to oxidation, the profile of this compound in vivo can thereby be drastically modified and result in improved pharmacokinetic properties.

When discovering and developing therapeutic agents, the person skilled in the art attempts to optimise pharmacokinetic parameters while retaining desirable in-vitro properties. It is reasonable to assume that many compounds with poor pharmacokinetic profiles are susceptible to oxidative metabolism. In-vitro liver microsomal assays currently available provide valuable information on the course of oxidative metabolism of this type, which in turn permits the rational design of deuterated compounds of the formula I with improved stability through resistance to such oxidative metabolism. Significant improvements in the pharmacokinetic profiles of the compounds of the formula I are thereby obtained and can be expressed quantitatively in terms of increases in the in-vivo half-life ($T/2$), concentration at maximum therapeutic effect (C_{max}), area under the dose response curve (AUC), and F ; and in terms of reduced clearance, dose and costs of materials.

The following is intended to illustrate the above: a compound of the formula I which has multiple potential sites of attack for oxidative metabolism, for example benzylic hydrogen atoms and hydrogen atoms bonded to a nitrogen atom, is prepared as a series of analogues in which various combinations of hydrogen atoms are replaced by deuterium atoms, so that some, most or all of these hydrogen atoms have been replaced by deuterium atoms. Half-life determinations enable favourable and accurate determination of the extent to which the improvement in resistance to oxidative metabolism has improved. In this way, it is determined that the half-life of the parent compound can be extended by up to 100% as the result of deuterium-hydrogen exchange of this type.

Deuterium-hydrogen exchange in a compound of the formula I can also be used to achieve a favourable modification of the metabolite spectrum of the starting compound in order to diminish or eliminate undesired toxic metabolites. For example, if a toxic metabolite arises through oxidative carbon-hydrogen (C-H) bond cleavage, it can reasonably be assumed that the deuterated analogue will greatly diminish or eliminate production of the undesired metabolite, even if the particular oxidation is not a rate-determining step. Further information on the state of the art with respect to deuterium-hydrogen exchange is given, for example in Harziik et al., J. Org. Chem. **55**, 3992-3997, 1990, Reider et al., J. Org. Chem. **52**, 3326-3334, 1987, Foster, Adv. Drug Res. **14**, 1-40, 1985, Gillette et al., Biochemistry **33**(10), 2927-2937, 1994, and Jarman et al., Carcinogenesis **16**(4), 683-688, 1993.

USE

The present compounds are suitable as pharmaceutical active compounds for mammals, especially for humans, in the treatment and control of diseases. These diseases include the proliferation of tumour cells, pathological neovascularisation (or angiogenesis), which promotes the growth of solid tumours, neovascularisation in the eye (diabetic retinopathy, age-induced macular degeneration and the like) and inflammation (psoriasis, rheumatoid arthritis and the like), and proliferative diseases of the mesangial cells.

The present invention encompasses the use of the compounds of the formula I and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment or prevention of tumours, tumour diseases and/or tumour metastases.

The tumour disease is preferably selected from the group tumour 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, the skin, monocytic leukaemia, lung adenocarcinoma, small-cell lung carcinoma, pancreatic cancer, glioblastoma, breast carcinoma, acute myeloid leukaemia, chronic myeloid leukaemia, acute lymphatic leukaemia, chronic lymphatic leukaemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma.

Likewise encompassed is the use of the compounds according to Claim 1 according to the invention and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of osteoporosis, diabetes and obesity.

Likewise encompassed is the use of the compounds according to Claim 1 according to the invention and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment or prevention of a disease in which angiogenesis is involved.

A disease of this type in which angiogenesis is involved is an eye disease, such as retina vascularisation, diabetic retinopathy, age-induced macular degeneration and the like.

The angiogenic disease is preferably selected from the group
diabetic retinopathy, arthritis, cancer, psoriasis, Kaposi's sarcoma, haemangioma, myocardial angiogenesis, atherosclerotic plaque neovascularisation, angiogenic eye diseases, choroidal neovascularisation, retrolental fibroplasia, macular degeneration, corneal transplant rejection, rubeosis iridis, neurovascular glaucoma, Oster Webber syndrome.

The proliferative disease of the mesangial cells is preferably selected from the group
glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathy syndrome, transplant rejection, glomerulopathy.

5 The use of compounds of the formula I and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment or prevention of inflammatory diseases likewise falls within the scope of the present invention. Examples of such inflammatory diseases include rheumatoid arthritis, psoriasis, contact dermatitis, delayed hypersensitivity reaction and the like.

10 The inflammatory disease is preferably selected from the group inflammatory bowel disease, arthritis, atherosclerosis, asthma, allergies, inflammatory kidney diseases, multiple sclerosis, chronic obstructive pulmonary disease, inflammatory skin diseases, pardontal diseases, psoriasis, T-cell-promoted immune disease.

15 The inflammatory bowel disease is preferably selected from the group ulcerative colitis, Crohn's disease, non-specific colitis.

20 The T-cell-promoted immune disease is preferably selected from the group allergic encephalomyelitis, allergic neuritis, transplant rejection, graft-versus-host reaction, myocarditis, thyroiditis, nephritis, systemic lupus erythematosus, insulin-dependent diabetes mellitus.

25 The arthritis disease is preferably selected from the group rheumatoid arthritis, osteoarthritis, Caplan's syndrome, Felty's syndrome, Sjogren's syndrome, spondylitis ankylosans, Still's disease, chondrocalcinosis, metabolic arthritis, rheumatic fever, Reiter's disease, Wissler's syndrome.

30 The inflammatory kidney disease is preferably selected from the group glomerulonephritis, glomerular injury, nephrotic syndrome, interstitial nephritis, lupus nephritis, Goodpasture's syndrome, Wegener's granulomatosis, renal vasculitis, IgA nephropathy, idiopathic glomerular disease.

35 The inflammatory skin disease is preferably selected from the group psoriasis, atopic dermatitis, contact sensitivity, acne.

5 Likewise encompassed is the use of the compounds of the formula I and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment or prevention of a disease or condition in a mammal, in which to this method a therapeutically effective amount of a compound according to the invention is administered to a sick mammal in need of such treatment. The therapeutic amount varies according to the specific disease and can be determined by the person skilled in the art without undue effort.

10 The present invention also encompasses the use compounds of the formula I and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment or prevention of retinal vascularisation.

15 Likewise encompassed is the use of the compounds of the formula I and/or physiologically acceptable salts thereof for the preparation of a medicament for the treatment and/or combating of a tumour-induced disease in a mammal, in which to this method a therapeutically effective amount of a compound according to the invention is administered to a sick mammal in need of such treatment. The therapeutic amount varies according to the specific disease and can be determined by the person skilled in the art without undue effort.

20 The disclosed compounds of the formula I can be administered in combination with other therapeutic agents, including anticancer agents. As used here, the term "anticancer agent" relates to any agent which is administered to a patient with cancer for the purposes of treating the cancer.

25 The compounds of the formula I may also be administered together with other well-known therapeutic agents that are selected for their particular suitability for the condition being treated.

30 The present compounds are also suitable for combination with known anti-cancer agents. These known anti-cancer agents include the following: oestrogen receptor modulators, androgen receptor modulators, retinoid receptor

35

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.

"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-dinitrophenylhydrazine 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 5 α -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-cis-retinoic acid, 9-cis-retinoic 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, dibromodulcitol, ranimustine, fotemustine, nedaplatin, oxaliplatin, temozolomide, heptaplatin, estramustine, improsulfan tosylate, trofosfamide, nimustine, dibrospidium chloride, pumitepa, lobaplatin, satra-

platin, profiromycin, cisplatin, irofulven, dexifosfamide, cis-aminedichloro(2-methylpyridine)platinum, benzylguanine, glufosfamide, GPX100,
 (trans,trans,trans)bis-mu-(hexane-1,6-diamine)-mu-[diamineplatinum(II)]bis-
 5 [diamine(chloro)platinum(II)] tetrachloride, diarisidinylspermine, arsenic tri-
 oxide, 1-(11-dodecylamino-10-hydroxyundecyl)-3,7-dimethylxanthine, zorubi-
 cin, idarubicin, daunorubicin, bisantrene, mitoxantrone, pirarubicin, pinafide,
 valrubicin, amrubicin, antineoplaston, 3'-deamino-3'-morpholino-13-deoxo-10-
 hydroxycarminomycin, annamycin, gal-arubicin, elinafide, MEN10755 and
 10 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'-norvincal leukoblastine, docetaxol, rhizoxin, dolastatin,
 15 mivobulin isethionate, auristatin, cemadotin, RPR109881, BMS184476, vin-
 flunine, cryptophycin, 2,3,4,5,6-pentafluoro-N-(3-fluoro-4-methoxy-
 phenyl)benzenesulfonamide, anhydrovinblastine, N,N-dimethyl-L-valyl-L-valyl-
 N-methyl-L-valyl-L-prolyl-L-proline-t-butylamide, TDX258 and BMS188797.
 Topoisomerase inhibitors are, for example, topotecan, hycaptamine, irino-
 20 tecan, rubitecan, 6-ethoxypropionyl-3' 4'-O-exobenzylidenechartreusin,
 9-methoxy-N,N-dimethyl-5-nitropyraclo[3,4,5-kl]acridine-2-(6H)propanamine,
 1-amino-9-ethyl-5-fluoro-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-
 25 (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-
 30 [N-[2-(dimethylamino)ethyl]-N-methylamino]ethyl]-5-[4-hydroxy-3,5-dimethoxy-
 phenyl]-5,5a,6,8,8a,9-hexahydrofuro(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-amino-
 propylamino)-7,10-dihydroxy-2-(2-hydroxyethylaminomethyl)-6H-pyrazolo-
 35 [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-car-

boxamide, 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 anti-
5 metabolites 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,
10 2'-fluoromethylene-2'-deoxycytidine, N-[5-(2,3-dihydrobenzofuryl)sulfonyl]-N'-(3,4-dichlorophenyl)urea, N6-[4-deoxy-4-[N2-[2(E),4(E)-tetradecadienoyl]glycyl-amino]-L-glycero-B-L-mannoheptopyranosyl]adenine, aplidine, ecteinascidin, troxacitabine, 4-[2-amino-4-oxo-4,6,7,3-tetrahydro-3H-pyrimidino[5,4-b]-1,4-
15 thiazin-6-yl-(S)ethyl]-2,5-thienoyl-L-glutamic acid, aminopterin, 5-fluorouracil, 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'-cyano-2'-deoxy-N4-palmitoyl-1-B-D-arabinofuranosyl cytosine and 3-aminopyridine-2-carboxaldehyde thio-
20 semicarbazone. "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 virus-mediated gene transfer (see US Patent No.
25 6,069,134, for example).

Evidence of the action of pharmacological inhibitors on the proliferation/vitality of tumour cells *in vitro*

1.0 Background

In the present experiment description, the inhibition of tumour cell proliferation/tumour cell vitality by active compounds is described.

The cells are sown in a suitable cell density in microtitre plates (96-well format)
35 and the test substances are added in the form of a concentration series. After four further days of cultivation in serum-containing medium, the tumour cell

proliferation/tumour cell vitality can be determined by means of an Alamar Blue test system.

2.0 Experimental procedure

2.1 Cell culture

For example commercially available colon carcinoma cell lines, ovary cell lines, prostate cell lines or breast cell lines, etc.

The cells are cultivated in medium. At intervals of several days, the cells are detached from the culture dishes with the aid of trypsin solution and sown in suitable dilution in fresh medium. The cells are cultivated at 37° Celsius and 10% CO₂.

2.2. Sowing of the cells

A defined number of cells (for example 2000 cells) per culture/well in a volume of 180 µl of culture medium are sown in microtitre plates (96 well cell-culture plates) using a multichannel pipette. The cells are subsequently cultivated in a CO₂ incubator (37°C and 10% CO₂).

2.3. Addition of the test substances

The test substances are dissolved, for example, in DMSO and subsequently employed in corresponding concentration (if desired in a dilution series) in the cell culture medium. The dilution steps can be adapted depending on the efficiency of the active compounds and the desired spread of the concentrations. Cell culture medium is added to the test substances in corresponding concentrations. The addition of the test substances to the cells can take place on the same day as the sowing of the cells. To this end, in each case 20 µl of substance solution from the predilution plate are added to the cultures/wells. The cells are cultivated for a further 4 days at 37° Celsius and 10% CO₂.

2.4. Measurement of the colour reaction

In each case, 20 µl of Alamar Blue reagent are added per well, and the microtitre plates are incubated, for example, for a further seven hours in a CO₂ incubator (at 37°C and 10% CO₂). The plates are measured in a reader with a fluorescence filter at a wavelength of 540 nm. The plates can be shaken gently immediately before the measurement.

3. Evaluation

The absorbance value of the medium control (no cells and test substances used) is subtracted from all other absorbance values. The controls (cells without test substance) are set equal to 100 per cent, and all other absorbance values are set in relation thereto (for example in% of control):

Calculation:

$$\frac{100 * (\text{value with cells and test substance} - \text{value of medium control})}{(\text{value with cells} - \text{value of medium control})}$$

IC₅₀ values (50% inhibition) are determined with the aid of statistics programs, such as, for example, RS1.

IC₅₀ data for compounds according to the invention are shown in Table 1.

25

Material	Order No.	Manufacturer
Microtitre plates for cell culture (Nunclon Surface 96-well plate)		167008 Nunc
DMEM	P04-03550	Pan Biotech
PBS (10x) Dulbecco	14200-067	Gibco
96-well plates (polypropylene)		267334 Nunc
AlamarBlue™	BUF01213	Serotec
FCS	1302	Pan Biotech GmbH

30

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	Trypsin/EDTA solution 10x	L 2153	Biochrom AG
	75cm ² culture bottles	353136	BD Falcon
5	A2780	93112519	ECACC
	Colo205	CCL222	ATCC
	MCF7	HTB22	ATCC
10	PC3	CRL-1435	ATCC

Determination of the proliferation inhibition by inhibitors of methionine aminopeptidase 2 in the BrdU proliferation test (cellular assay)

15 The inhibition of proliferation is determined by incorporation of bromodesoxyuridine (BrdU) into human umbilical vein endothelial cells (HUVECs, PromoCell, C-12200). The HUVECs are cultivated at 37°C and 5% CO₂ in basal medium (PromoCell, C-22200) with supplement mix (PromoCell, C-39225).

20 After detachment of the cells by means of trypsin/EDTA, the number of living cells is determined, and the cells are sown in a density of 1000 cells per cavity in a total volume of 175 µl (cavities are coated in advance either with supplemented culture medium for 1-2 hours at 37°C or with 1.5% gelatine for 0.5 – 2 hours at 37°C). After cultivation for 24 hours, the test substances are added in

25 various concentrations (for example final concentrations 30 µM to 0.03 nM in 10-fold dilution steps) and a volume of 25 µl. The DMSO concentration is kept constant at 0.3%. After cultivation for a total of 48 or 72 hours, 20 µl of bromodesoxyuridine (Roche, # 11647229001 diluted 1:1000 in culture medium, final concentration 10µM) are added, and cultivation is continued for a further 20 to

30 24 hours. After incubation with test substances for a total of 72 or 96 hours, the culture medium is removed, and an immunohistochemical determination is carried out for detection of BrdU incorporation (BrdU ELISA, Roche, #

35 11647229001). To this end, the cells are treated with a fixative for 30 min at room temperature and subsequently incubated with a peroxidase-labelled

anti-BrdU antibody (diluted 1:100 in antibody dilution buffer) for 60 min at room temperature. After washing three times with 1-fold-concentrated DPBS buffer (Gibco, # 14200), the enzymatic reaction is initiated in TMB substrate solution. The colour development is stopped after 15 min by addition of 25 μ l of a 1M sulfuric acid solution. A determination of the optical density is carried out within 5 min by measurement at a wavelength of 450 nm. The controls used are cavities containing DMSO-treated cells (100% control) or empty cavities (blank value). The sensitivity of this test to inhibitors of methionine aminopeptidase is checked and confirmed using the inhibitor fumagillin.

MetAP-2 activity measurement

The MetAP-2 activity is determined by coupling enzymatic reactions. The tripeptide Met-Arg-Ser (MAS) is employed as substrate. The methionine liberated is firstly converted into Met_{ox} and H₂O₂ by L-aminooxidase (AAO). In the second step, the peroxidase (POD) with the aid of the H₂O₂ catalyses the oxidation of the leukodye dianisidine to dianisidine_{ox}, the increase of which is detected photometrically at 450 nm.

MetAP-2 activity can be recorded continuously as kinetics. The reaction scheme illustrates that one mol of dianisidine_{ox} is formed per mol of methionine. The MetAP-2 enzyme activity can therefore be calculated directly as Δ absorption per time unit. Qualification of the MetAP-2 activity (mol of Met/time unit) is possible with the aid of the dianisidine_{ox} extinction coefficient.

The change in extinction per time unit is depicted graphically and a slope calculation is carried out in the visually linear region of the reaction.

The activities of the compounds are summarised in Table 1.

Solubility measurement

Determination by shake flask solubility measurement

Eluent preparation:

- Eluent A: 2 ml of diethylamine, for synthesis +
1000 ml of methanol, LiChrosolv
- 5 Eluent B: 5 g of ammonium acetate, for analysis +
5 ml of methanol, LiChrosolv +
995 ml of ultrapure water
-
- 10 Sample solvent:
- Buffer: 3.954 g of sodium dihydrogenphosphate monohydrate + 6.024 g of
sodium chloride + 950 ml of ultrapure water the pH is adjusted using 0.1 M
- 15 NaOH or 0.1 M HCl.
Sample preparation:
- The samples are shaken at 37°C and 450 rpm for 24 h.
After about 7h, the pH of the samples is checked and adjusted if necessary.
- 20 It is also checked whether the sample is still present in excess.
- Just before the end of the 24h shaking time, the samples are again checked
for pH and a precipitate.
- 25 Ultrapure water unit: MilliQ gradient, Milipore, instrument: F3PN37462D
Shaker: TiMix control, Bühler
Incubation hood: TH 15 Bühler
- 30 pH meter: 766 Calimatic Knick instrument: pH 1
pH electrode: InLab 423 Mettler
- 35 APCI-MS (atmospheric pressure chemical ionisation - mass spectrometry)
(M+H)⁺.

The racemic end products of the compounds according to the invention or the racemic intermediates can be separated simply and both on an analytical and also on a preparative scale via a chiral HPLC or SFC column.

5

LCMS:

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5 μ) + ve mode

10

Time	% of B
------	--------

0	05
---	----

8.0	100
-----	-----

8.1	100
-----	-----

15

8.5	05
-----	----

10	05
----	----

\$

20

LC-MS method: (instrument: Agilent 1100 series)

Column: Chromolith Speed Rod RP18e 50-4.6

Flow rate: 2.4ml/min

Solvent A: water + 0.05% of HCOOH

Solvent B: acetonitrile + 0.04% of HCOOH

25

WL: 220 nm

Gradient: 0-2.8 min: 4% of B to 100% of B, 2.8-3.3 min: 100% of B.

\$\$

30

Method: A- 10 mM NH₄HCO₃, B- ACN: flow – 1.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5 μ) - ve mode

Time	% of B
------	--------

0	05
---	----

8.0	100
-----	-----

35

8.1	100
-----	-----

8.5	05
-----	----

10 05

HPLC:

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5u) + ve mode

5

Time % of B

0 5

8.0 100

8.1 100

10

8.5 5

10 5

\$\$\$

15

Method: isopropanol: flow – 0.8 ml/min.

Run time: 20 min

Column: Chiralpak AD

1)

20

Enantiomer separation:

Separation on Chiralcel OD-H with n-heptane/ethanol = 70/30.

The substance is dissolved in 10 ml of n-heptane/EtOH = 1/1 and separated via 5x25cm Chiralcel OD column with 20 µm material at a flow rate of

25

100ml/min of n-heptane/ethanol = 70/30.

Above and below, all temperatures are indicated in °C. In the following examples, "conventional work-up" means: water is added if necessary, the pH is adjusted, if necessary, to values 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.

35

M.p.: melting point

Mass spectrometry (MS): EI (electron impact ionisation) M^+

FAB (fast atom bombardment) $(M+H)^+$

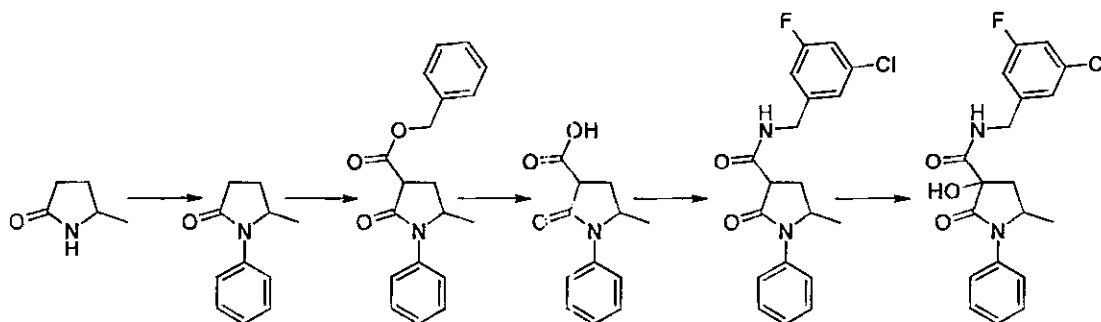
ESI (electrospray ionisation) $(M+H)^+$

APCI-MS (atmospheric pressure chemical ionisation - mass spectrometry) $(M+H)^+$.

Synthesis schemes for the preparation of compounds of the formula I:

Example 1

Preparation of N-(3-chloro-5-fluorobenzyl)-3-hydroxy-5-methyl-2-oxo-1-phenylpyrrolidine-3-carboxamide ("A119")



Example 2

Preparation of 3-[(3-chloro-5-fluorobenzylamino)methyl]-1-phenylpyrrolidin-3-ol ("A120")



N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide (100 mg) is dissolved in dry THF (2 ml), and borane/tetrahydrofuran complex (1.0 M in THF; 1 ml) is added dropwise at -78°C .

The mixture is stirred at 60°C for a further five hours and then worked up at 0°C by addition of 3 ml of methanol. After evaporation, the residue is purified by chromatography, giving 3-[(3-chloro-5-fluorobenzylamino)methyl]-1-phenylpyrrolidin-3-ol (22 mg) as amorphous solid.

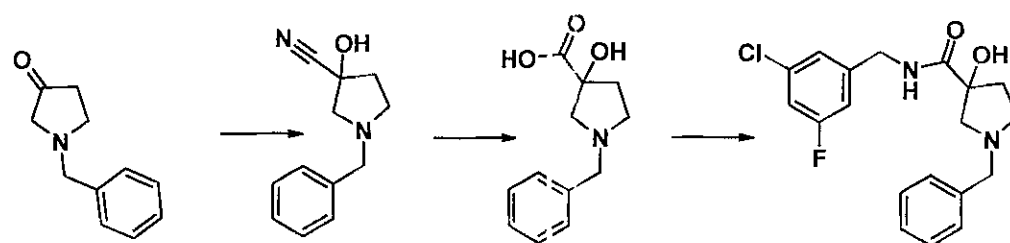
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Example 3

Preparation of N-(3-chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypyrrolidine-3-carboxamide ("A121")

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3.1 1 ml of commercially available 1-benzylpyrrolidin-3-one is dissolved in 30 ml of water and 10 ml of 1N HCl. A solution of 460 mg of sodium cyanide in 10 ml of water is added dropwise, and the mixture is stirred at RT for one hour. The product is not isolated and is reacted directly in the next step.

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The crude product from the preceding step is dissolved in 50 ml of 25% HCl and heated at reflux for 2 h. Volatile constituents are removed in vacuo, and the residue is purified by chromatography, giving 400 mg of 1-benzyl-3-hydroxypyrrolidine-3-carboxylic acid as amorphous solid;

25

^1H (400 MHz, DMSO- d_6) δ [ppm] 7.35 (5 H, m), 3.90 (2 H, s), 3.06 (1 H, d, J 10.5), 2.99 (1 H, m), 2.87 (1 H, m), 2.75 (1 H, d, J 10.4), 2.25 (1 H, dt, J 13.0, 7.7), 1.83 (1 H, m).

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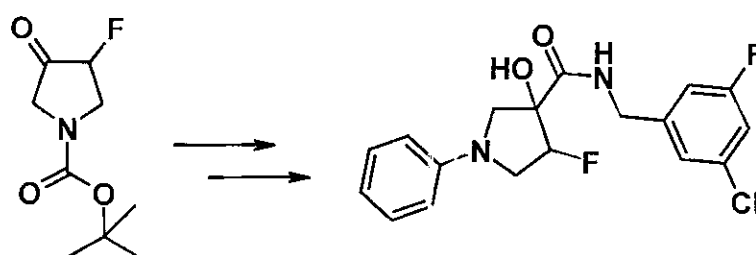
3.2 1-Benzyl-3-hydroxypyrrolidine-3-carboxylic acid (100 mg) and 3-chloro-5-fluorobenzylamine (79 mg) are dissolved in one millilitre of dried DMSO and cooled to 0°C. o-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (206 mg) and 4-methylmorpholine (0.124 ml) are then added. The batch is stirred at 25°C for 2 hours and then immediately purified by chro-

35

matography, giving N-(3-chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypyrrolidine-3-carboxamide (37 mg) as colourless amorphous solid.

Example 4

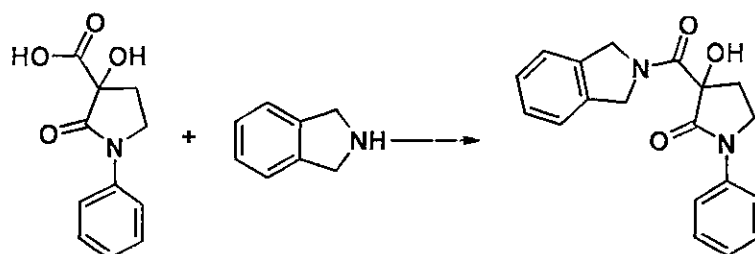
Preparation of N-[(3-chloro-5-fluorophenyl)methyl]-4-fluoro-3-hydroxy-1-phenylpyrrolidine-3-carboxamide ("B1")



Commercially available t-butyl 3-fluoro-4-oxopyrrolidine-1-carboxylate (Shanghai AQBioPharma) can be reacted by known methods and in an analogous manner, giving "B1".

Example 5

Preparation of 3-(1,3-dihydroisoindole-2-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one ("A267")



A solution of 3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxylic acid (100 mg) and 2,3-dihydro-1H-isoindole (66 mg) in N,N-dimethylformamide (1 ml) is cooled in an ice bath. o-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium

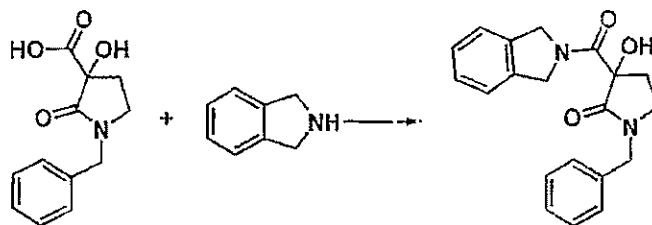
hexafluorophosphate (206 mg) and 4-methylmorpholine (0.1 ml) are added, and the mixture is stirred at 25°C for 20 h, giving 3-(1,3-dihydroisoindole-2-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one (63 mg).

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Example 6

Preparation of 1-benzyl-3-(1,3-dihydroisoindole-2-carbonyl)-3-hydroxy-pyrrolidin-2-one ("A268")

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1-Benzyl-3-hydroxy-2-oxopyrrolidine-3-carboxylic acid (100 mg) and 2,3-dihydro-1H-isoindole (62 mg) are dissolved in N,N-dimethylformamide (1 ml), and the solution is cooled to 0°C. o-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (194 mg) and 4-methylmorpholine (0.1 ml) are added dropwise, and the batch is stirred at 25°C for 20 hours, giving 1-benzyl-3-(1,3-dihydroisoindole-2-carbonyl)-3-hydroxypyrrolidin-2-one (57 mg) as colourless amorphous solid.

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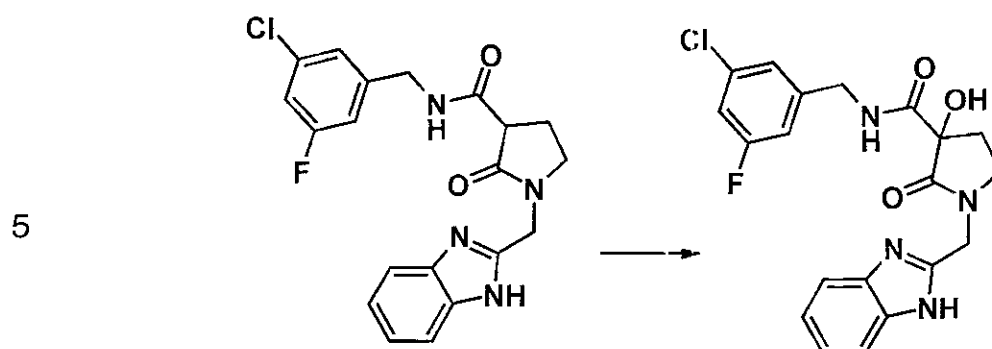
25

Example 7a

Preparation of N-(3-chloro-5-fluorobenzyl)-1-(1H-benzimidazol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide ("A269")

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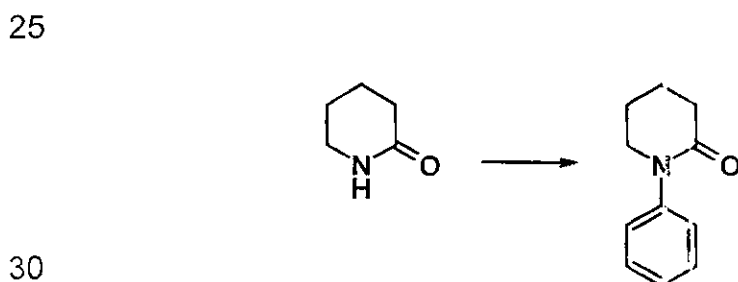
10 N-(3-Chloro-5-fluorobenzyl)-1-(1H-benzimidazol-2-ylmethyl)-2-oxopyrrolidine-3-carboxamide (396 mg) is dissolved in tert-butanol (5 ml), sodium ethoxide (20% solution in ethanol, 0.6 ml) and tert-butyl hydroperoxide (70% solution in water, 0.2 ml). The mixture is stirred at 80°C for one hour and then evaporated. After equal parts of water and ethyl acetate have been added, the product pre-

15 cipitates out as colourless solid, giving N-(3-chloro-5-fluorobenzyl)-1-(1H-benzimidazol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide (237 mg).

Example 7

20 Preparation of N-(3-chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxamide ("A65")

7.1 1-Phenylpiperidin-2-one:



35 δ -Valerolactam (2 g) is dissolved in 1,4-dioxane (10 ml), bromobenzene (3.32 g) and caesium carbonate (13.2 g) are added, and the reaction vessel is sealed. Nitrogen is subsequently passed through the suspension for 15 min. Xantphos (1.16 g) and tris(dibenzylidene acetone)dipalladium (0) (1.84 g) is

then added, and the mixture is warmed at 100°C for 12 h. When the reaction is complete, the constituents which are insoluble at RT are filtered off, and the reaction solution is evaporated. The crude product obtained in this way is chromatographed on silica gel, giving 1.3 g (37%) of the product as pale-yellow solid;

^1H NMR (400 MHz, DMSO- d_6) δ [ppm] 7.38-7.34 (m, 2H), 7.26-7.20 (m, 3H), 3.58 (t, J = 6.08 Hz, 2H), 2.37 (t, J = 6.12 Hz, 2H), 1.87-1.80 (m, 4H);

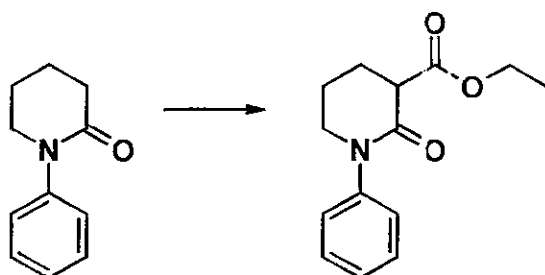
LCMS: mass found ($M+1$, 176.2);

Method: A- 0.1% of TFA in H_2O , B- 0.1% of TFA in ACN; flow – 2.0 ml/min.

Column: X Bridge C8 (50x4.6mm.3.5 μ) + ve mode

Rt (min) : 3.91 area% 76.24 (max), 74.74(220nm)

7.2 Ethyl 2-oxo-1-phenylpiperidine-3-carboxylate:



A solution of 1-phenylpiperidin-2-one (1.3 g) in THF (20 ml) is deprotonated using lithium bistrimethylsilylamide (1M in THF) (15 ml) at -78°C under nitrogen. After one hour, ethyl chloroformate (0.806 g) is added dropwise at the temperature indicated, and the cooling bath is removed. When the reaction is complete, the mixture is worked up using ice-water and extracted with ethyl acetate. The organic phase is washed with 10% sodium bicarbonate solution and saturated sodium chloride solution. After drying and evaporation, the residue is chromatographed on silica gel, giving 600 mg (32%) of a pale-brown liquid;

^1H NMR (400 MHz, DMSO- d_6) δ [ppm] 7.40-7.37 (m, 2H), 7.27-7.23 (m, 3H), 4.14-4.08 (m, 2H), 3.67-3.60 (m, 2H), 3.56-3.52 (m, 1H), 2.12-2.11 (m, 1H), 2.06-2.03 (m, 1H), 1.94-1.90 (m, 1H), 1.19 (t, J = 7.08 Hz, 3H);

LCMS: mass found (M+1, 248.2)

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

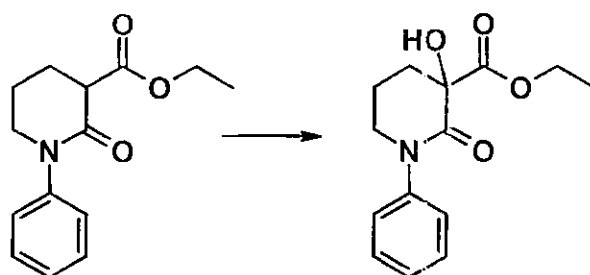
Column: X Bridge C8 (50x4.6mm.3.5 μ) + ve mode

Rt (min) : 2.61 area% 96.52 (max), 96.55 (254 nm)

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7.3 Ethyl 3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxylate:

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Cerium chloride heptahydrate (85 mg) is added to a solution of ethyl 2-oxo-1-phenylpiperidine-3-carboxylate (280 mg) in IPA (10 ml), and the mixture is treated with oxygen gas for 15 min. The mixture is subsequently stirred under an O₂ atmosphere for 12 h. When the reaction is complete, the mixture is evaporated in vacuo and purified by chromatography, giving 100 mg (34%) of the product shown and also the chlorine analogue;

20

LCMS: mass found (M+1, 264)

25

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0ml/min.

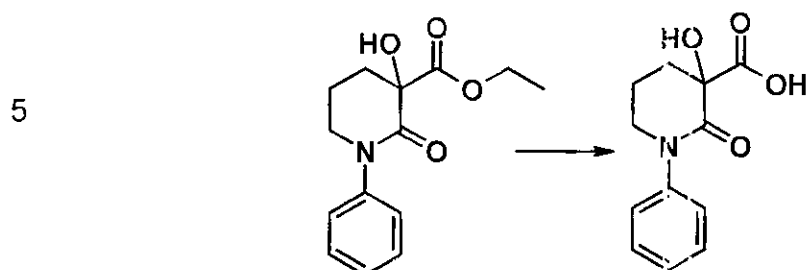
Column: X Bridge C8 (50x4.6mm.3.5 μ) + ve mode

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¹H NMR (400 MHz, DMSO-d₆) δ [ppm] 7.40-7.38 (m, 2H), 7.28-7.24 (m, 3H), 6.25 (s, 1H), 4.18-4.12 (m, 2H), 3.69-3.66 (m, 2H), 2.22 (m, 1H), 1.99 (m, 2H), 1.94-1.89 (m, 1H), 1.21 (t, J = 7.08 Hz, 3H).

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7.4 3-Hydroxy-2-oxo-1-phenylpiperidine-3-carboxylic acid:



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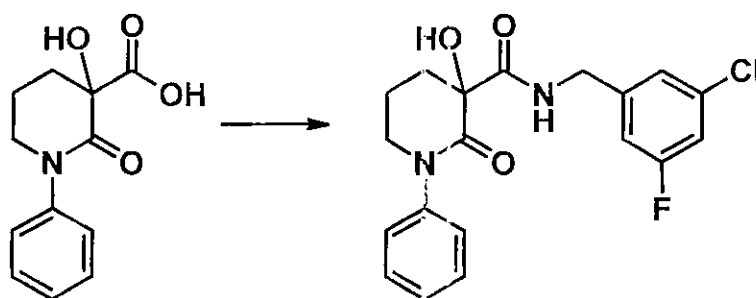
15

LiOH.H₂O (32 mg) is added to a solution of ethyl 3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxylate (100 mg) in THF/H₂O = 8:2 (10 ml), and the mixture is stirred for 1 h. When the reaction is complete, the mixture is neutralised using 1.5 N HCl solution, dried over sodium sulfate, evaporated in vacuo, giving the product as colourless solid with a yield of 89% (80 mg).

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7.5 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxamide ("A65"):



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A solution of 3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxylic acid (80 mg) and 3-chloro-5-fluorobenzylamine (65 mg) in dichloromethane (15 ml) is stirred with triethylamine (0.14 ml) and propanephosphoric anhydride (T3P; 0.33 g) firstly at 0°C, then at RT for 1h under nitrogen. When the reaction is complete, the mixture is diluted with dichloromethane and washed with 10% sodium bicarbonate solution and saturated NaCl solution. Filtration, evaporation and chromatography gives the product as colourless solid with a yield of 12% (15 mg);

LCMS: mass found (M+1,377.0)

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6mm.3.5μ) + ve mode

Rt (min) : 4.03 area% 92.24 (max), 91.79 (220nm)

HPLC:

Method: A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate:2.0ml/min

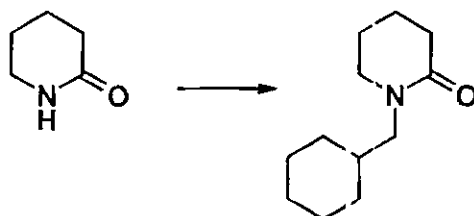
COLUMN: XBridge C8 (50X4.6)mm, 3.5 μm

Rt (min) : 4.01 area% 94.30 (max), 94.44 (220 nm);

Example 8

Preparation of N-(3-fluorobenzyl)-(S)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide ("A256") and N-(3-fluorobenzyl)-(R)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide ("A263")

8.1 1-Cyclohexylmethylpiperidin-2-one:



δ-Valerolactam (5 g) is dissolved in dry N,N-dimethylformamide (25 ml), and this solution is added at 0°C to a suspension of sodium hydride (2.42 g) in N,N-dimethylformamide (25 ml). After stirring at the temperature indicated for 30 minutes, bromomethylcyclohexane (11.60 g, 65.57 mmol) is added dropwise. The batch is subsequently stirred at RT for 8 h and, for work-up, evaporated to dryness in a Rotavapor. The residue is taken up with water and extracted to exhaustion with ethyl acetate. The organic phases are dried over sodium sulfate and evaporated, giving the title compound as pale-brown liquid; Yield: 6.6 g (67%);

^1H NMR (400 MHz, DMSO-d_6) δ [ppm] 3.21-3.18 (m, 2H), 3.10-3.08 (m, 2H), 2.18 (t, $J = 6.00$ Hz, 2H), 1.72-1.54 (m, 11H), 1.20-1.08 (m, 4H), 0.89-0.80 (m, 2H), .

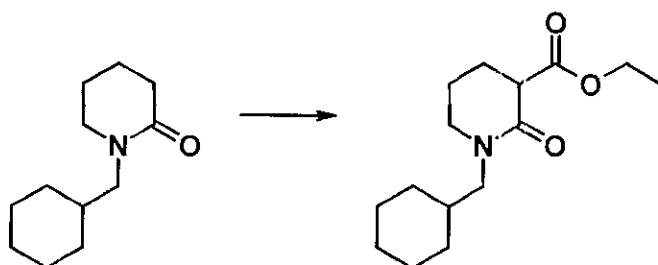
LCMS: mass found ($M+1$, 196.2)

Method: A- 0.1% of TFA in H_2O , B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50x4.6 mm.3.5u) + ve mode

Rt (min) : 3.91 area% 92.59 (ELSD).

Ethyl 1-cyclohexylmethyl-2-oxopiperidine-3-carboxylate:



Lithium bistrimethylsilylamide (1M in THF; 68 ml) is added dropwise at -78°C under nitrogen to a solution of the 1-cyclohexylmethylpiperidin-2-one prepared above (6.6 g) in THF (70 ml). After one hour, ethyl chloroformate (3.67 g) is added dropwise at the temperature indicated, and, when the addition is complete, the cooling bath is removed. For work-up, ice-water is added to the batch, and the mixture is extracted with ethyl acetate. After the organic phase has been washed with 10% sodium bicarbonate solution and saturated NaCl solution, the mixture is dried over sodium sulfate, filtered off and evaporated. The residue is chromatographed on silica gel, giving the product as brown liquid.

Yield: 5 g (55%);

^1H NMR (400 MHz, DMSO-d_6) δ [ppm] 4.08-4.03 (m, 2H), 3.32-3.18 (m, 3H), 3.04-3.00 (m, 1H), 1.98-1.87 (m, 1H), 1.68-1.56 (m, 9H), 1.20-1.12 (m, 7H), 0.87-0.84 (m, 2H);

LCMS: mass found ($M+1$, 268.2)

Method: A- 0.1% of TFA in H_2O , B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

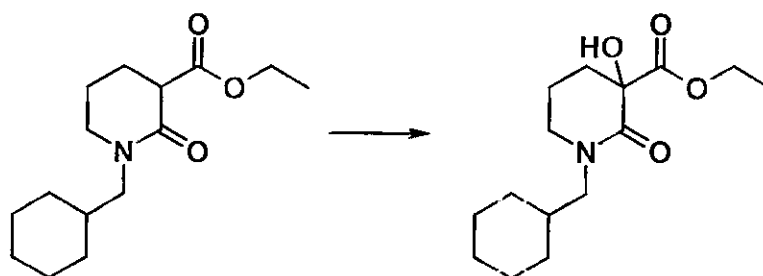
Column: X Bridge C8 (50 x 4.6 mm.3.5u) + ve mode

Rt (min) : 4.41 area% 95.21 (max), 93.63 (220 nm)

Ethyl 1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxylate:

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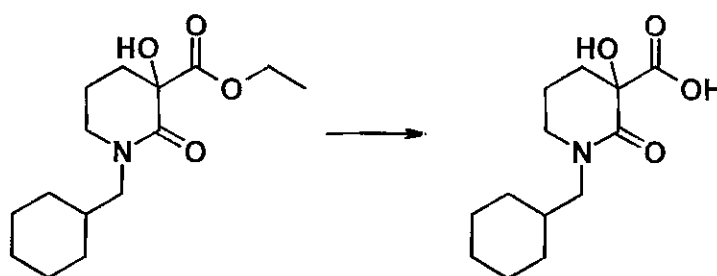
15

Cerium chloride heptahydrate (0.697 g) is added to a solution of ethyl 1-cyclohexylmethyl-2-oxopiperidine-3-carboxylate (2.5 g) in IPA (20 ml), and the mixture is treated with O₂ gas for 15 min. After 12 h under an O₂ atmosphere, all volatile constituents are removed, and the residue is purified on silica gel.

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1-Cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxylic acid

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The ester prepared above (700 mg) is dissolved in THF/H₂O = 16:4 (20 ml), and LiOH x H₂O (207 mg) is added. After one hour, all volatile constituents are removed in vacuo, and the mixture is acidified using 1.5 N HCl. The aqueous phase is extracted with ethyl acetate, and the organic phase is dried as described, giving the title compound as yellow liquid (600 mg, 95%) without further purification;

35

LCMS: mass found (M+1, 256)

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0ml/min.

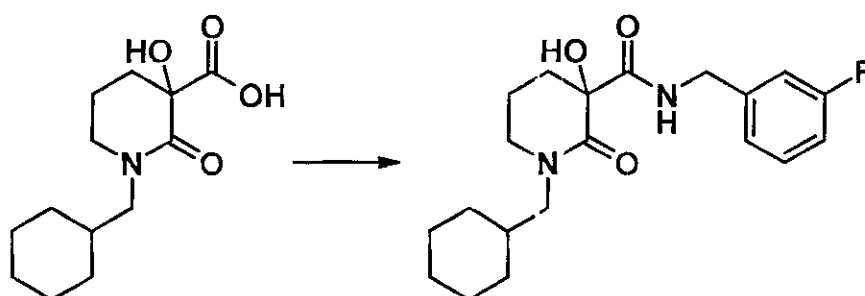
Column: X Bridge C8 (50x4.6mm.3.5 μ) + ve mode

Rt (min) : 6.00 area% 96.63 (ELSD).

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N-(3-Fluorobenzyl)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide

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Triethylamine (0.33 ml) and propanephosphoric anhydride (T3P - 748 g) are added at 0°C to a solution of 1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxylic acid (200 mg) and 3-fluorobenzylamine (116 mg) in dichloromethane (20 ml). After one hour at RT, the mixture is worked up as described. Since reduction of the hydroxyl group is partially observed, the batch is re-oxidised using tert-butyl hydroperoxide in tert-butanol.

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After conventional work-up, the mixture is purified on chiral HPLC;

Mobile phase: 0.1% of DEA in HEXANE/IPA = 60:40

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Column: CHIRALPAK AD-H (250x4.6)mm, 5 μ m

FLOW: 1.0ml/min

Rt (min) : 5.1 & 10.3 area% 53.43 & 46.56

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The S-enantiomer is obtained in a yield of 3% ("A256");

LCMS: mass found (M+1,363.3)

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5 μ) + ve mode

Rt (min) : 4.42 area% 95.85 (max), 95.34 (220 nm)

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HPLC:

Method: A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate: 2.0 ml/min

COLUMN: XBridge C8 (50 x 4.6) mm, 3.5 μ m

Rt (min) : 4.44 area% 95.49 (max), 95.20 (220 nm);

^1H NMR (400 MHz, DMSO- d_6) δ [ppm] 8.40-8.39 (m, 1H), 7.31 (t, J = 7.48 Hz, 1H), 7.11 (m, 2H), 7.05-7.00 (m, 1H), 6.08 (s, 1H), 4.39-4.33 (m, 1H), 4.26-4.20 (m, 1H), 3.28-3.22 (m, 3H), 3.04-3.01 (m, 1H), 2.17 (m, 1H), 1.85-1.77 (m, 3H), 1.63-1.62 (m, 6H), 1.23-1.13 (m, 3H), 0.89-0.83 (m, 2H).

The R-enantiomer is obtained in a yield of 13% ("A263" from table)

LCMS: mass found (M+1, 363.3)

Method: A- 0.1% of TFA in H₂O, B- 0.1% of TFA in ACN: flow – 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5 μ) + ve mode

Rt (min) : 4.45 area% 96.21 (max), 96.17 (220 nm)

HPLC:

Method: A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate: 2.0 ml/min

COLUMN: XBridge C8 (50 x 4.6) mm, 3.5 μ m

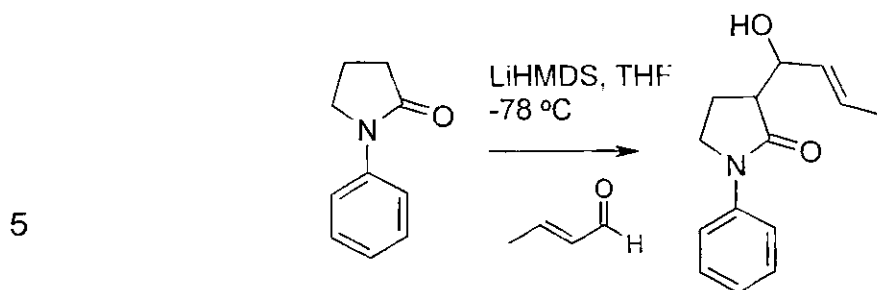
Rt (min) : 4.44 area% 98.19 (max), 97.90 (220 nm)

^1H NMR (400 MHz, DMSO- d_6) δ [ppm] 8.40-8.39 (m, 1H), 7.31 (t, J = 7.48 Hz, 1H), 7.11 (m, 2H), 7.05-7.00 (m, 1H), 6.08 (s, 1H), 4.39-4.33 (m, 1H), 4.26-4.20 (m, 1H), 3.28-3.22 (m, 3H), 3.04-3.01 (m, 1H), 2.17 (m, 1H), 1.85-1.77 (m, 3H), 1.63-1.62 (m, 6H), 1.23-1.13 (m, 3H), 0.89-0.83 (m, 2H).

Example 9

Preparation of (S)-3-((E)-but-2-enoyl)-3-hydroxy-1-phenylpyrrolidin-2-one ("A70")

9.1 (E)-3-(1-Hydroxybut-2-en-1-yl)-1-phenylpyrrolidin-2-one

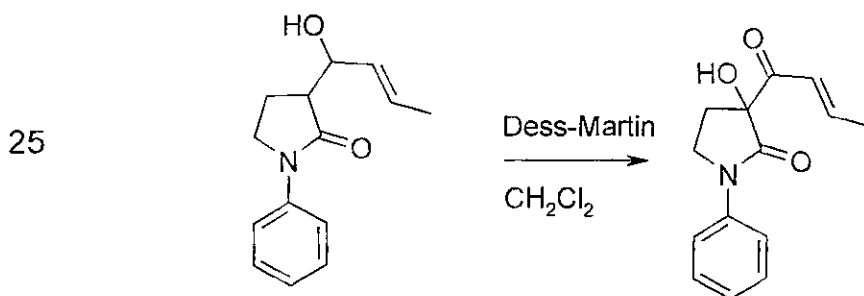


Commercially available 1-phenylpyrrolidin-2-one (483 mg) is dissolved in THF (10 ml), and LiHMDS (3.6 ml, 1M in THF) is added dropwise at -78°C . After 30 minutes, crotonaldehyde (252 mg) in THF (5 ml) is added dropwise, and the cooling bath is subsequently removed. The batch is worked up using NH_4Cl solution (5 ml) and extracted with ethyl acetate. After drying over sodium sulfate, the product is purified on silica gel, giving a colourless solid. (66%; 455 mg).

^1H NMR: 400 MHz, $\text{DMSO}-d_6$: δ 7.61-7.68 (m, 2H), 7.33-7.37 (m, 2H), 7.11-7.14 (m, 1H), 5.63-5.65 (m, 1H), 5.54-5.54 (m, 1H), 5.03 (d, $J = 3.88$ Hz) & 4.96 (d, $J = 4.88$ Hz, 1H), 4.41 (t, $J = 72.00$ Hz, 1H), 3.70-3.75 (m, 2H), 2.60-2.80 (m, 1H), 1.98-2.09 (m, 2H), 1.61-1.67 (m, 3H).

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9.2 (E)-3-(But-2-enoyl)-3-hydroxy-1-phenylpyrrolidin-2-one



A solution of (E)-3-(1-hydroxybut-2-en-1-yl)-1-phenylpyrrolidin-2-one (226 mg) in dichloromethane (10 ml) is reacted with Dess-Martin periodinane (850 mg) at 0°C . When the reaction is complete, the mixture is subjected to conventional work-up and purification, giving the product as colourless solid (75%, 185 mg);

^1H NMR: 400 MHz, $\text{DMSO}-d_6$: δ [ppm] 7.66-7.69 (m, 2H), 7.38-7.42 (m, 2H), 7.16-7.19 (m, 1H), 6.90-6.95 (m, 1H), 6.79 (d, $J = 15.56$ Hz, 1H), 6.65 (s, 1H),

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3.82-3.84 (m, 1H), 3.71-3.74 (m, 1H), 2.49-2.53 (m, 1H), 2.06-2.09 (m, 1H),
1.90 (d, $J = 6.72$ Hz, 3H);

LCMS: (method A) 246.0 (M+H), RT. 3.16 min, 98.5% (max), 96.8% (254 nm).

HPLC: (method A) RT 3.3 min, 98.1% (max), 95.9% (254 nm).

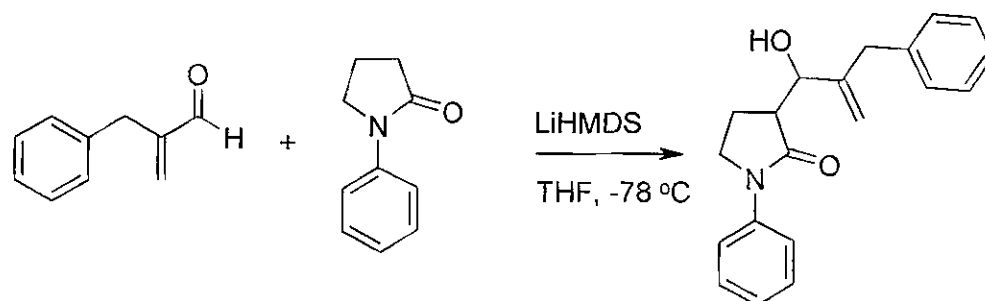
Enantiomer separation by means of chiral HPLC gives (S)-3-((E)-but-2-enoyl)-
3-hydroxy-1-phenylpyrrolidin-2-one:

^1H NMR (400 MHz, DMSO- d_6) δ [ppm] 7.70 – 7.65 (m, 2H), 7.43 – 7.37 (m,
2H), 7.21 – 7.15 (m, 1H), 6.83 – 6.76 (m, 1H), 6.65 (s, 1H), 3.84 (td, $J = 9.2$,
3.0 Hz, 1H), 3.73 (dt, $J = 9.6$, 7.5 Hz, 1H), 2.57 – 2.50 (m, 1H), 2.13 – 2.03 (m,
1H), 1.90 (dd, $J = 6.7$, 1.5 Hz, 3H).

Example 10

Preparation of 3-(2-benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one ("A89")

10.1 3-(2-Benzyl-1-hydroxyallyl)-1-phenylpyrrolidin-2-one

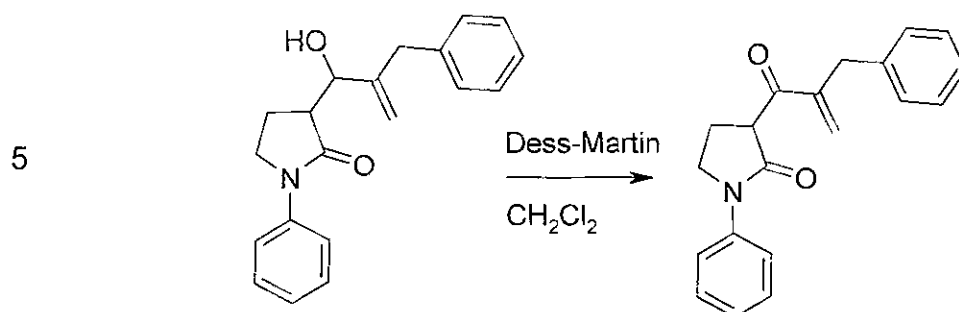


The reaction is carried out as described above for crotonaldehyde.

^1H NMR: 400 MHz, DMSO- d_6 : δ [ppm] 7.64-7.67 (m, 2H), 7.12-7.39 (m, 10H),
5.23 (d, $J = 3.56$ Hz, 1H), 5.13 (d, $J = 4.32$ Hz, 1H), 4.65 (d, $J = 1.20$ Hz, 1H),
4.30-4.45 (m, 1H), 3.72-7.75 (m, 2H), 3.30-3.50 (m, 3H), 2.85-3.00 (m, 1H),
1.80-2.20 (m, 2H);

LCMS: (method A) 308.2 (M+H), RT. 4.71 min, 30.39% (max) and 308.2
(M+H), RT. 4.96 min, 42.73% (max).

10.2 3-(2-Benzylacryloyl)-1-phenylpyrrolidin-2-one



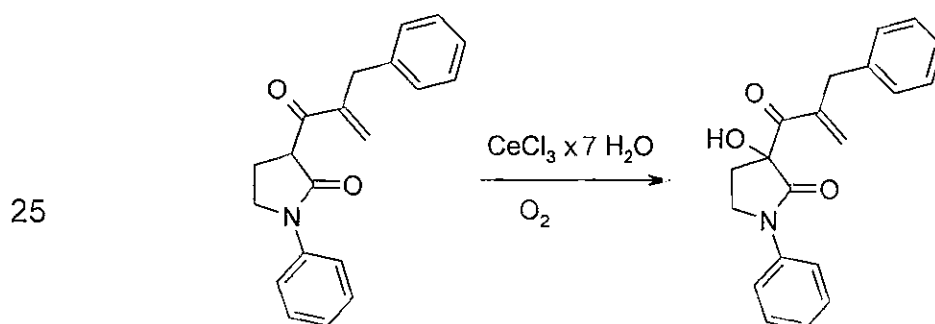
10 The reaction is carried out analogously to the reaction described above, where here only the hydroxyl group already present is oxidised to the ketone, and the second OH function is not, as above, also simultaneously introduced.

LCMS: (method A) 306.2 (M+H), RT. 4.98 min, 80.6% (max), 91.59%

(254 nm);

15 ¹H NMR: 400 MHz, DMSO-d₆: δ [ppm] 7.60-7.62 (m, 2H), 7.35-7.39 (m, 2H), 7.25-7.29 (m, 2H), 7.13-7.19 (m, 5H), 6.46 (s, 1H), 6.02 (s, 1H), 4.67-4.71 (m, 1H), 3.83 (t, J = 6.96 Hz, 2H), 3.58 (s, 2H).

20 10.3 3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one



30 Oxygen is added to a solution of 3-(2-benzylacryloyl)-1-phenylpyrrolidin-2-one (400 mg) and CeCl₃ x 7 H₂O (37 mg) in 2-propanol (15 ml) for 30 min, and the mixture is then stirred for 14 h. The mixture is subsequently subjected to conventional work-up and purification.

LCMS: (method A) 322.0 (M+H), RT. 4.63 min, 98.2% (max), 98.9% (254 nm);

HPLC: (method A) RT 4.6 min, 99.1% (max), 99.6% (254 nm);

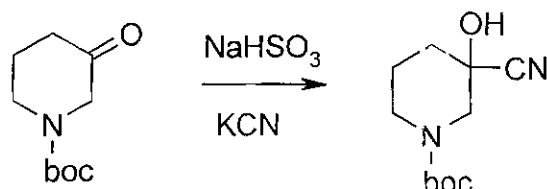
35 ¹H NMR: 400 MHz, DMSO-d₆: δ [ppm] 7.65 (t, J = 0.88 Hz, 2H), 7.37-7.41 (m, 2H), 7.24-7.28 (m, 2H), 7.15-7.19 (m, 4H), 6.79 (s, 1H), 6.66 (s, 1H), 5.91 (d, J

= 1.00 Hz, 1H), 3.81-3.82 (m, 1H), 3.57-3.59 (m, 1H), 3.54 (s, 2H), 3.34-3.35 (m, 1H), 2.52-2.55 (m, 1H), 2.13-2.16 (m, 1H).

Example 11

Preparation of 1-benzyl-N-(3-chloro-5-fluorobenzyl)-3-hydroxypiperidine-3-carboxamide ("A301")

11.1 tert-Butyl 3-cyano-3-hydroxypiperidine-1-carboxylate

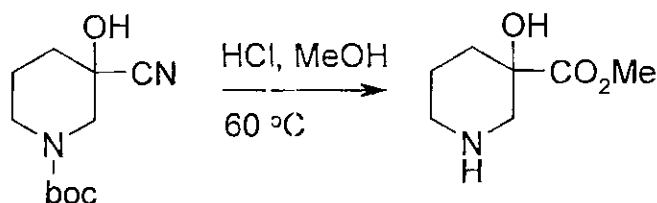


NaHSO₃ (3.8 g) is added to a solution of tert-butyl 3-oxopiperidine-1-carboxylate (5 g) in water / diethyl ether (50 : 25 ml), and the mixture is stirred for 15 min. KCN (2.4 g) is subsequently added. When the reaction is complete, the phases are separated, and the product is isolated by extraction and chromatography, giving 4.2 g (74%) of an orange solid;

LCMS: (method A) 100.2 (M+H), RT. 3.32 min, 92.85% (max);

¹H NMR: 400 MHz, DMSO-d₆: δ [ppm] 6.86 (s, 1H), 4.01-4.09 (m, 1H), 3.75 (s, 1H), 2.76-2.90 (m, 2H), 2.08 (d, J = 12.24 Hz, 1H), 1.30-1.50 (m, 2H).

11.2 Methyl 3-hydroxypiperidine-3-carboxylate



Concentrated HCl (20 ml) is added to a solution of tert-butyl 3-cyano-3-hydroxypiperidine-1-carboxylate (4.2 g) in MeOH (40 ml), and the mixture is warmed to reflux. The water is subsequently removed in vacuo, the mixture is neutralised using saturated NaHCO₃ solution, extracted with ethyl acetate,

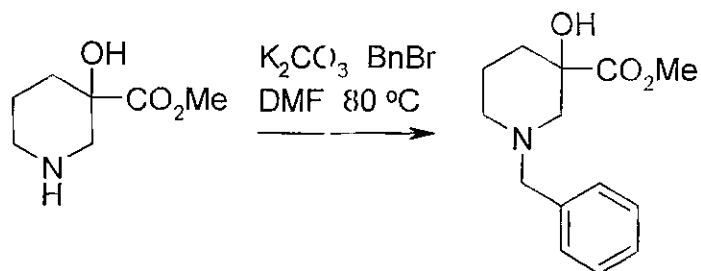
dried over Na_2SO_4 , and, after evaporation, the residue is reacted without further purification.

LCMS: (method A) 160.2 (M+H), RT. 0.52 min, 14.78% (max).

5

11.3 Methyl 1-benzyl-3-hydroxypiperidine-3-carboxylate

10



15

The crude product from the previous step is suspended in 40 ml of DMF, and stoichiometric amounts of K_2CO_3 and benzyl bromide are added. The mixture is warmed at 80°C for 14 h, and the solvent is subsequently removed in vacuo. The residue is taken up in water and extracted with ethyl acetate. The combined organic phases are washed with saturated NaCl solution, dried over Na_2SO_4 and, after concentration, purified on silica gel, giving 400 mg of a yellow oil;

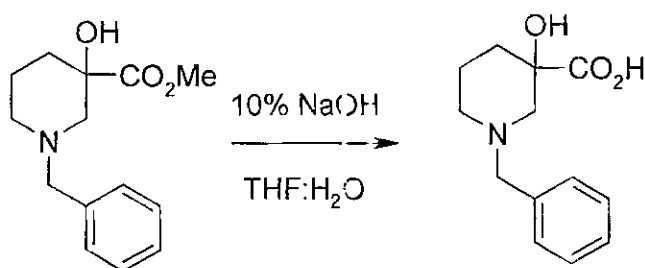
20

LCMS: (method A) 150.0 (M+H), RT. 1.34 min, 26.66% (max).

25

11.4 1-Benzyl-3-hydroxypiperidine-3-carboxylic acid

30



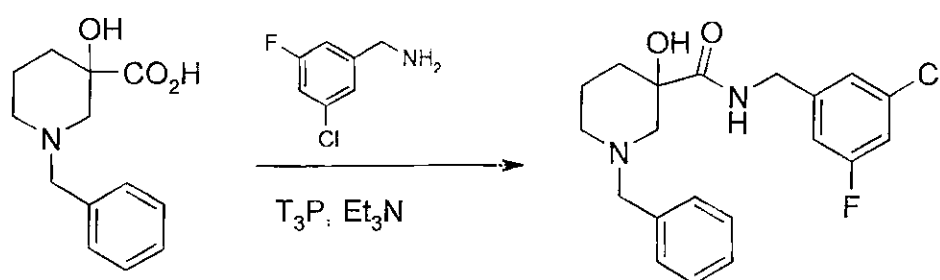
35

10% NaOH solution (2 ml) is added to a solution of methyl 1-benzyl-3-hydroxypiperidine-3-carboxylate (400 mg) in THF : H_2O (10 ml, 1:1), and the mixture is stirred at RT for 3 h. The mixture is subsequently concentrated in vacuo and neutralised using 1.5 N HCl solution. The residue is suspended in

CH₃OH : CH₂Cl₂ (1:1, 25 ml), and the inorganic residue is filtered off. Re-evaporation gives 200 mg of a colourless solid;

¹H NMR: 400 MHz, DMSO-d₆: δ [ppm] 13.31 (s, 1H), 9.58 (s, 1H), 7.45-7.57 (m, 5H), 6.16 (s, 1H), 4.38 (d, J = 10.80 Hz, 1H), 4.17-4.22 (m, 1H), 3.18-3.23 (m, 1H), 2.98 (d, J = 11.56 Hz, 2H), 2.04-2.08 (m, 1H), 1.60-1.90 (m, 3H).

11.5 1-Benzyl-N-(3-chloro-5-fluorobenzyl)-3-hydroxypiperidine-3-carboxamide



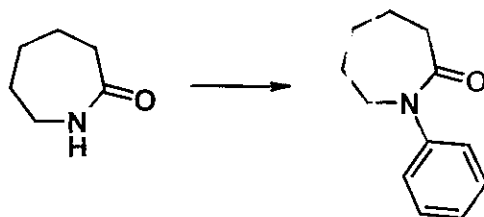
The acid prepared above is reacted with 3-chloro-5-fluorobenzylamine under the conditions described for amide coupling to T3P and subjected to conventional work-up and purification;

LCMS: (method A) 378.0 (M+H), RT. 3.56 min, 95.42% (max).

Example 12

Preparation of N-(3-chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide ("A66") and of N-(3-chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide ("A67")

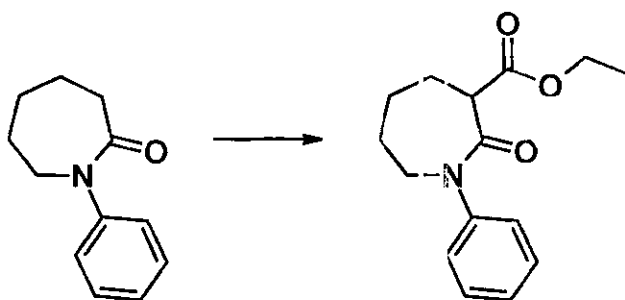
12.1 1-Phenylazepan-2-one:



A solution of ϵ -caprolactam (1 g) in 1,4-dioxane (10 ml) is sealed in a reaction vessel with bromobenzene (1.66 g) and Cs_2CO_3 (4.3 g). The mixture is degassed with N_2 for 15 min. Xanthphos (0.307 g) and tris(dibenzylideneacetone)dipalladium(0) (0.243 g) are then added, and the mixture is warmed at 100°C for 12 h. When the reaction is complete, insoluble constituents are filtered off, and the solvent is removed by evaporation. The residue is purified by chromatography, giving 1.2 g (72%) of the product as pale-yellow solid; LCMS: mass found ($M+1$, 190.0)

Method: A-0.1% of TFA in H_2O , B-0.1% of TFA in ACN: flow-2.0 ml/min.
Column: X Bridge C8 (50 x 4.6 mm, 3.5 μ) + ve mode
Rt (min) : 3.09 area% 95.94 (max), 97.13 (254 nm)

12.2 Ethyl 2-oxo-1-phenylazepane-3-carboxylate:

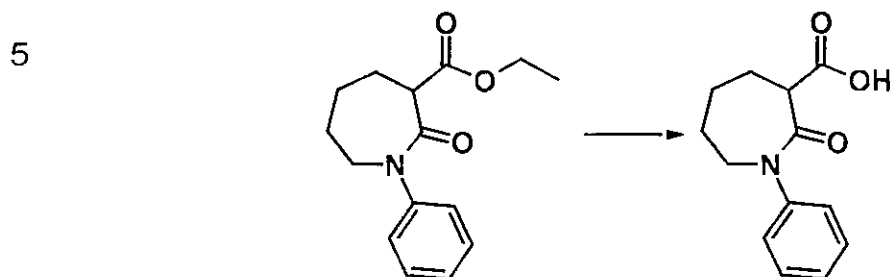


Lithium bistrimethylsilylamide (1M in THF; 13 ml) is added at -78°C to a solution of 1-phenylazepan-2-one (1.2 g) in THF (20 ml). After one hour at the temperature indicated, ethyl chloroformate (0.65 g) is added dropwise. The mixture is subsequently left to stir at RT until the reaction is complete. When the reaction is complete, the mixture is worked up using ice-water and extracted with ethyl acetate. The organic phase is washed with 10% sodium bicarbonate solution and saturated NaCl solution. The organic phase is subsequently dried over sodium sulfate, filtered and evaporated. Purification by chromatography gives 300 mg (19%) of the product; LCMS: mass found ($M+1$, 262.2)

Method: A- 0.1% of TFA in H_2O , B-0.1% of TFA in ACN: flow-2.0 ml/min.
Column: X Bridge C8 (50 x 4.6 mm, 3.5 μ) + ve mode

Rt (min) : 3.84 area% 90.35 (max), 86.73 (220 nm).

12.3 2-Oxo-1-phenylazepane-3-carboxylic acid



LiOH x H₂O (111 mg) is added to a solution of ethyl 2-oxo-1-phenylazepane-3-carboxylate (300 mg) in THF/H₂O = 8:2 (15 ml), and the mixture is stirred for 1 h. When the reaction is complete, the solvent is removed in vacuo, and the mixture is neutralised using 1.5 N HCl solution. The aqueous solution is extracted with ethyl acetate, and the combined organic phases are dried over sodium sulfate, filtered and evaporated, giving the product with a yield of 97% (250 mg);

LCMS: mass found (M+1, 234.0)

20 Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN: flow-2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm, 3.5 µm) + ve mode

Rt (min) : 2.95 area% 97.57 (max), 97.38 (220 nm);

HPLC:

25 Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate: 2.0ml/min

Column: X Bridge C8 (50 x 4.6) mm, 3.5 µm

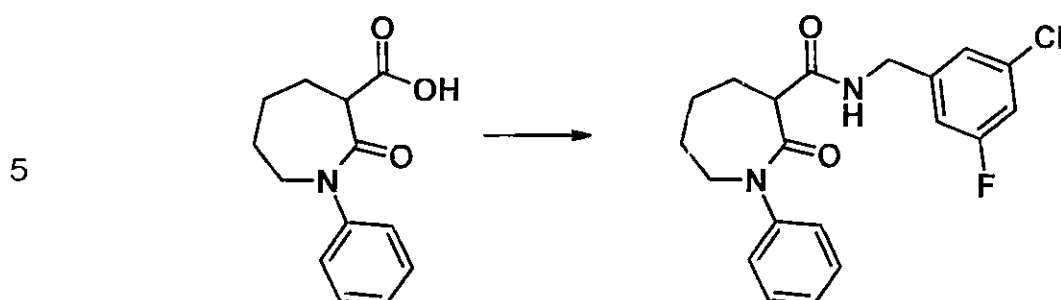
Rt (min) : 2.90 area% 99.67 (max), 99.24 (254 nm)

¹H NMR (400 MHz, DMSO-d₆): δ [ppm] 12.45 (s, 1H), 7.39-7.35 (m, 2H), 7.25-7.19 (m, 3H), 3.98-3.87 (m, 2H), 3.53-3.47 (m, 1H), 2.00 (m, 1H), 1.88 (m, 1H), 1.77-1.60 (m, 4H).

30

35

12.4 N-(3-Chloro-5-fluorobenzyl)-2-oxo-1-phenylazepane-3-carboxamide:



Triethylamine (0.74 ml) and propanephosphoric anhydride (T3P; 1.02 g) are added at 0°C to a solution of 2-oxo-1-phenylazepane-3-carboxylic acid (250 mg) and 3-chloro-5-fluorobenzylamine (205 mg) in dichloromethane (15 ml). When the reaction has been brought to completion at RT, the mixture is diluted with further dichloromethane and washed with 10% sodium bicarbonate solution and saturated NaCl solution. The organic phase is treated in the usual manner, and the residue is purified, giving the product as colourless solid in a yield of 87% (350 mg);

LCMS: mass found (M+1, 375.2)

Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN: flow-2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm, 3.5 μm) + ve mode

Rt (min) : 4.57 area% 98.66 (max), 97.22 (220 nm)

HPLC:

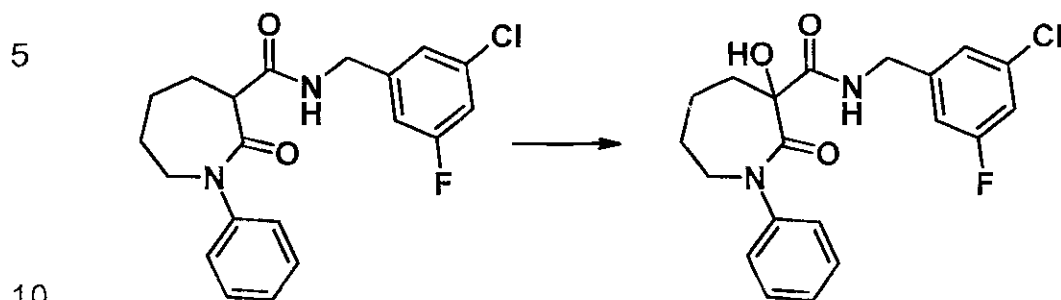
Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate: 2.0 ml/min

Column: XBridge C8 (50 x 4.6) mm, 3.5 μm

Rt (min) : 4.63 area% 97.55 (max), 97.87 (220 nm);

¹H NMR (400 MHz, DMSO-d₆): δ [ppm] 8.37-8.36 (m, 1H), 7.40-7.36 (m, 2H), 7.27-7.20 (m, 6H), 4.44-4.38 (m, 1H), 4.25-4.20 (m, 1H), 3.92-3.83 (m, 2H), 3.60-3.59 (m, 1H), 2.03-2.01 (m, 1H), 1.98-1.95 (m, 1H), 1.78-1.63 (m, 4H).

12.5 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide



Sodium ethoxide (20% in ethanol) (0.91 ml) and tert-butyl hydroperoxide (70% aqueous solution; 0.37 ml) are slowly added at 0°C to a solution of N-(3-chloro-5-fluorobenzyl)-2-oxo-1-phenylazepane-3-carboxamide (350 mg) in tert-butanol (10 ml). When the addition is complete, the mixture is stirred at 75°C for 1 h and, after completion, volatile constituents are removed in vacuo. The residue is taken up with water and ethyl acetate, the organic phase is treated as described, and the residue is purified on chiral HPLC.

"A66":

LCMS: mass found (M+1, 391.0)

Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN: flow - 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm, 3.5 μm) + ve mode

Rt (min) : 4.86 area% 98.24 (max), 94.59 (254nm)

HPLC:

Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate: 2.0 ml/min

Column: X Bridge C8 (50 x 4.6) mm, 3.5 μm

Rt (min) : 5.01 area% 99.39 (max), 96.44 (254 nm);

¹H NMR (400 MHz, DMSO-d₆) δ [ppm] 8.62 (t, J = 6.2 Hz, 1H), 7.39 (m, 2H), 7.26 (m, 2H), 7.22 (s, 1H), 7.17 (m, 2H), 7.13 (dd, J = 9.3, 1.8 Hz, 1H), 5.85 (s, 1H), 4.37 (dd, 1H), 4.27 (dd, 1H), 3.95 (dd, J = 14.5, 9.0 Hz, 1H), 3.77 (dd, J = 14.8, 5.4 Hz, 1H), 2.26 (m, 2H), 1.82 (m, 4H), 1.66 (m, 1H).

"A67":

LCMS: mass found (M+1, 391.0)

Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN: flow- 2.0 ml/min.

Column: X Bridge C8 (50 x 4.6 mm.3.5µm) + ve mode

Rt (min) : 4.86 area% 98.09 (max), 95.22 (254nm)

HPLC:

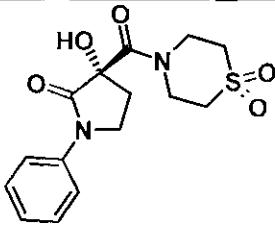
Method A: 0.1% of TFA in H₂O, B: 0.1% of TFA in ACN, flow rate -2.0 ml/min

Column: XBridge C8 (50 x 4.6 mm, 3.5 µm)

Rt (min) : 5.01 area% 99.15 (max), 96.19 (254 nm);

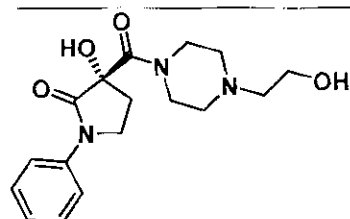
¹H NMR (400 MHz, DMSO-d₆) δ [ppm] 8.62 (t, J = 6.2 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.30 – 7.23 (m, 2H), 7.22 (s, 1H), 7.19 – 7.15 (m, 2H), 7.13 (d, J = 9.7 Hz, 1H), 5.85 (s, 1H), 4.37 (dd, J = 15.9, 6.4 Hz, 1H), 4.27 (dd, J = 15.8, 6.0 Hz, 1H), 4.01 – 3.88 (m, 1H), 3.78 (dd, J = 14.7, 5.6 Hz, 1H), 2.25 (m, 1H), 1.90 – 1.72 (m, 4H), 1.66 (m, 1H).

The following compounds are obtained analogously

No.	Structure / name	¹ H NMR (400 MHz, DMSO-d ₆) δ [ppm] * (DMSO-d ₆ + TFA-d ₁) ** 500 MHz	LC-MS; rt; [M+H ⁺]
"A56"	 (S)-3-(1,1-Dioxo-116-thiomorpholine-4-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one		3.73 [475.3]

5

"A57"



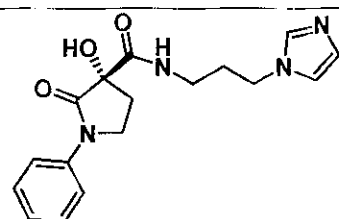
(S)-3-Hydroxy-3-[4-(2-hydroxyethyl)piperazine-1-carbonyl]-1-phenylpyrrolidin-2-one

1.87

[334.3]

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"A58"



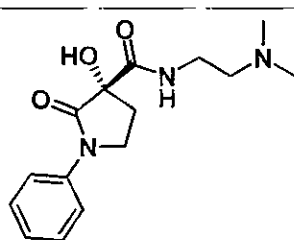
N-(3-Imidazol-1-ylpropyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide

1.87

[329.3]

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"A59"



N-(2-Dimethylaminoethyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide

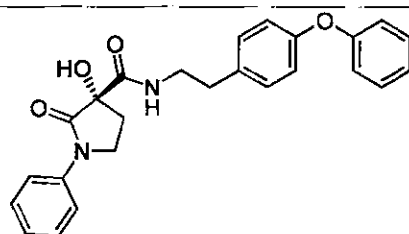
1.82

[292.3]

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"A60"



N-[2-(4-Phenoxyphenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide

4.75

[417.3]

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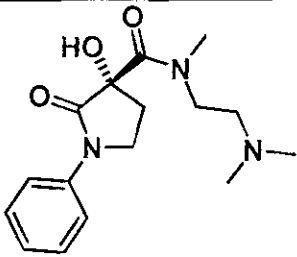
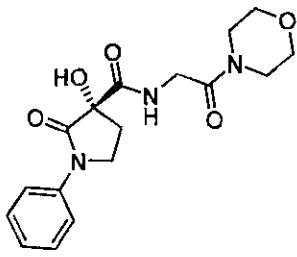
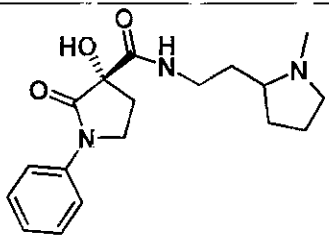
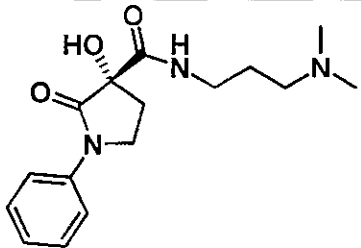
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"A61"	 N-(2-Dimethylaminoethyl)methyl-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide	1.94 [306.3]
"A62"	 N-(2-Morpholin-4-yl-2-oxoethyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide	2.18 [348.3]
"A63"	 N-[2-(1-Methylpyrrolidin-2-yl)ethyl]-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide	1.99 [332.3]
"A64"	 N-(3-Dimethylaminopropyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide	1.86 [306.3]

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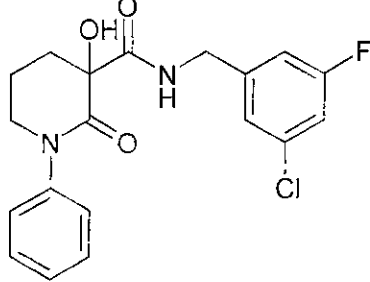
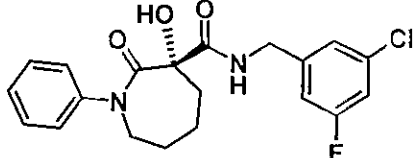
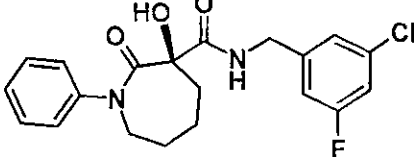
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"A65"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxamide	8.62 (t, $J = 6.2$ Hz, 1H), 7.39 (m, 2H), 7.26 (m, 2H), 7.22 (s, 1H), 7.17 (m, 2H), 7.13 (dd, $J = 9.3, 1.8$ Hz, 1H), 5.85 (s, 1H), 4.37 (dd, 1H), 4.27 (dd, 1H), 3.95 (dd, $J = 14.5, 9.0$ Hz, 1H), 3.77 (dd, $J = 14.8, 5.4$ Hz, 1H), 2.26 (m, 2H), 1.82 (m, 4H), 1.66 (m, 1H)	4.01 [377]
"A66"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide	8.62 (t, $J = 6.2$ Hz, 1H), 7.43 – 7.35 (m, 2H), 7.30 – 7.23 (m, 2H), 7.22 (s, 1H), 7.19 – 7.15 (m, 2H), 7.13 (d, $J = 9.7$ Hz, 1H), 5.85 (s, 1H), 4.37 (dd, $J = 15.9, 6.4$ Hz, 1H), 4.27 (dd, $J = 15.8, 6.0$ Hz, 1H), 4.01 – 3.88 (m, 1H), 3.78 (dd, $J = 14.7, 5.6$ Hz, 1H), 2.25 (m, 1H), 1.90 – 1.72 (m, 4H), 1.66 (m, 1H).	5.01 [391]
"A67"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide	11.11 (s, 1H), 8.71 (t, $J = 6.4$ Hz, 1H), 7.84 – 7.74 (m, 1H), 7.53 (d, $J = 8.6$ Hz, 1H), 7.38 – 7.29 (m, 1H), 7.29 – 7.20 (m, 3H), 7.12 (d, $J = 9.7$ Hz, 1H), 6.71 (s, 1H), 6.40 (ddd, $J = 2.9, 1.9, 0.8$ Hz, 1H), 4.40 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.89 (t, $J = 6.8$ Hz, 2H), 2.64 – 2.56 (m, 1H), 2.13 (m, 1H).	5.01 [391]

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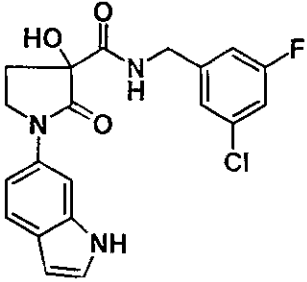
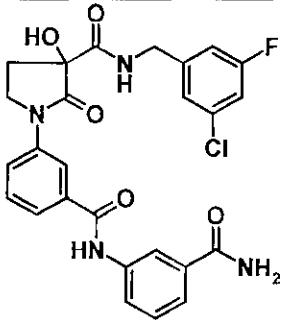
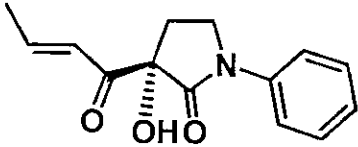
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"A68"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1H-indol-6-yl)-2-oxo-pyrrolidine-3-carboxamide	10.44 (s, 1H), 8.77 (s, 1H), 8.20 (d, $J = 20.2$ Hz, 2H), 7.96 (dd, $J = 22.7, 8.6$ Hz, 3H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.58 (dd, $J = 14.7, 7.5$ Hz, 2H), 7.42 (t, $J = 7.9$ Hz, 1H), 7.35 (s, 1H), 7.27 (d, $J = 9.0$ Hz, 1H), 7.21 (s, 1H), 7.11 (d, $J = 9.7$ Hz, 1H), 6.83 (s, 1H), 4.39 (d, $J = 14.9$ Hz, 1H), 4.26 (d, $J = 15.6$ Hz, 1H), 3.95 (t, $J = 6.7$ Hz, 2H), 2.69 – 2.57 (m, 1H), 2.22 – 2.10 (m, 1H).	4.13 [402]
"A69"	 N-(3-Chloro-5-fluorobenzyl)-1-[3-(3-carbamoylphenylcarbamoyl)-phenyl]-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	7.70 – 7.65 (m, 2H), 7.43 – 7.37 (m, 2H), 7.21 – 7.15 (m, 1H), 6.83 – 6.76 (m, 1H), 6.65 (s, 1H), 3.84 (td, $J = 9.2, 3.0$ Hz, 1H), 3.73 (dt, $J = 9.6, 7.5$ Hz, 1H), 2.57 – 2.50 (m, 1H), 2.13 – 2.03 (m, 1H), 1.90 (dd, $J = 6.7, 1.5$ Hz, 3H).	3.63 [525.2]
"A70"	 (S)-3-((E)-But-2-enoyl)-3-hydroxy-1-phenylpyrrolidin-2-one	8.62 (t, $J = 6.2$ Hz, 1H), 7.39 (m, 2H), 7.26 (m, 2H), 7.22 (s, 1H), 7.17 (m, 2H), 7.13 (dd, $J = 9.3, 1.8$ Hz, 1H), 5.85 (s, 1H), 4.37 (dd, 1H), 4.27 (dd, 1H), 3.95 (dd, $J = 14.5, 9.0$ Hz, 1H), 3.77 (dd, $J = 14.8, 5.4$ Hz, 1H), 2.26 (m, 2H), 1.82 (m, 4H), 1.66 (m, 1H)	3.26 [246]

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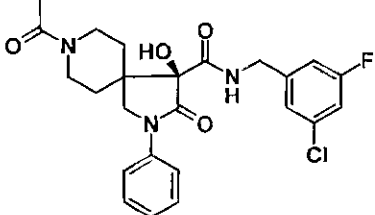
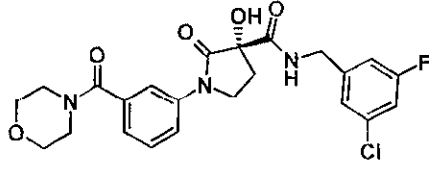
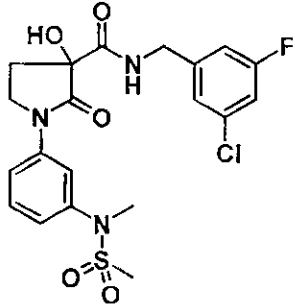
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"A71"	 N-(3-Chloro-5-fluorobenzyl)-(S)-8-acetyl-4-hydroxy-3-oxo-2-phenyl-2,8-diazaspiro[4.5]decane-4-carboxamide	3.78 (dd, $J = 13.6, 6.5$ Hz, 1H), 4.04 [474] 7.70 (d, $J = 8.5$ Hz, 2H), 7.40 (t, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.18 (dd, $J = 13.1, 5.8$ Hz, 2H), 7.09 (d, $J = 9.7$ Hz, 1H), 6.87 (d, $J = 3.9$ Hz, 1H), 4.39 – 4.27 (m, 1H), 4.25 – 4.13 (m, 2H), 4.08 (m, 1H), 3.86 (dd, $J = 9.5, 5.1$ Hz, 1H), 3.74 (m, 2H), 3.67 (m, 1H), 3.41 – 3.33 (m, 1H), 3.12 (m, 1H), 2.93 (m, 1H), 2.75 (s, 1H), 1.86 – 1.74 (m, 1H), 1.66 (m, 1H), 1.57 – 1.18 (m, 5H).
"A72"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(morpholine-4-carbonyl)phenyl]-2-oxopyrrolidine-3-carboxamide	3.67 [476] 8.74 (t, $J = 6.3$ Hz, 1H), 7.80 (s, 1H), 7.74 (d, $J = 8.1$ Hz, 1H), 7.48 (t, $J = 7.9$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.21 (d, $J = 4.1$ Hz, 2H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.6, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.6, 5.9$ Hz, 1H), 3.88 (t, $J = 7.0$ Hz, 2H), 3.61 (m, 6H), 3.38 (m, 2H), 2.65 – 2.55 (m, 1H), 2.22 – 2.08 (m, 1H).
"A73"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[3-(methanesulfonyl)-4-(methanesulfonyl)phenyl]-2-oxopyrrolidine-3-carboxamide	3.96 [470] 8.73 (t, $J = 6.4$ Hz, 1H), 7.77 (t, $J = 2.1$ Hz, 1H), 7.63 (dd, $J = 8.3, 1.3$ Hz, 1H), 7.44 (t, $J = 3.1$ Hz, 1H), 7.29 – 7.25 (m, 1H), 7.24 (dd, $J = 8.5, 1.8$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.79 (s, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.87

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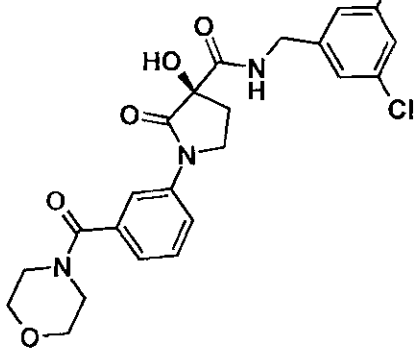
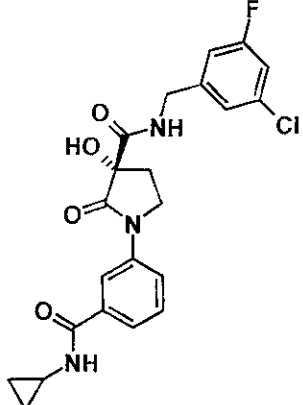
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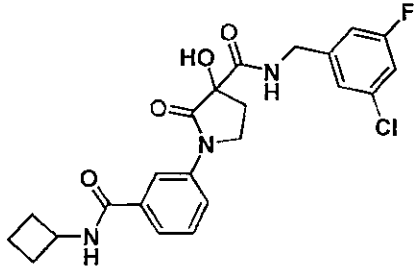
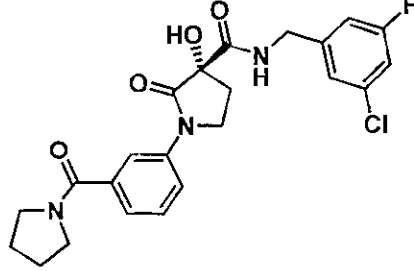
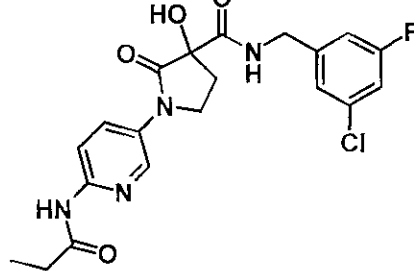
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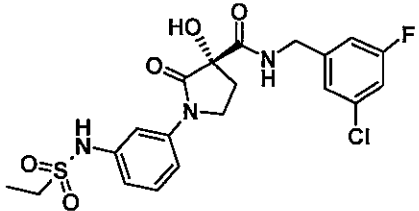
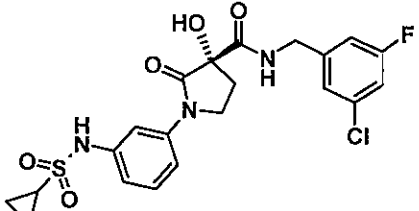
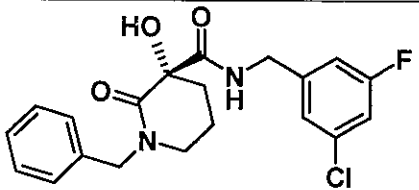
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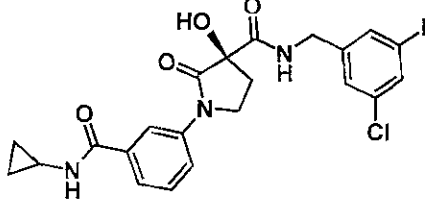
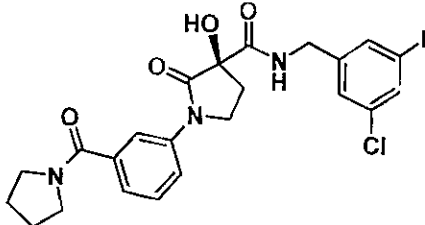
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	methlamino)phenyl]-2-oxo- pyrrolidine-3-carboxamide	(dd, $J = 8.8, 5.7$ Hz, 2H), 3.24 (s, 3H), 2.59 (dt, $J = 11.8, 5.6$ Hz, 1H), 2.13 (dt, $J = 12.9, 7.6$ Hz, 1H).	
"A74"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3- hydroxy-1-[3-(morpholine-4- carbonyl)phenyl]-2-oxopyrrolidine- 3-carboxamide	8.74 (t, $J = 6.4$ Hz, 1H), 7.82 – 7.78 (m, 1H), 7.73 (ddd, $J =$ 8.3, 2.3, 0.9 Hz, 1H), 7.48 (t, J $= 7.9$ Hz, 1H), 7.27 (dt, $J = 8.8,$ 2.2 Hz, 1H), 7.23 – 7.19 (m, 2H), 7.10 (d, $J = 8.8$ Hz, 1H), 6.80 (s, 1H), 4.38 (dd, $J =$ 15.7, 6.7 Hz, 1H), 4.24 (dd, $J =$ 15.8, 6.0 Hz, 1H), 3.88 (dd, $J =$ 8.4, 5.7 Hz, 2H), 3.61 (m, 7H), 3.43 – 3.35 (m, 1H), 2.64 – 2.55 (m, 1H), 2.13 (dt, $J =$ 12.9, 7.6 Hz, 1H).	3.67 [476]
"A75"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1- (3-cyclopropylcarbonylphenyl)-3- hydroxy-2-oxopyrrolidine-3- carboxamide	3.75 (t, $J = 6.4$ Hz, 1H), 8.49 (d, $J = 4.0$ Hz, 1H), 7.98 (t, $J =$ 1.8 Hz, 1H), 7.91 (dd, $J = 8.1,$ 1.4 Hz, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J =$ 9.5 Hz, 1H), 6.80 (s, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.89 (t, $J = 6.9$ Hz, 2H), 2.91 – 2.77 (m, 1H), 2.64 – 2.54 (m, 1H), 2.14 (dt, $J = 13.0, 7.7$ Hz, 1H), 0.69 (td, $J = 7.1, 4.7$ Hz, 2H), 0.59 – 0.53 (m, 2H).	3.84 [446]

5	"A76"	 N-(3-Chloro-5-fluorobenzyl)-1-(3-cyclobutylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.75 (t, $J = 6.3$ Hz, 1H), 8.66 (d, $J = 7.5$ Hz, 1H), 8.00 (s, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.64 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 7.9$ Hz, 1H), 7.27 (dd, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.80 (s, 1H), 4.48 – 4.33 (m, 2H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.91 (t, $J = 6.9$ Hz, 2H), 2.65 – 2.55 (m, 1H), 2.27 – 1.98 (m, 5H), 1.74 – 1.61 (m, 2H).	4.07 [460]
15	"A77"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-[3-(pyrrolidine-1-carbonyl)phenyl]pyrrolidine-3-carboxamide	3.75 (t, $J = 6.4$ Hz, 1H), 7.88 (s, 1H), 7.72 (dd, $J = 8.2, 1.4$ Hz, 1H), 7.46 (t, $J = 7.9$ Hz, 1H), 7.32 – 7.25 (m, 2H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.92 – 3.84 (m, 2H), 3.46 (t, $J = 6.8$ Hz, 2H), 3.37 (t, $J = 6.5$ Hz, 2H), 2.59 (dt, $J = 6.9, 5.7$ Hz, 1H), 2.13 (dt, $J = 13.0, 7.6$ Hz, 1H), 1.91 – 1.74 (m, 4H).	3.97 [460.2]
30	"A78"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(6-	10.48 (s, 1H), 8.75 (t, $J = 6.4$ Hz, 1H), 8.65 (s, 1H), 8.09 (dt, $J = 9.1, 5.8$ Hz, 2H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.4$ Hz, 1H), 6.80 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.86 (t, $J = 6.1$ Hz,	3.39 [435.2]

		propionylaminopyridin-3-yl)-pyrrolidine-3-carboxamide	2H), 2.65 – 2.56 (m, 1H), 2.38 (q, $J = 7.5$ Hz, 2H), 2.21 – 2.07 (m, 1H), 1.06 (t, $J = 7.5$ Hz, 3H)..	
5	"A79"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-ethanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.88 (s, 1H), 8.73 (t, $J = 6.4$ Hz, 1H), 7.70 (d, $J = 1.7$ Hz, 1H), 7.37 – 7.30 (m, 2H), 7.27 (dt, $J = 8.8, 2.2$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 8.9$ Hz, 1H), 7.05 – 7.00 (m, 1H), 6.79 (s, 1H), 4.37 (dd, $J = 16.0, 6.8$ Hz, 1H), 4.24 (dd, $J = 15.9, 6.0$ Hz, 1H), 3.81 (dd, $J = 13.0, 5.7$ Hz, 2H), 3.10 (q, $J = 7.4$ Hz, 2H), 2.63 – 2.53 (m, 1H), 2.18 – 2.05 (m, 1H), 1.18 (t, $J = 7.3$ Hz, 3H).	3.94 [470]
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20	"A80"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyclopropanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.82 (s, 1H), 8.73 (t, $J = 6.4$ Hz, 1H), 7.73 (s, 1H), 7.37 – 7.30 (m, 2H), 7.29 – 7.25 (m, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 7.06 – 7.02 (m, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.8, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.82 (m, 2H), 3.29 (m, 1H), 2.59 (m, 2H), 2.19 – 2.05 (m, 1H), 1.00 – 0.89 (m, 4H).	4.05 [482]
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35	"A81"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyl-3-hydroxy-2-oxopiperidine-3-carboxamide	8.60 (t, $J = 6.3$ Hz, 1H), 7.36 – 7.29 (m, 2H), 7.26 (d, $J = 7.6$ Hz, 5H), 7.16 (d, $J = 9.9$ Hz, 1H), 6.38 (s, 1H), 4.59 (d, $J = 15.1$ Hz, 1H), 4.47 (d, $J = 15.1$ Hz, 1H), 4.40 (dd, $J = 15.9, 7.0$	4.55 [391.2]

		3-carboxamide	Hz, 1H), 4.24 (dd, $J = 15.9, 5.7$ Hz, 1H), 3.28 – 3.15 (m, 2H), 2.25 – 2.11 (m, 1H), 1.83 (m, 3H), 1.21 (m, 2H).	
5	"A82"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclopropylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 8.49 (d, $J = 4.0$ Hz, 1H), 7.98 (s, 1H), 7.94 – 7.87 (m, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.4$ Hz, 1H), 6.80 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.89 (t, $J = 6.8$ Hz, 2H), 2.89 – 2.78 (m, 1H), 2.64 – 2.55 (m, 1H), 2.14 (dt, $J = 13.0, 7.6$ Hz, 1H), 0.69 (td, $J = 7.1, 4.7$ Hz, 2H), 0.60 – 0.50 (m, 2H).	3.84 [446]
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25	"A83"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-[3-(pyrrolidine-1-carbonyl)phenyl]pyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 7.88 (s, 1H), 7.76 – 7.69 (m, 1H), 7.46 (t, $J = 7.9$ Hz, 1H), 7.29 (m, 2H), 7.24 – 7.15 (m, 1H), 7.10 (d, $J = 9.2$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.92 – 3.85 (m, 1H), 3.46 (t, $J = 6.8$ Hz, 1H), 3.37 (t, $J = 6.5$ Hz, 2H), 2.64 – 2.55 (m, 1H), 2.13 (dt, $J = 13.0, 7.8$ Hz, 1H), 1.92 – 1.74 (m, 3H).	3.97 [460.2]
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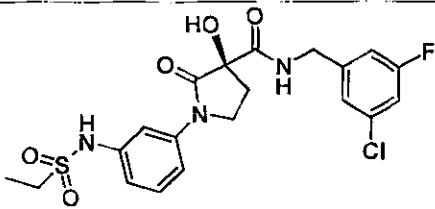
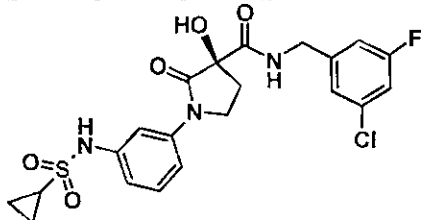
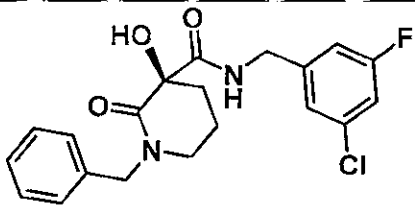
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"A84"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-ethanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.88 (s, 1H), 8.73 (t, $J = 6.4$ Hz, 1H), 7.70 (s, 1H), 7.34 (m, 2H), 7.27 (dt, $J = 8.8, 2.2$ Hz, 1H), 7.20 (s, 1H), 7.09 (m, 1H), 7.03 (dt, $J = 5.0, 2.2$ Hz, 1H), 6.79 (s, 1H), 4.37 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.82 (dd, $J = 13.0, 5.6$ Hz, 2H), 3.10 (q, $J = 7.4$ Hz, 2H), 2.56 (dd, $J = 13.0, 7.4$ Hz, 1H), 2.16 – 2.06 (m, 1H), 1.18 (t, $J = 7.4$ Hz, 3H).	3.94 [470]
"A85"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclopropanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.82 (s, 1H), 8.73 (t, $J = 6.4$ Hz, 1H), 7.73 (s, 1H), 7.33 (d, $J = 5.1$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.9$ Hz, 1H), 7.04 (dd, $J = 7.1, 4.0$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.6, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.82 (m, 2H), 2.59 (m, 2H), 2.13 (m, 1H), 1.01 – 0.79 (m, 4H).	4.05 [482]
"A86"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyl-3-hydroxy-2-oxopiperidine-3-carboxamide	8.60 (t, $J = 6.1$ Hz, 1H), 7.36 – 7.29 (m, 2H), 7.26 (d, $J = 7.7$ Hz, 5H), 7.16 (d, $J = 9.8$ Hz, 1H), 6.38 (s, 1H), 4.59 (d, $J = 15.0$ Hz, 1H), 4.47 (d, $J = 15.3$ Hz, 1H), 4.40 (dd, $J = 15.9, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.9, 5.6$ Hz, 1H), 3.28 – 3.14 (m, 2H), 2.17 (dd, $J = 15.1, 10.1$ Hz, 1H), 1.83 (s, 3H).	4.55 [391.2]

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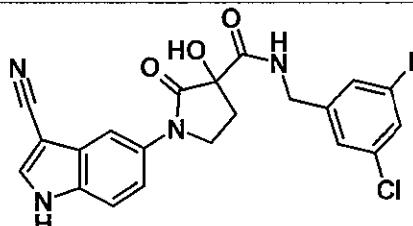
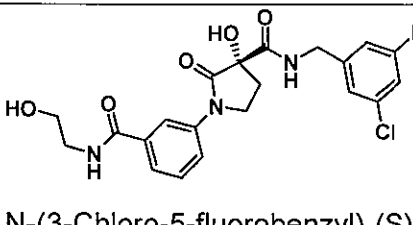
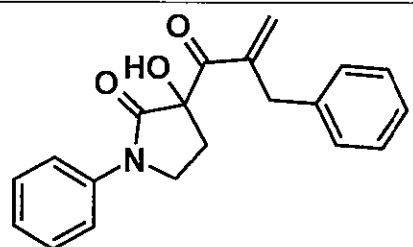
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"A87"	 N-(3-Chloro-5-fluorobenzyl)-1-(3-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.74 (t, $J = 6.3$ Hz, 1H), 8.27 (s, 1H), 7.90 (d, $J = 1.8$ Hz, 1H), 7.61 (dd, $J = 8.9, 1.9$ Hz, 1H), 7.57 (d, $J = 8.9$ Hz, 1H), 7.27 (d, $J = 8.8$ Hz, 1H), 7.22 (s, 1H), 7.11 (d, $J = 9.9$ Hz, 1H), 6.76 (s, 1H), 4.39 (dd, $J = 15.7, 6.6$ Hz, 1H), 4.25 (dd, $J = 15.6, 6.0$ Hz, 1H), 3.93 (t, $J = 7.2$ Hz, 2H), 2.65 – 2.57 (m, 1H), 2.20 – 2.08 (m, 1H).	3.82 [427]
"A88"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(2-hydroxyethylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.3$ Hz, 1H), 8.50 (t, $J = 5.5$ Hz, 1H), 8.02 (s, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 8.0$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.1$ Hz, 1H), 6.80 (s, 1H), 4.73 (t, $J = 5.6$ Hz, 1H), 4.38 (dd, $J = 15.6, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 3.50 (q, $J = 6.1$ Hz, 2H), 2.60 (dt, $J = 11.8, 5.8$ Hz, 1H), 2.21 – 2.08 (m, 1H).	3.16 [450]
"A89"	 3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one		4.63 [322]

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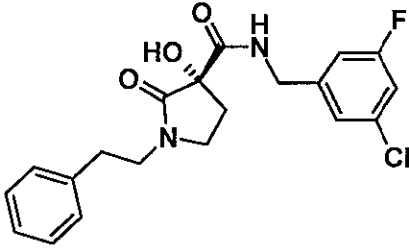
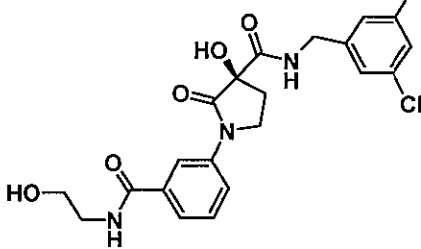
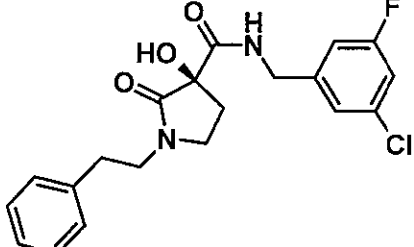
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"A90"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-phenethylpyrrolidine-3-carboxamide	3.61 (d, $J = 6.4$ Hz, 1H), 7.40 – 7.23 (m, 5H), 7.20 (s, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 6.53 (d, $J = 15.8$ Hz, 1H), 5.21 (dd, $J = 10.1, 7.1$ Hz, 1H), 4.37 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.04 – 2.93 (m, 1H), 2.45 – 2.36 (m, 1H), 2.00 – 1.84 (m, 1H), 1.50 (d, $J = 7.2$ Hz, 1H), 1.45 (d, $J = 7.2$ Hz, 1H).	4.36 [391]
"A91"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(2-hydroxyethylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 8.50 (t, $J = 5.6$ Hz, 1H), 8.02 (s, 1H), 7.96 – 7.88 (m, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 7.9$ Hz, 1H), 7.27 (dd, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.80 (s, 1H), 4.73 (t, $J = 5.6$ Hz, 1H), 4.38 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 3.50 (q, $J = 6.1$ Hz, 2H), 2.65 – 2.56 (m, 1H), 2.20 – 2.09 (m, 1H).	3.16 [450]
"A92"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-phenethylpyrrolidine-3-carboxamide	8.61 (t, $J = 6.3$ Hz, 1H), 7.40 – 7.23 (m, 5H), 7.20 (s, 1H), 7.10 (d, $J = 9.8$ Hz, 1H), 6.51 (s, 1H), 5.20 (q, $J = 7.4$ Hz, 1H), 4.37 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.40 – 3.33 (m, 1H), 2.98 (td, $J = 8.8, 3.4$ Hz, 1H), 2.45 – 2.35 (m, 1H), 1.96 – 1.83 (m, 1H), 1.45 (d, $J = 7.2$ Hz, 2H).	4.36 [391]

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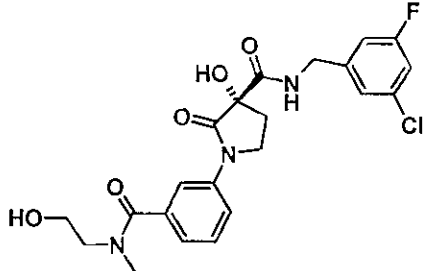
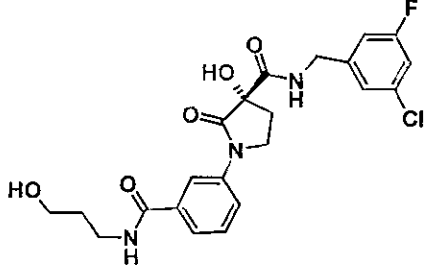
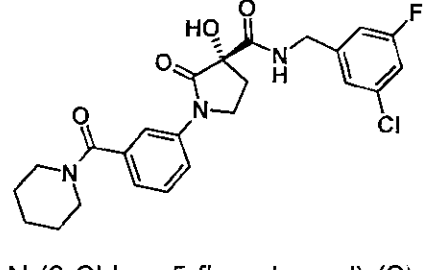
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"A93"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-[(2-hydroxyethyl)methylcarbamoyl]phenyl]-2-oxopyrrolidine-3-carboxamide	8.74 (t, $J = 6.4$ Hz, 1H), 7.73 (s, 2H), 7.45 (d, $J = 7.3$ Hz, 1H), 7.31 – 7.25 (m, 1H), 7.19 (d, $J = 7.4$ Hz, 2H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.79 (s, 1H), 4.79 (t, $J = 5.5$ Hz, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.87 (m, 2H), 3.61 (m, 1H), 3.48 (m, 2H), 3.26 (m, 1H), 2.95 (s, 3H), 2.58 (m, 1H), 2.20 – 2.07 (m, 1H).	3.21 [464]
"A94"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(3-hydroxypropylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 8.50 (t, $J = 5.6$ Hz, 1H), 8.01 (d, $J = 1.7$ Hz, 1H), 7.95 – 7.88 (m, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 7.9$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.80 (s, 1H), 4.47 (t, $J = 5.2$ Hz, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.8, 3.1$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 3.45 (dd, $J = 11.6, 6.2$ Hz, 2H), 3.30 – 3.26 (m, 1H), 2.65 – 2.55 (m, 1H), 2.22 – 2.09 (m, 1H), 1.72 – 1.62 (m, 2H).	3.24 [464.2]
"A95"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(piperidin-1-yl)carbamoyl]phenyl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 7.81 – 7.77 (m, 1H), 7.69 (dd, $J = 8.3, 1.4$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.16 (d, $J = 7.7$ Hz, 1H), 7.10 (d, $J =$	4.15 [474]

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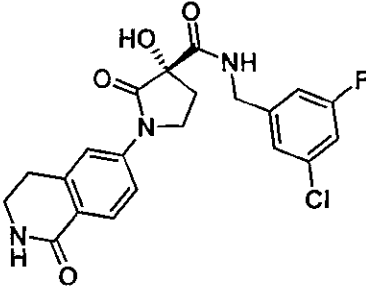
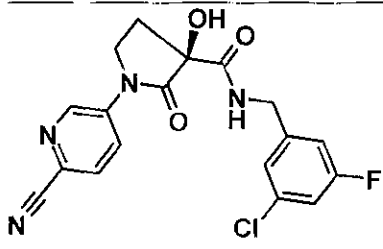
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	3-hydroxy-2-oxo-1-[3-(piperidin-1-carbonyl)phenyl]pyrrolidine-3-carboxamide	9.7 Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.8, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.94 – 3.83 (m, 2H), 3.57 (m, 2H), 3.26 (m, 2H), 2.64 – 2.55 (m, 1H), 2.13 (dt, $J = 13.0, 7.6$ Hz, 1H), 1.69 – 1.34 (m, 6H).	
"A96"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-6-yl)pyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 7.91 – 7.81 (m, 2H), 7.71 (dd, $J = 8.6, 2.1$ Hz, 1H), 7.63 (s, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.5$ Hz, 1H), 6.82 (s, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.89 (m, 2H), 3.40 – 3.33 (m, 2H), 2.91 (t, $J = 6.6$ Hz, 2H), 2.64 – 2.55 (m, 1H), 2.14 (dt, $J = 13.0, 7.7$ Hz, 1H).	3.38 [432]
"A97"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(6-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.12 (d, $J = 2.4$ Hz, 1H), 8.82 (t, $J = 6.4$ Hz, 1H), 8.38 (dd, $J = 8.7, 2.6$ Hz, 1H), 8.10 (d, $J = 8.7$ Hz, 1H), 7.28 (d, $J = 8.8$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.1$ Hz, 1H), 6.96 (s, 1H), 4.37 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.1$ Hz, 1H), 4.02 – 3.85 (m, 2H), 2.66 – 2.58 (m, 1H), 2.19 (dt, $J = 13.1, 7.7$ Hz, 1H).	3.84 [389]

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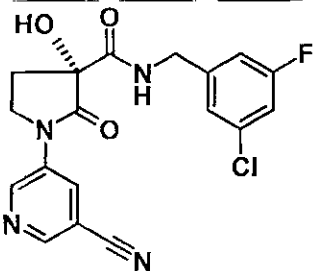
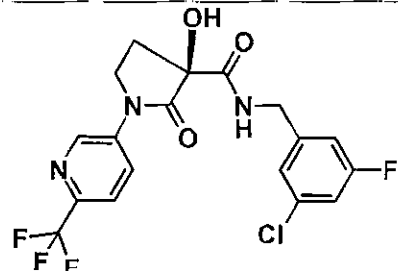
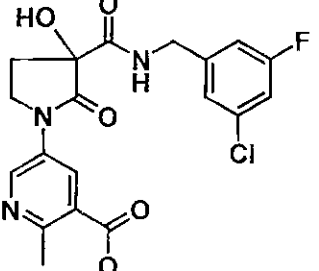
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"A98"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(5-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.28 (d, $J = 2.6$ Hz, 1H), 8.83 (d, $J = 1.8$ Hz, 1H), 8.80 (d, $J = 6.4$ Hz, 1H), 8.61 – 8.55 (m, 1H), 7.28 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.5$ Hz, 1H), 6.93 (s, 1H), 4.37 (dd, $J = 15.7, 6.9$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.94 (m, 2H), 3.40 – 3.34 (m, 1H), 2.62 (m, 1H), 2.27 – 2.12 (m, 1H).	3.63 [389]
"A99"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(6-trifluoromethylpyridin-3-yl)pyrrolidine-3-carboxamide	9.10 (d, $J = 2.4$ Hz, 1H), 8.81 (t, $J = 6.3$ Hz, 1H), 8.44 (dd, $J = 8.6, 2.2$ Hz, 1H), 7.97 (d, $J = 8.7$ Hz, 1H), 7.28 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.94 (s, 1H), 4.38 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.02 – 3.91 (m, 2H), 3.40 – 3.34 (m, 1H), 2.65 – 2.55 (m, 1H), 2.20 (dt, $J = 13.2, 7.8$ Hz, 2H).	4.44 [432]
"A100"	 Methyl 5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-2-methylnicotinate	8.88 (d, $J = 2.7$ Hz, 1H), 8.79 (t, $J = 6.4$ Hz, 1H), 8.59 (d, $J = 2.7$ Hz, 1H), 7.28 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.0$ Hz, 1H), 6.87 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.94 (m, 2H), 3.87 (s, 3H), 2.69 (s, 3H), 2.61 (m, 1H), 2.21 – 2.11 (m, 1H).	3.35 [436]

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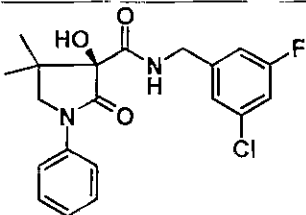
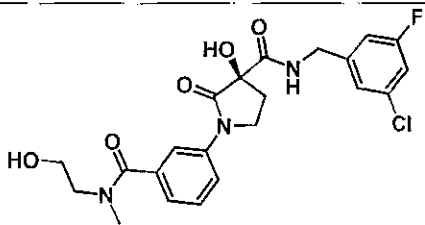
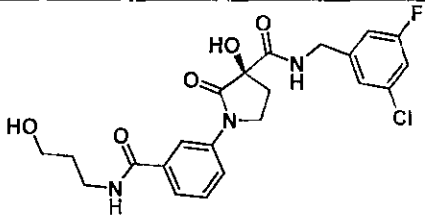
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"A101"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxamide	8.72 (t, $J = 6.3$ Hz, 1H), 7.65 (d, $J = 7.7$ Hz, 2H), 7.44 – 7.35 (m, 2H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.16 (t, $J = 7.4$ Hz, 1H), 7.09 (d, $J = 9.0$ Hz, 1H), 6.68 (s, 1H), 4.31 (dd, $J = 15.5, 6.5$ Hz, 1H), 4.22 (dd, $J = 15.5, 6.2$ Hz, 1H), 3.77 (d, $J = 8.9$ Hz, 1H), 3.41 (d, $J = 8.9$ Hz, 1H), 1.06 (s, 3H), 1.01 (s, 3H).	4.92 [391]
"A102"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-{3-[(2-hydroxyethyl)methylcarbamoyl]phenyl}-2-oxopyrrolidine-3-carboxamide	8.74 (t, $J = 6.4$ Hz, 1H), 7.73 (s, 2H), 7.45 (d, $J = 7.2$ Hz, 1H), 7.31 – 7.25 (m, 1H), 7.19 (d, $J = 7.4$ Hz, 2H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.79 (s, 1H), 4.79 (t, $J = 5.4$ Hz, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.87 (m, 2H), 3.62 (m, 1H), 3.49 (m, 2H), 3.27 (m, 1H), 2.95 (s, 3H), 2.64 – 2.53 (m, 1H), 2.21 – 2.05 (m, 1H).	3.21 [464]
"A103"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(3-hydroxypropylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 8.50 (t, $J = 5.6$ Hz, 1H), 8.02 (s, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 8.0$ Hz, 1H), 7.27 (d, $J = 3.8$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.2$ Hz, 1H), 6.80 (s, 1H), 4.47 (t, $J = 5.2$ Hz, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 3.45	3.24 [464]

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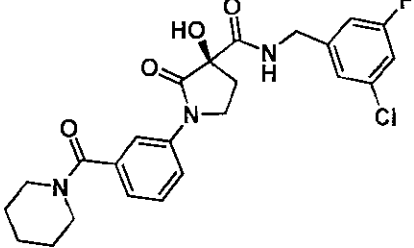
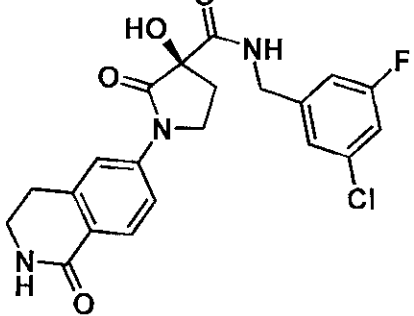
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		(dd, $J = 11.6, 6.2$ Hz, 2H), 3.30 – 3.26 (m, 1H), 2.64 – 2.55 (m, 1H), 2.24 – 2.09 (m, 1H), 1.75 – 1.59 (m, 2H).	
"A104"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-[3-(piperidin-1-carbonyl)phenyl]pyrrolidine-3-carboxamide	8.75 (t, $J = 6.3$ Hz, 1H), 7.79 (s, 1H), 7.69 (d, $J = 8.1$ Hz, 1H), 7.47 (t, $J = 7.9$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.16 (d, $J = 7.6$ Hz, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.88 (m, 2H), 3.57 (m, 2H), 3.26 (m, 2H), 2.64 – 2.53 (m, 1H), 2.20 – 2.08 (m, 1H), 1.70 – 1.37 (m, 6H).	4.15 [474]
"A105"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-6-yl)pyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 1H), 7.91 – 7.81 (m, 2H), 7.71 (dd, $J = 8.6, 2.1$ Hz, 1H), 7.63 (d, $J = 1.9$ Hz, 1H), 7.30 – 7.24 (m, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.9$ Hz, 1H), 6.82 (s, 1H), 4.37 (dt, $J = 12.6, 6.3$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.89 (m, 2H), 3.36 (td, $J = 6.8, 2.7$ Hz, 3H), 2.91 (t, $J = 6.5$ Hz, 2H), 2.63 – 2.53 (m, 1H), 2.21 – 2.07 (m, 1H).	3.38 [432]

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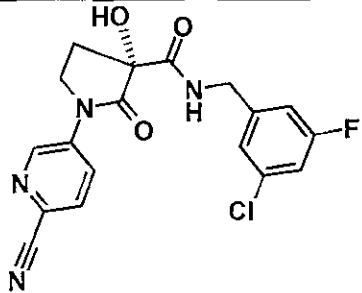
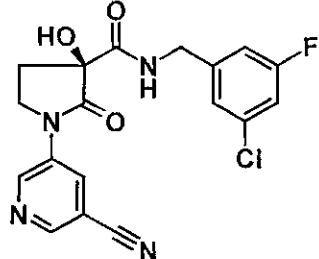
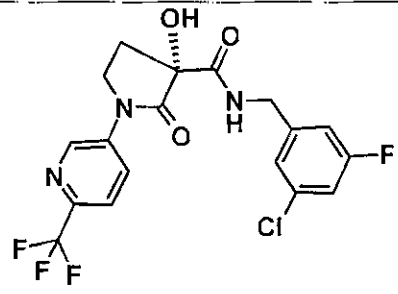
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"A106"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(6-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.13 (s, 1H), 8.83 (d, $J = 6.3$ Hz, 1H), 8.38 (d, $J = 8.6$ Hz, 1H), 8.10 (d, $J = 8.6$ Hz, 1H), 7.28 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.9$ Hz, 1H), 6.96 (s, 1H), 4.37 (dd, $J = 15.6, 6.5$ Hz, 1H), 4.25 (dd, $J = 15.6, 6.1$ Hz, 1H), 3.94 (m, 2H), 2.71 – 2.59 (m, 1H), 2.27 – 2.10 (m, 1H).	3.84 [389]
"A107"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(5-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	9.28 (d, $J = 2.6$ Hz, 1H), 8.82 (dd, $J = 11.5, 4.1$ Hz, 2H), 8.58 (dd, $J = 2.5, 1.8$ Hz, 1H), 7.28 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 8.8$ Hz, 1H), 6.94 (s, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.94 (m, 2H), 2.65 – 2.58 (m, 1H), 2.25 – 2.09 (m, 1H).	3.79 [389]
"A108"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(6-(trifluoromethyl)pyridin-3-yl)pyrrolidine-3-carboxamide	9.10 (d, $J = 2.5$ Hz, 1H), 8.82 (t, $J = 6.4$ Hz, 1H), 8.44 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.97 (d, $J = 8.7$ Hz, 1H), 7.28 (dt, $J = 8.8, 2.2$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.95 (s, 1H), 4.38 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.25 (dd, $J = 15.9, 6.1$ Hz, 1H), 4.04 – 3.91 (m, 2H), 2.67 – 2.58 (m, 1H), 2.20 (dt, $J = 13.1, 7.7$ Hz, 1H).	4.43 [432]

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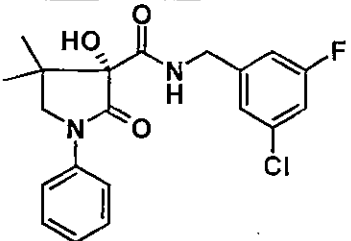
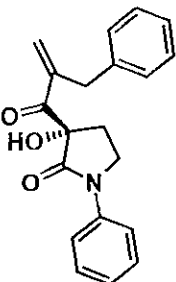
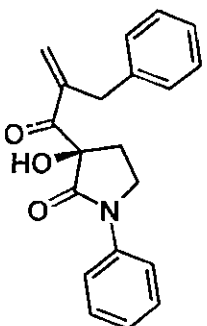
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"A109"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxamide	8.72 (t, $J = 6.3$ Hz, 1H), 7.65 (d, $J = 7.8$ Hz, 2H), 7.39 (t, $J = 8.0$ Hz, 2H), 7.31 – 7.23 (m, 1H), 7.20 (s, 1H), 7.16 (t, $J = 7.4$ Hz, 1H), 7.09 (d, $J = 9.5$ Hz, 1H), 6.68 (s, 1H), 4.31 (dd, $J = 15.5, 6.5$ Hz, 1H), 4.22 (dd, $J = 15.5, 6.2$ Hz, 1H), 3.77 (d, $J = 8.9$ Hz, 1H), 3.41 (d, $J = 8.9$ Hz, 1H), 1.06 (s, 3H), 1.01 (s, 3H).	4.92 [391]
"A110"	 (S)-3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one	7.69 – 7.62 (m, 2H), 7.43 – 7.36 (m, 2H), 7.26 (t, $J = 7.3$ Hz, 2H), 7.22 – 7.14 (m, 4H), 6.79 (s, 1H), 6.66 (s, 1H), 5.91 (d, $J = 1.0$ Hz, 1H), 3.81 (td, $J = 9.2, 2.7$ Hz, 1H), 3.63 – 3.55 (m, 1H), 3.54 (s, 2H), 2.54 (m, 1H), 2.14 (dt, $J = 13.0, 8.5$ Hz, 1H).	4.61 [322.3]
"A111"	 (R)-3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one	7.69 – 7.62 (m, 2H), 7.43 – 7.36 (m, 2H), 7.26 (t, $J = 7.3$ Hz, 2H), 7.22 – 7.12 (m, 4H), 6.79 (s, 1H), 6.66 (s, 1H), 5.91 (d, $J = 0.9$ Hz, 1H), 3.81 (td, $J = 9.3, 2.6$ Hz, 1H), 3.58 (m, 1H), 3.54 (s, 2H), 2.57 – 2.51 (m, 1H), 2.14 (dt, $J = 13.0, 8.4$ Hz, 1H).	4.61 [322.3]

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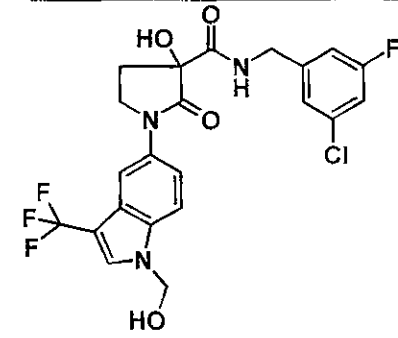
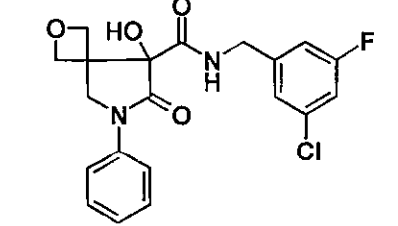
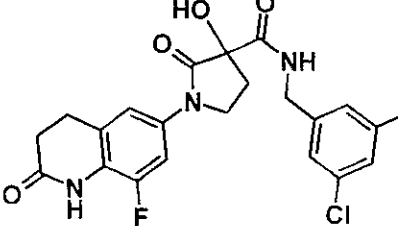
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"A112"  N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-hydroxymethyl-3-trifluoromethyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	8.73 (t, $J = 6.4$ Hz, 1H), 8.08 (s, 1H), 7.92 (s, 1H), 7.73 (d, $J = 9.0$ Hz, 1H), 7.57 (dd, $J = 9.0, 2.0$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.22 (s, 1H), 7.11 (d, $J = 9.4$ Hz, 1H), 6.75 (s, 1H), 6.70 (t, $J = 7.4$ Hz, 1H), 5.58 (d, $J = 7.4$ Hz, 2H), 4.39 (dd, $J = 15.7, 6.6$ Hz, 1H), 4.26 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.92 (t, $J = 6.7$ Hz, 2H), 3.36 (m, 1H), 2.66 – 2.56 (m, 1H), 2.20 – 2.08 (m, 1H).	4.4 [500]
"A113"  N-(3-Chloro-5-fluorobenzyl)-8-hydroxy-7-oxo-6-phenyl-2-oxa-6-azaspiro[3.4]octane-8-carboxamide	8.97 (t, $J = 6.3$ Hz, 1H), 7.69 (d, $J = 7.9$ Hz, 2H), 7.41 (t, $J = 7.9$ Hz, 2H), 7.29 – 7.25 (m, 1H), 7.25 (s, 1H), 7.22 – 7.15 (m, 2H), 7.06 (d, $J = 9.4$ Hz, 1H), 4.95 (d, $J = 6.1$ Hz, 1H), 4.48 (d, $J = 6.8$ Hz, 1H), 4.44 (d, $J = 6.8$ Hz, 1H), 4.38 (d, $J = 6.1$ Hz, 1H), 4.28 (m, 4H).	4.19 [405]
"A114"  N-(3-Chloro-5-fluorobenzyl)-1-(8-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.14 (s, 1H), 8.74 (s, 1H), 7.59 (dd, $J = 12.9, 1.9$ Hz, 1H), 7.34 – 7.24 (m, 2H), 7.20 (s, 1H), 7.09 (d, $J = 9.4$ Hz, 1H), 6.78 (s, 1H), 4.37 (d, $J = 15.6$ Hz, 1H), 4.23 (d, $J = 15.6$ Hz, 1H), 3.81 (m, 2H), 2.93 (t, $J = 7.4$ Hz, 2H), 2.63 – 2.52 (m, 1H), 2.18 – 2.04 (m, 1H).	3.68 [450]

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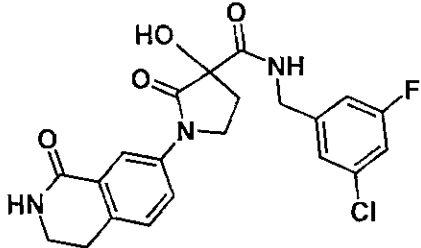
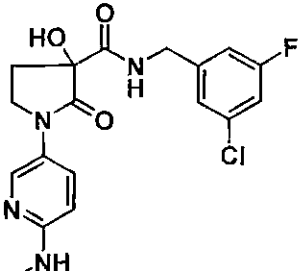
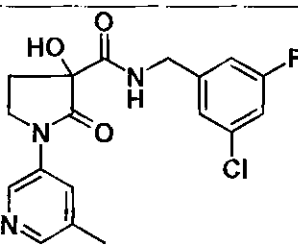
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"A115"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)-pyrrolidine-3-carboxamide	10.12 (s, 1H), 8.72 (t, $J = 6.4$ Hz, 1H), 7.31 (s, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.17 (s, 1H), 7.15 – 7.11 (m, 1H), 7.09 (d, $J = 9.7$ Hz, 1H), 6.75 (s, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.78 m, 2H), 2.84 (t, $J = 7.5$ Hz, 2H), 2.60 – 2.53 (m, 1H), 2.46 – 2.38 (m, 2H), 2.16 – 2.05 (m, 1H).	3.57 [432]
"A116"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-methylaminopyridin-3-yl)-2-oxopyrrolidine-3-carboxamide	8.69 (t, $J = 6.3$ Hz, 1H), 8.17 (d, $J = 2.6$ Hz, 1H), 7.71 (dd, $J = 9.0, 2.7$ Hz, 1H), 7.27 (d, $J = 8.8$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.69 (s, 1H), 6.52 (d, $J = 4.8$ Hz, 1H), 5.47 (d, $J = 9.0$ Hz, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.75 (t, $J = 6.7$ Hz, 2H), 2.75 (d, $J = 4.9$ Hz, 3H), 2.63 – 2.52 (m, 1H), 2.17 – 2.04 (m, 1H).	2.83 [393.2]
"A117"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(5-methylpyridin-3-yl)-2-oxopyrrolidine-3-carboxamide	8.77 (t, $J = 6.3$ Hz, 1H), 7.95 (s, 2H), 7.31 – 7.25 (m, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.83 (s, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.87 (t, $J = 6.1$ Hz, 2H), 2.65 – 2.56 (m, 1H), 2.33 (s, 3H), 2.15 (dt, $J = 13.1, 7.6$ Hz, 1H).	2.9 [378]

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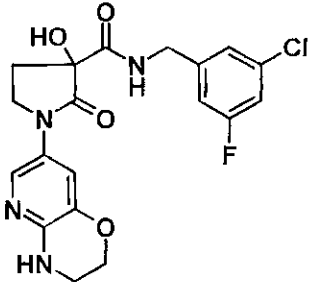
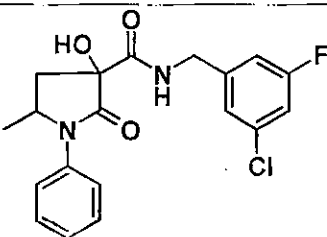
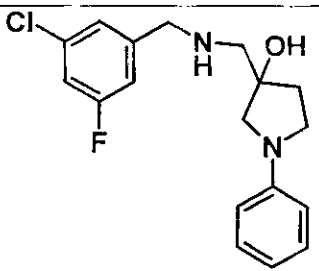
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"A118"	 N-(3-Chloro-5-fluorobenzyl)-1-(3,4-Dihydro-2H-pyrido[3,2-b]-1,4-oxazin-7-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.69 (t, $J = 6.3$ Hz, 1H), 7.79 (d, $J = 2.1$ Hz, 1H), 7.38 (d, $J = 2.0$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.74 (s, 1H), 6.70 (s, 1H), 4.38 (dd, $J = 15.7, 6.9$ Hz, 1H), 4.23 (dd, $J = 15.7, 6.1$ Hz, 1H), 4.17 – 4.04 (m, 2H), 3.75 (t, $J = 6.6$ Hz, 2H), 3.36 (m, 2H), 2.62 – 2.52 (m, 1H), 2.08 (dt, $J = 14.9, 7.6$ Hz, 1H).	3.06 [421]
"A119"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-5-methyl-2-oxo-1-phenylpyrrolidine-3-carboxamide	8.72 (dt, $J = 24.7, 6.3$ Hz, 1H), 7.50 – 7.31 (m, 4H), 7.31 – 7.17 (m, 3H), 7.11 (dd, $J = 29.9, 9.3$ Hz, 1H), 6.73 (s, 1H), 4.50 – 4.32 (m, 2H), 4.32 – 4.19 (m, 1H), 2.78 (dd, $J = 13.2, 7.1$ Hz, 1H), 2.36 (dd, $J = 13.2, 7.4$ Hz, 1H), 2.26 (dd, $J = 13.5, 6.4$ Hz, 1H), 1.75 (dd, $J = 13.0, 6.9$ Hz, 1H), 1.13 (dd, $J = 6.2, 1.7$ Hz, 3H).	4.27 [377]
"A120"	 3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-phenylpyrrolidin-3-ol	7.31 (1 H, s), 7.23 (2 H, dd, $J = 11.9, 9.8$), 7.13 (2 H, t, $J = 7.8$), 6.56 (1 H, t, $J = 7.2$), 6.46 (2 H, d, $J = 8.1$), 4.86 (2 H, bs, $J = 166.8$), 3.81 (2 H, s), 3.30 (3 H, m), 3.11 (1 H, d, $J = 10.0$), 2.00 (1 H, dt, $J = 12.4, 8.6$), 1.90 (1 H, m).	1.69 [335.0]

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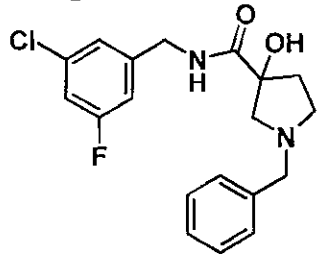
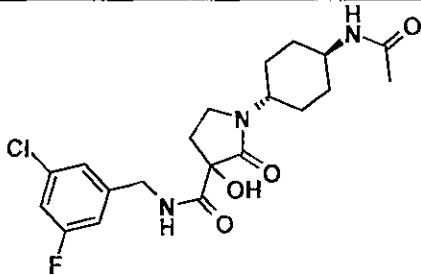
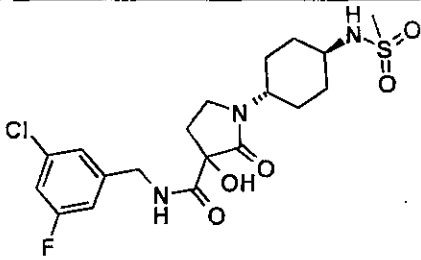
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"A121"	 N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypyrrolidine-3-carboxamide	7.58 (2 H, s), 7.47 (3 H, d, J 2.3), 7.20 (2 H, d, J 10.6), 7.10 (1 H, d, J 9.2), 4.48 (2 H, s), 4.37 (2 H, s), 3.68 (2 H, m), 3.42 (2 H, m), 2.29 (2 H, m).	1.56 [363.0]
"A122"	 N-(3-Chloro-5-fluorobenzyl)-1-(4-acetylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.52 (t, J = 6.4 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.25 (dt, J = 8.8, 2.1 Hz, 1H), 7.19 (s, 1H), 7.11 – 7.05 (m, 1H), 6.40 (s, 1H), 4.36 (dd, J = 15.8, 6.8 Hz, 1H), 4.21 (dd, J = 15.8, 6.0 Hz, 1H), 3.67 (m, 1H), 3.48 (m, 1H), 3.38 – 3.30 (m, 2H), 2.50 (s, 3H), 2.42 (m, 1H), 1.91 (m, 1H), 1.88 – 1.79 (m, 2H), 1.63 – 1.50 (m, 4H), 1.31 – 1.17 (m, 2H).	1.74 [426.1]
"A123"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methanesulfonylamino-cyclohexyl)-2-oxopyrrolidine-3-carboxamide	8.53 (t, J = 6.4 Hz, 1H), 7.27 (dt, J = 8.7, 2.1 Hz, 1H), 7.20 (s, 1H), 7.10 (d, J = 9.0 Hz, 1H), 7.01 (d, J = 7.4 Hz, 1H), 6.42 (s, 1H), 4.37 (dd, J = 15.8, 6.8 Hz, 1H), 4.23 (dd, J = 15.8, 5.9 Hz, 1H), 4.16 (s, 1H), 3.66 (m, 1H), 3.58 (s, 3H), 3.11 (m, 1H), 2.43 (m, 1H), 2.03 – 1.86 (m, 3H), 1.66 – 1.52 (m, 4H), 1.34 (m, 2H).	1.81 [462.0]

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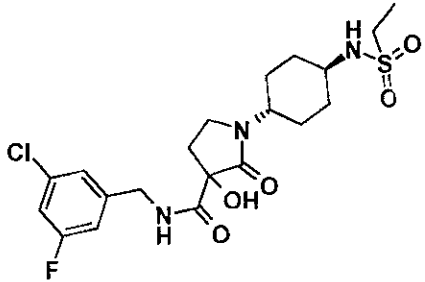
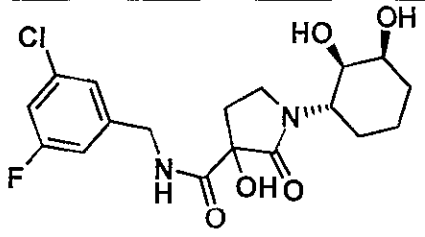
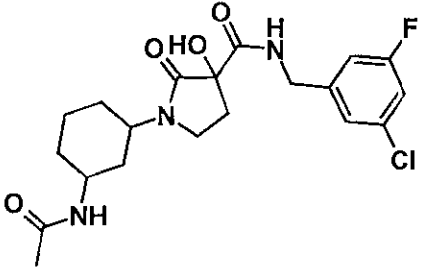
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"A124"	 N-(3-Chloro-5-fluorobenzyl)-1-(4-ethanesulfonylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.51 (t, $J = 6.3$ Hz, 1H), 7.27 – 7.21 (m, 1H), 7.18 (s, 1H), 7.09 (d, $J = 9.3$ Hz, 1H), 7.01 (d, $J = 7.7$ Hz, 1H), 6.39 (s, 1H), 4.36 (dd, $J = 15.8, 6.6$ Hz, 1H), 4.21 (dd, $J = 15.9, 6.1$ Hz, 1H), 3.73 – 3.59 (m, 1H), 3.06 (m, 1H), 2.97 (q, $J = 7.4$ Hz, 2H), 2.46 – 2.35 (m, 1H), 1.92 (m, 3H), 1.65 – 1.48 (m, 4H), 1.36 (s, 3H), 1.19 (t, $J = 7.3$ Hz, 3H).	1.87 [476.0]
"A125"	 N-(3-Chloro-5-fluorobenzyl)-1-((1S,2R,3S)-2,3-dihydroxycyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.57 (t, $J = 6.3$ Hz, 1H), 8.50 (t, $J = 6.4$ Hz, 1H), 7.28 – 7.23 (m, 2H), 7.21 (t, $J = 7.1$ Hz, 2H), 7.10 (t, $J = 9.8$ Hz, 2H), 4.41 – 4.33 (m, 3H), 4.27 – 4.19 (m, 2H), 3.98 (m, 4.2 Hz, 2H), 3.90 (m, 2H), 3.49 – 3.43 (m, 3H), 2.47 – 2.37 (m, 2H), 2.02 – 1.88 (m, 2H), 1.74 – 1.56 (m, 4H), 1.56 – 1.47 (m, 2H), 1.46 – 1.39 (m, 2H), 1.39 – 1.28 (m, 5H), 1.26 – 1.14 (m, 1H).	1.75 [401.0]
"A126"	 N-(3-Chloro-5-fluorobenzyl)-1-(3-acetylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.55 (t, $J = 6.4$ Hz, 1H), 7.78 (d, $J = 7.6$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.11 (d, $J = 9.6$ Hz, 1H), 4.44 – 4.31 (m, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.83 – 3.71 (m, 1H), 3.67 – 3.60 (m, 1H), 3.37 – 3.24 (m, 2H), 2.48	

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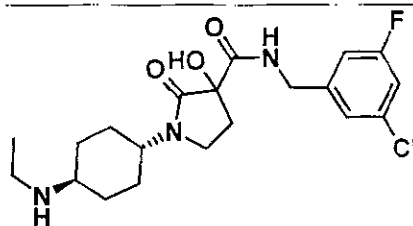
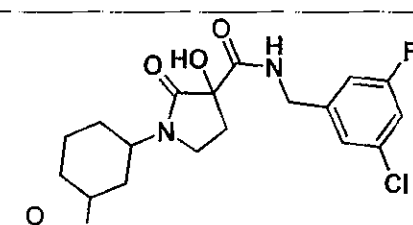
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	carboxamide	- 2.39 (m, 1H), 1.99 – 1.88 (m, 1H), 1.80 – 1.77 (s, 3H), 1.74 (m, 2H), 1.51 (m, 1H), 1.46 – 1.26 (m, 3H), 1.15 – 0.95 (m, 1H).
"A127"	 N-(3-Chloro-5-fluorobenzyl)-1-(4-ethylaminocyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.55 (t, $J = 6.4$ Hz, 1H), 8.36 (s, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 4.37 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.23 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.69 (m, 2H), 3.38 – 3.24 (m, 4H), 2.73 (m, 2H), 2.63 (m, 1H), 2.44 (m, 1H), 2.05 – 1.97 (m, 2H), 1.97 – 1.87 (m, 1H), 1.69 – 1.56 (m, 3H), 1.51 (m, 2H), 1.31 – 1.16 (m, 2H), 1.09 (t, $J = 7.1$ Hz, 3H).
"A128"	 N-(3-Chloro-5-fluorobenzyl)-1-(3-ethanesulfonylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.53 (t, $J = 6.4$ Hz, 1H), 7.25 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (t, $J = 7.6$ Hz, 2H), 6.42 (s, 1H), 4.35 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.75 (m, 1H), 3.37 – 3.31 (m, 1H), 3.25 (m, 2H), 3.22 – 3.06 (m, 1H), 2.97 (q, $J = 7.3$ Hz, 2H), 2.42 (m, 1H), 1.92 (m, 1H), 1.80 (m, 3H), 1.52 (s, 1H), 1.46 – 1.27 (m, 3H), 1.23 – 1.14 (m, 3H), 1.11 (s, 1H).

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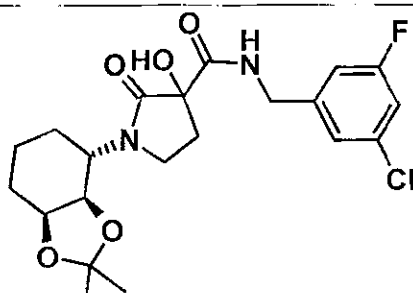
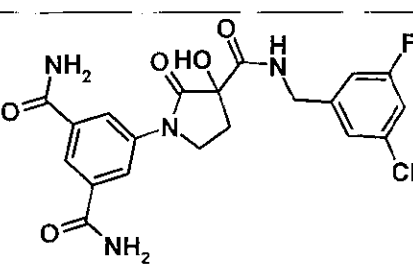
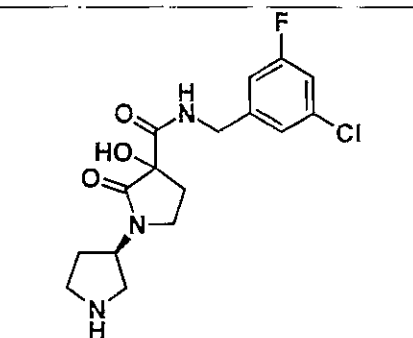
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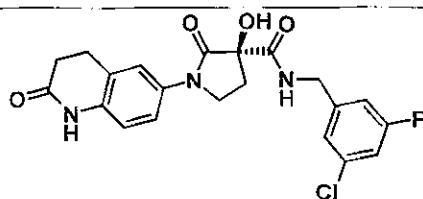
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"A129"	 N-(3-Chloro-5-fluorobenzyl)-1-((3aR,4S,7aS)-2,2-dimethylhexahydrobenzo-1,3-dioxol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.49 (t, $J = 6.2$ Hz, 1H), 7.23 (m, 2H), 7.09 (t, $J = 8.6$ Hz, 1H), 6.41 (m, 1H), 4.36 (m, 1H), 4.28 – 4.17 (m, 2H), 4.17 – 4.05 (m, 1H), 3.73 (m, 1H), 3.48 – 3.36 (m, 1H), 3.36 – 3.21 (m, 2H), 2.51 (m, 1H), 2.04 – 1.87 (m, 2H), 1.64 (m, 1H), 1.59 – 1.47 (s, 3H), 1.42 (m, 5H), 1.25 (s, 3H).	
"A130"	 5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-isophthalamide	** 8.73 (t, $J = 6.4$ Hz, 1H), 8.26 (d, $J = 1.4$ Hz, 2H), 8.16 (t, $J = 1.4$ Hz, 1H), 8.04 (s, 2H), 7.50 (d, $J = 26.6$ Hz, 2H), 7.29 – 7.23 (m, 1H), 7.21 (s, 1H), 7.11 (d, $J = 9.6$ Hz, 1H), 6.80 (s, 1H), 4.39 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.28 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.95 (dd, $J = 14.8, 8.4$ Hz, 2H), 2.69 – 2.58 (m, 1H), 2.17 (dt, $J = 13.0, 7.5$ Hz, 1H).	
"A131"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-[1,3']bipyrrolidinyl-3-carboxamide	8.58 (dd, $J = 12.2, 6.1$ Hz, 1H), 7.25 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 9.4$ Hz, 1H), 4.51 (dd, $J = 14.4, 7.5$ Hz, 1H), 4.36 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.23 (dd, $J = 15.6, 6.0$ Hz, 1H), 3.50 – 3.33 (m, 5H), 3.16 – 2.99 (m, 3H), 2.47 – 2.38 (m, 1H), 2.13 – 1.82 (m, 3H).	1.44 [356.1]

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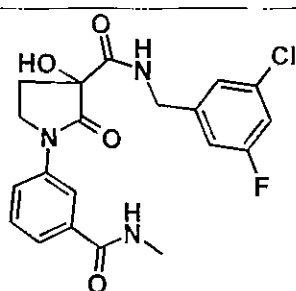
"A132"



N-(3-Chloro-5-fluorobenzyl)-(R)-
3-hydroxy-2-oxo-1-(2-oxo-
1,2,3,4-tetrahydroquinolin-6-yl)-
pyrrolidine-3-carboxamide

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"A133"

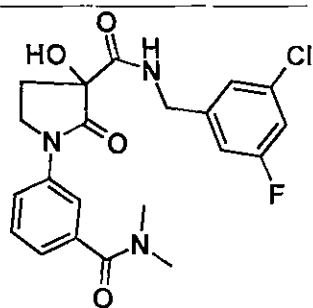


N-(3-Chloro-5-fluorobenzyl)-3-
hydroxy-1-(3-methylcarbamoyl-
phenyl)-2-oxopyrrolidine-3-
carboxamide

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"A134"

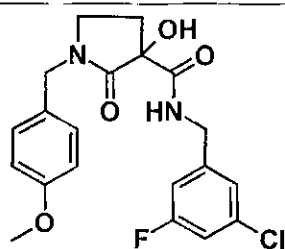


N-(3-Chloro-5-fluorobenzyl)-1-
(3-Dimethylcarbamoylphenyl)-3-
hydroxy-2-oxopyrrolidine-3-
carboxamide

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"A135"



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1.93

[420.1]

1.99

[434.1]

2.21

[407.1]

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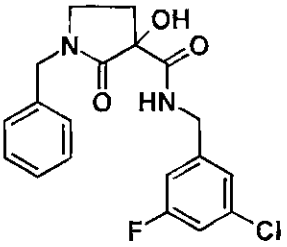
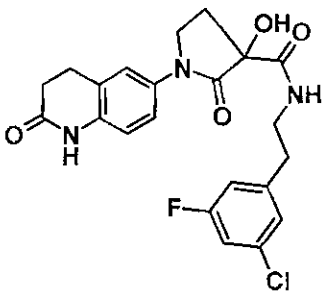
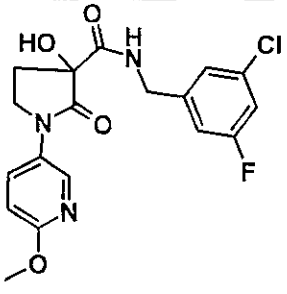
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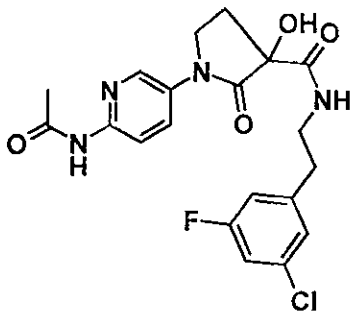
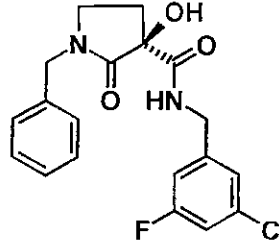
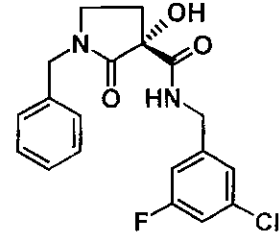
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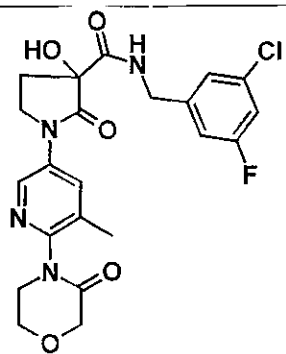
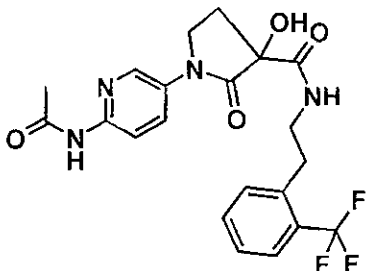
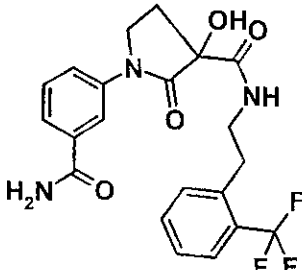
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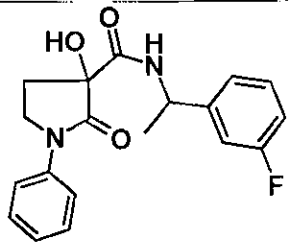
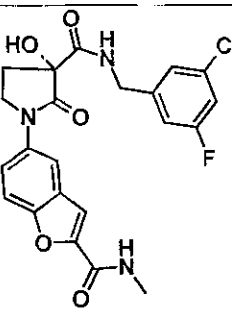
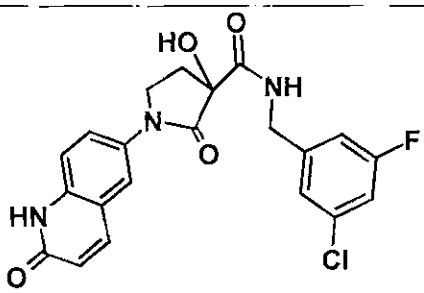
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	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methoxybenzyl)-2-oxopyrrolidine-3-carboxamide		
"A136"	 N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide		2.21 [377.1]
"A137"	 N-[2-(3-Chloro-5-fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	10.05 (s, 1H), 7.99 (t, $J = 6.0$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.42 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.23 (dt, $J = 8.9, 2.2$ Hz, 1H), 7.16 (s, 1H), 7.11 – 7.04 (m, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.54 (s, 1H), 3.80 – 3.73 (m, 2H), 3.45 – 3.30 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.79 (t, $J = 7.0$ Hz, 2H), 2.47 – 2.38 (m, 3H), 2.10 – 1.96 (m, 1H).	2.03 [446.1]
"A138"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-methoxypyridin-3-yl)-2-oxopyrrolidine-3-carboxamide		2.06 [394.0]

"A139"	 N-[2-(3-Chloro-5-fluorophenyl)-ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 10.50 (s, 1H), 8.64 (dd, $J = 2.5, 0.8$ Hz, 1H), 8.15 – 8.02 (m, 3H), 7.23 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.16 (s, 1H), 7.08 (dt, $J = 12.8, 6.4$ Hz, 1H), 6.65 (s, 1H), 3.91 – 3.76 (m, 2H), 3.44 – 3.36 (m, 2H), 2.80 (t, $J = 6.9$ Hz, 2H), 2.49 – 2.43 (m, 1H), 2.09 (s, 3H).	1.99 [435.0]
"A140"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide		2.25 [377.0]
"A141"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide		2.23 [377.0]

"A142"  N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[5-methyl-6-(3-oxomorpholin-4-yl)-pyridin-3-yl]-2-oxopyrrolidine-3-carboxamide	8.75 (t, $J = 6.4$ Hz, 2H), 8.06 (s, 1H), 7.28 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.11 (d, $J = 9.5$ Hz, 1H), 6.84 (s, 1H), 4.39 (dt, $J = 18.6, 9.4$ Hz, 1H), 4.31 – 4.17 (m, 3H), 4.01 (t, $J = 5.0$ Hz, 2H), 3.97 – 3.87 (m, 2H), 2.69 – 2.58 (m, 1H), 2.24 – 2.12 (m, 4H).	2.02 [477.1]
"A143"  N-[2-(2-Trifluoromethylphenyl)ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.50 (s, 1H), 8.64 (d, $J = 1.6$ Hz, 1H), 8.17 (t, $J = 6.0$ Hz, 1H), 8.13 – 8.04 (m, 2H), 7.67 (d, $J = 7.9$ Hz, 1H), 7.60 (t, $J = 7.4$ Hz, 1H), 7.49 (d, $J = 7.6$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 1H), 6.63 (s, 1H), 3.89 – 3.78 (m, 2H), 3.44 – 3.31 (m, 2H), 2.94 (t, $J = 7.2$ Hz, 2H), 2.56 – 2.52 (m, 1H), 2.17 – 2.09 (m, 1H), 2.09 (s, 3H).	2.03 [451.1]
"A144"  N-[2-(2-Trifluoromethylphenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.17 (t, $J = 6.0$ Hz, 1H), 8.06 – 8.03 (m, 1H), 8.00 (s, 1H), 7.96 – 7.90 (m, 1H), 7.72 – 7.65 (m, 2H), 7.60 (t, $J = 7.6$ Hz, 1H), 7.49 (d, $J = 8.0$ Hz, 2H), 7.46 – 7.35 (m, 2H), 6.62 (s, 1H), 3.88 (m, 2H), 3.38 (m, 2H), 2.94 (t, $J = 7.2$ Hz, 2H), 2.54 (m, 1H), 2.10 (dt, $J = 12.9, 7.9$ Hz, 1H).	1.98 [436.1]

"A145"	 N-[1-(3-Fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide	** 8.32 – 8.24 (m, 1H), 7.73 – 7.65 (m, 2H), 7.44 – 7.37 (m, 2H), 7.37 – 7.29 (m, 1H), 7.25 – 7.15 (m, 3H), 7.07 – 6.99 (m, 1H), 6.69 (d, $J = 19.3$ Hz, 1H), 5.01 – 4.91 (m, 1H), 3.89 – 3.78 (m, 2H), 2.66 – 2.57 (m, 1H), 2.49 – 2.43 (m, 1H), 2.17 – 2.05 (m, 1H), 1.43 (d, $J = 7.0$ Hz, 3H).	2.16 [343.1]
"A146"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methylcarbamoylbenzofuran-5-yl)-2-oxopyrrolidine-3-carboxamide		2.11 [460.1]
"A147"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide	** 11.76 (s, 1H), 9.18 – 8.53 (m, 1H), 7.90 (dd, $J = 6.3, 3.1$ Hz, 3H), 7.36 – 7.29 (m, 1H), 7.26 (d, $J = 8.7$ Hz, 1H), 7.21 (s, 1H), 7.11 (d, $J = 9.5$ Hz, 1H), 6.52 (d, $J = 9.6$ Hz, 1H), 4.39 (dd, $J = 15.6, 5.1$ Hz, 1H), 4.26 (dd, $J = 15.6, 4.2$ Hz, 1H), 3.89 (t, $J = 6.8$ Hz, 2H), 2.66 – 2.57 (m, 1H), 2.16 (dt, $J = 13.0, 7.6$ Hz, 1H).	2.07 [430.0]

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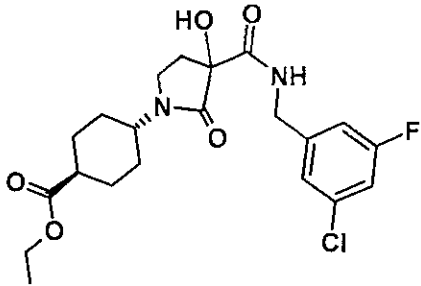
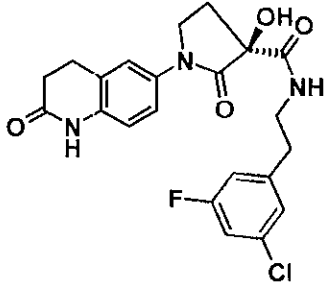
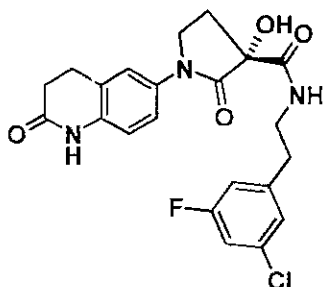
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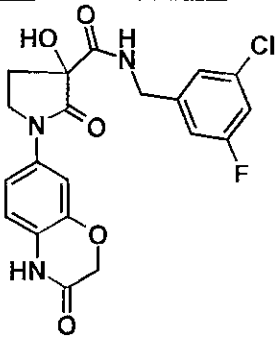
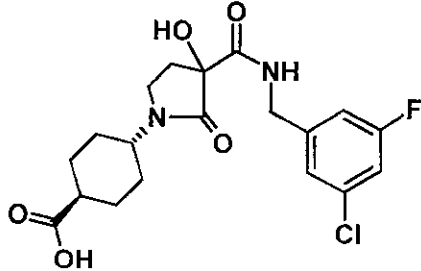
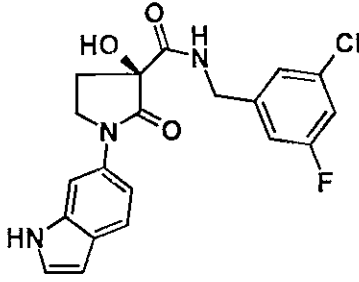
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"A148"	 Ethyl 4-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-cyclohexanecarboxylate	3.52 (t, $J = 6.3$ Hz, 1H), 7.25 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 8.9$ Hz, 1H), 6.40 (d, $J = 4.5$ Hz, 1H), 4.36 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.22 (dd, $J = 15.8, 5.9$ Hz, 1H), 4.05 (q, $J = 7.1$ Hz, 2H), 3.76 – 3.62 (m, 1H), 2.42 (ddd, $J = 11.9, 7.1, 4.5$ Hz, 1H), 2.25 (ddd, $J = 11.9, 8.5, 3.5$ Hz, 1H), 2.02 – 1.85 (m, 3H), 1.71 – 1.33 (m, 6H), 1.17 (t, $J = 7.1$ Hz, 3H).	2.25 [441.1]
"A149"	 N-[2-(3-Chloro-5-fluorophenyl)-ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide		2.08 [446.1]
"A150"	 N-[2-(3-Chloro-5-fluorophenyl)-ethyl]-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide		2.06 [446.1]

5	"A151"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide	2.08 [434.0]
15	"A152"	 4-[3-(3-Chloro-5-fluorobenzyl-carbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-cyclohexanecarboxylic acid	2.02 [413.1]
25	"A153"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(1H-indol-6-yl)-2-oxopyrrolidine-3-carboxamide	11.08 (d, $J = 10.1$ Hz, 1H), 8.68 (t, $J = 6.3$ Hz, 1H), 7.78 (dd, $J = 3.4, 2.5$ Hz, 1H), 7.54 (d, $J = 8.6$ Hz, 1H), 7.35 – 7.33 (m, 1H), 7.28 – 7.22 (m, 3H), 7.11 (t, $J = 7.5$ Hz, 1H), 6.70 (s, 1H), 6.46 – 6.38 (m, 1H), 4.41 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 2.65 – 2.58 (m, 1H), 2.15 (dt, $J =$ 13.0, 7.5 Hz, 1H).
30			2.19 [402.0]
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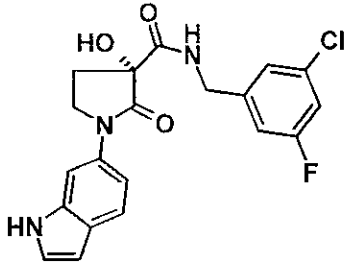
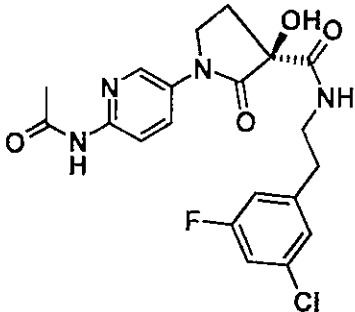
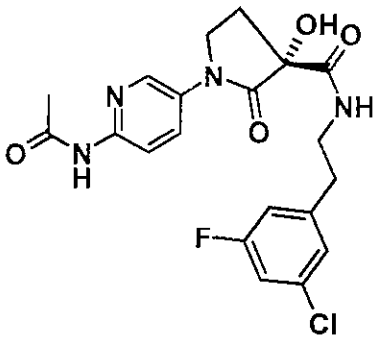
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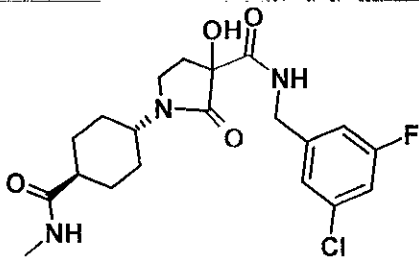
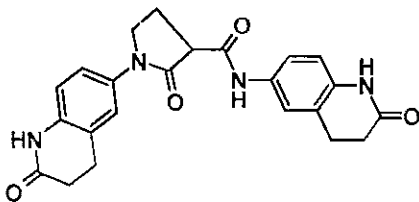
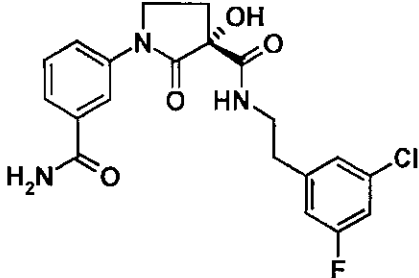
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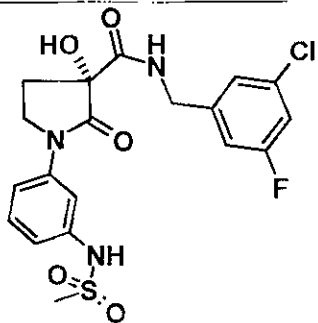
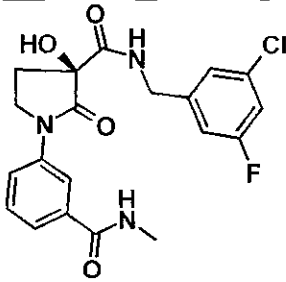
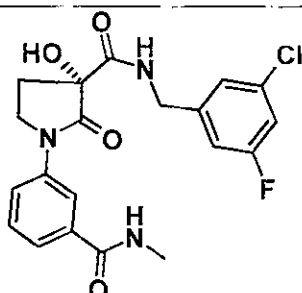
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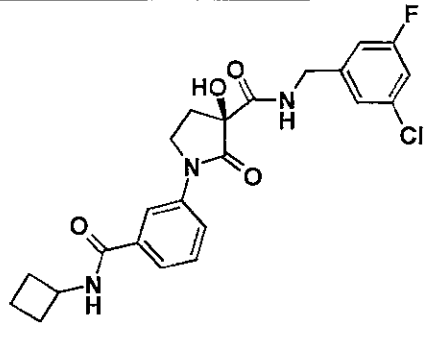
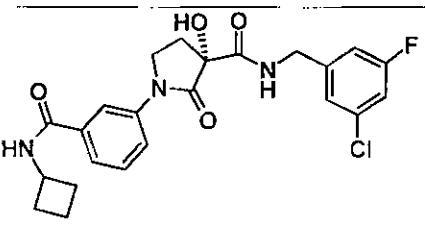
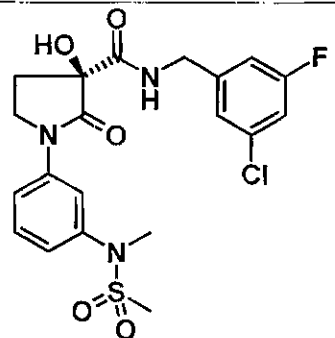
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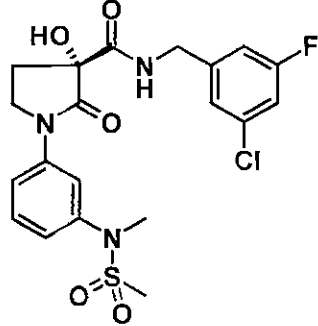
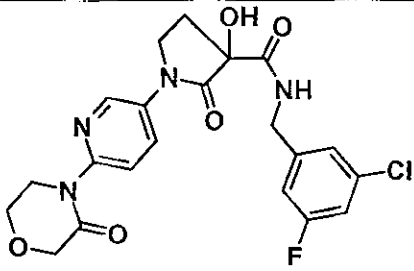
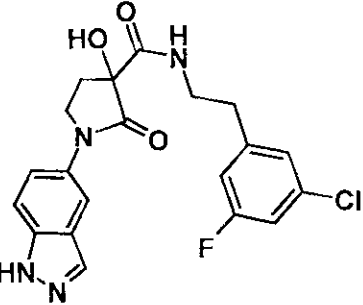
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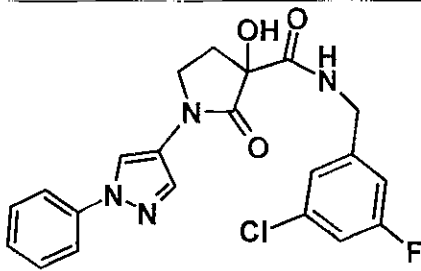
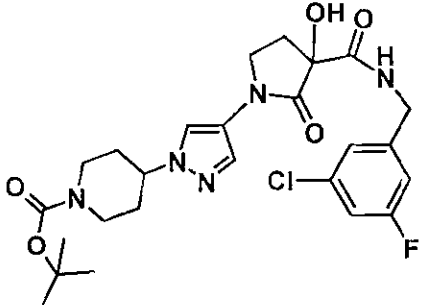
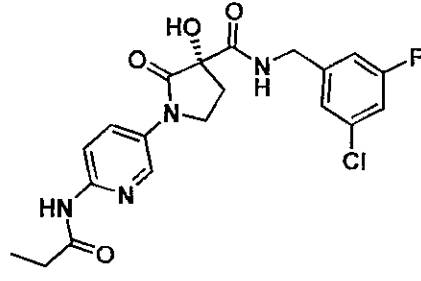
"A154"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(1H-indol-6-yl)-2-oxopyrrolidine-3-carboxamide	2.18 [402.0]
"A155"	 N-[2-(3-Chloro-5-fluorophenyl)-ethyl]-(S)-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	2.04 [435.1]
"A156"	 N-[2-(3-Chloro-5-fluorophenyl)-ethyl]-(R)-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	2.06 [435.1]

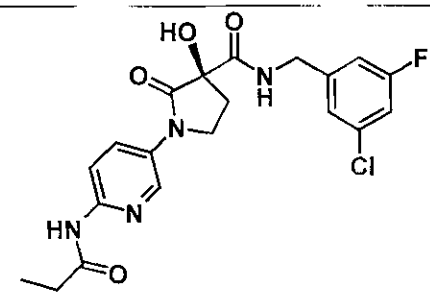
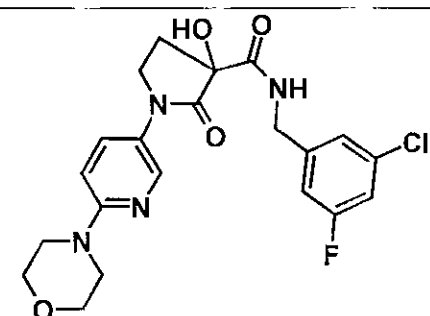
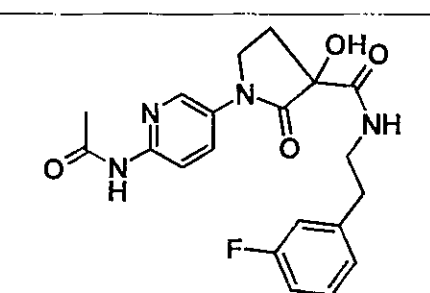
5	"A157"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcarbamoylcyclohexyl)-2-oxopyrrolidine-3-carboxamide	1.98 [426.1]
15	"A158"	 N-(2-Oxo-1,2,3,4-tetrahydroquinolin-6-yl)-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.16 – 9.99 (m, 1H), 7.47 (d, $J = 7.4$ Hz, 1H), 7.37 (ddd, $J = 23.0, 8.6, 1.9$ Hz, 1H), 6.90 – 6.74 (m, 1H), 3.90 – 3.77 (m, 1H), 3.24 (d, $J = 7.1$ Hz, 1H), 2.93 – 2.81 (m, 2H), 2.47 – 2.39 (m, 2H), 2.38 – 2.25 (m, 1H), 1.22 – 1.10 (m, 1H).
20	"A159"	 N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(R)-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	2.13 [420.1]

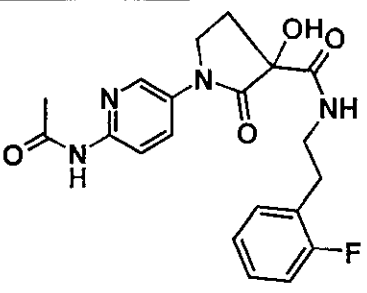
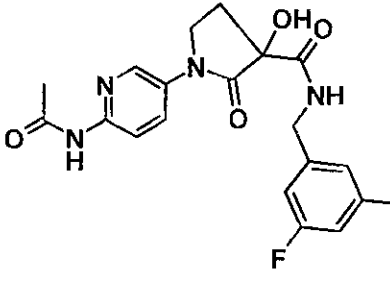
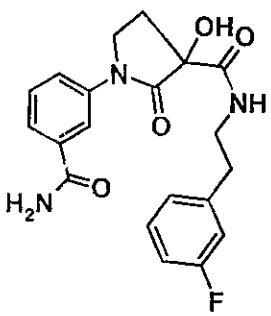
5	"A160"		
10		N-(3-Chloro-5-fluorobenzyl)-(R)- 3-hydroxy-1-(3-methane- sulfonylamino-phenyl)-2-oxo- pyrrolidine-3-carboxamide	
15	"A161"		1.93 [420.1]
20		N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-1-(3-methyl- carbamoylphenyl)-2-oxo- pyrrolidine-3-carboxamide	
25	"A162"		1.93 [420.1]
30		N-(3-Chloro-5-fluorobenzyl)-(R)- 3-hydroxy-1-(3-methyl- carbamoylphenyl)-2-oxo- pyrrolidine-3-carboxamide	

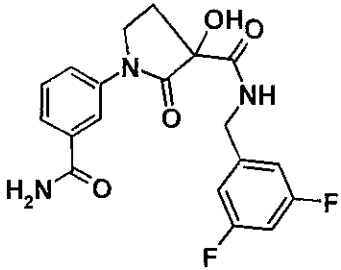
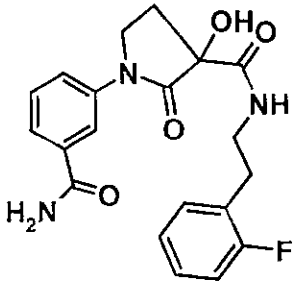
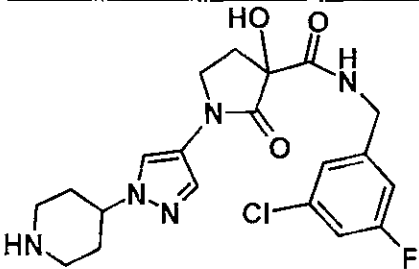
5	"A163"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyclobutylcarbamoyl-phenyl)-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	2.22 [460.1]
15	"A164"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclobutylcarbamoyl-phenyl)-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	2.22 [460.1]
25	"A165"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(methanesulfonylmethylamino)phenyl]-2-oxopyrrolidine-3-carboxamide	2.24 [470.1]

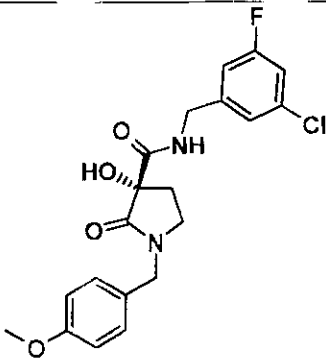
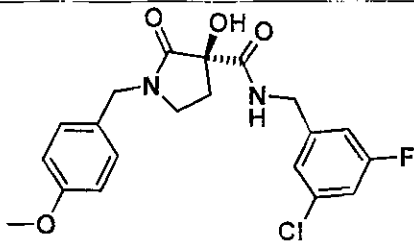
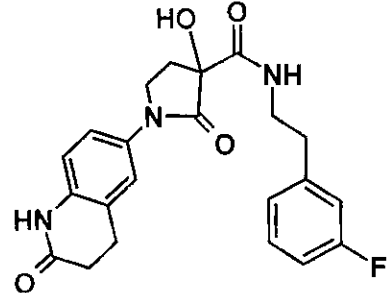
"A166" 5 10	 N-(3-Chloro-5-fluorobenzyl)- (R)-3-hydroxy-1-[3-(methane- sulfonylmethylamino)phenyl]-2- oxopyrrolidine-3-carboxamide		2.19 [470.0]
"A167" 15 20	 N-(3-Chloro-5-fluorobenzyl)-3- hydroxy-2-oxo-1-[6-(3-oxo- morpholin-4-yl)-pyridin-3-yl]- pyrrolidine-3-carboxamide		2.14 [463.1]
"A168" 25 30 35	 N-[2-(3-Chloro-5-fluorophenyl)- ethyl]-3-hydroxy-1-(1H-indazol- 5-yl)-2-oxopyrrolidine-3- carboxamide	13.06 (s, 1H), 8.07 (s, 1H), 8.01 (t, $J = 5.9$ Hz, 1H), 7.89 (s, 1H), 7.75 (dd, $J = 9.0, 1.9$ Hz, 1H), 7.55 (d, $J = 9.0$ Hz, 1H), 7.23 (dt, $J = 8.9, 2.1$ Hz, 1H), 7.17 (s, 1H), 7.09 (d, $J =$ 9.4 Hz, 1H), 6.57 (s, 1H), 3.94 – 3.84 (m, 2H), 3.47 – 3.29 (m, 2H), 2.80 (t, $J = 7.0$ Hz, 2H), 2.46 (t, $J = 6.4$ Hz, 1H), 2.09 (dt, $J = 12.9, 7.7$ Hz, 1H).	2.15 [417.0]

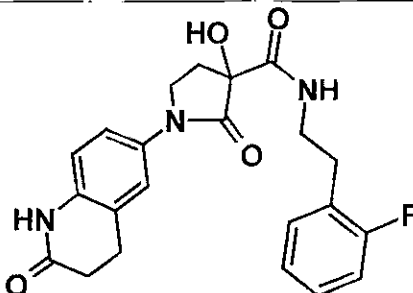
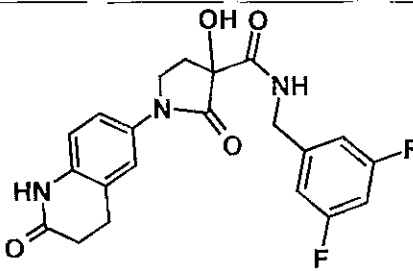
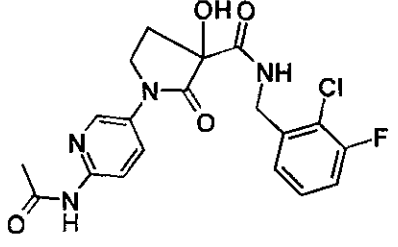
5	"A169"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-phenyl-1H-pyrazol-4-yl)pyrrolidine-3-carboxamide	¹ H NMR (CDCl ₃) δ: 8.72 (t, <i>J</i> = 6.3 Hz, 1H), 8.66 (s, 1H), 8.11 (s, 1H), 7.83 (d, <i>J</i> = 7.8 Hz, 2H), 7.51 (t, <i>J</i> = 7.9 Hz, 2H), 7.32 (t, <i>J</i> = 7.4 Hz, 1H), 7.27 (d, <i>J</i> = 8.7 Hz, 1H), 7.22 (s, 1H), 7.11 (d, <i>J</i> = 9.5 Hz, 1H), 6.76 (s, 1H), 4.39 (dd, <i>J</i> = 15.7, 6.7 Hz, 1H), 4.27 (dd, <i>J</i> = 15.7, 6.1 Hz, 1H), 3.86 – 3.74 (m, 2H), 2.71 – 2.61 (m, 1H), 2.25 – 2.13 (m, 1H).	2.28 [429.0]
15	"A170"	 tert-Butyl 4-{4-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-pyrazol-1-yl}-piperidine-1-carboxylate	¹ H NMR (CDCl ₃) δ: 8.67 (t, <i>J</i> = 6.4 Hz, 1H), 8.06 (s, 1H), 7.70 (s, 1H), 7.26 (dt, <i>J</i> = 8.7, 2.1 Hz, 1H), 7.20 (s, 1H), 7.09 (d, <i>J</i> = 9.0 Hz, 1H), 6.66 (s, 1H), 4.42 – 4.30 (m, 2H), 4.28 – 4.16 (m, 1H), 4.03 (m, 2H), 3.73 – 3.62 (m, 2H), 2.61 (ddd, <i>J</i> = 12.1, 7.6, 4.2 Hz, 1H), 2.14 (ddd, <i>J</i> = 13.0, 8.5, 6.8 Hz, 1H), 1.96 (m, 2H), 1.76 (m, 2H), 1.41 (s, 9H).	
25	"A171"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(6-propionylaminopyridin-3-yl)-pyrrolidine-3-carboxamide		3.39 [435.2]

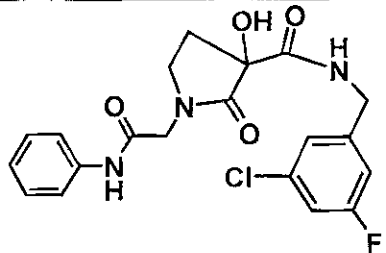
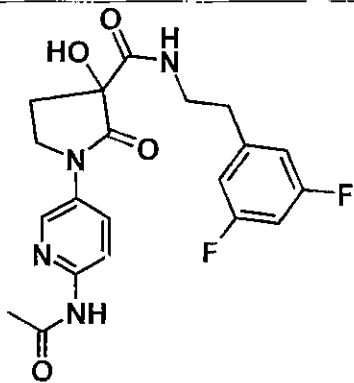
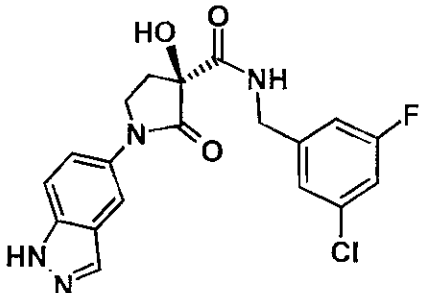
5	"A172"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(6-propionylaminopyridin-3-yl)-pyrrolidine-3-carboxamide		
15	"A173"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-morpholin-4-ylpyridin-3-yl)-2-oxopyrrolidine-3-carboxamide		1.70 [449.1]
25	"A174"	 N-[2-(3-Fluorophenyl)ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.49 (s, 1H), 8.63 (s, 1H), 8.17 – 7.85 (m, 3H), 7.31 (dd, $J = 14.3, 7.6$ Hz, 1H), 7.13 – 6.81 (m, 3H), 6.61 (s, 1H), 3.83 (t, $J = 6.7$ Hz, 2H), 3.43 – 3.30 (m, 3H), 2.78 (t, $J = 7.2$ Hz, 2H), 2.08 (s, 3H).	1.77 [401.1]

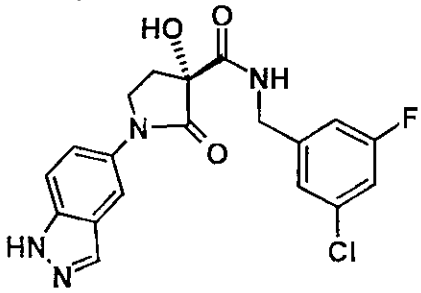
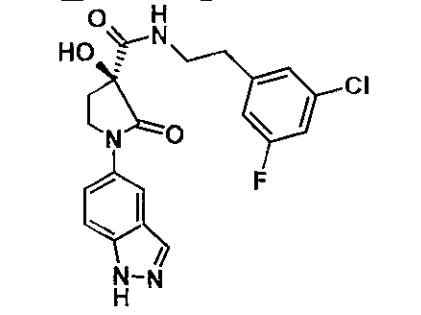
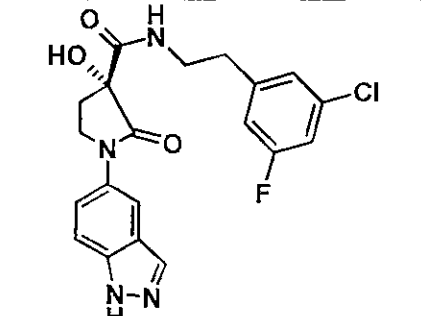
5	"A175"	 N-[2-(2-Fluorophenyl)ethyl]-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.49 (s, 1H), 8.63 (s, 1H), 8.12 – 8.03 (m, 3H), 7.26 (dt, J = 7.7, 6.7 Hz, 2H), 7.17 – 7.08 (m, 2H), 6.60 (s, 1H), 3.83 (m, 2H), 3.39 (m, 1H), 2.86 – 2.73 (m, 2H), 2.08 (s, 3H).	1.75 [401.1]
15	"A176"	 N-(3,5-Difluorobenzyl)-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.50 (s, 1H), 8.70 (t, J = 6.2 Hz, 1H), 8.64 (s, 1H), 8.13 – 8.01 (m, 2H), 7.04 (dd, J = 19.0, 9.4 Hz, 1H), 6.98 (d, J = 7.5 Hz, 2H), 6.76 (s, 1H), 4.40 (dd, J = 15.7, 6.7 Hz, 1H), 4.26 (dd, J = 15.8, 5.9 Hz, 1H), 3.87 (t, J = 6.7 Hz, 2H), 2.68 – 2.56 (m, 1H), 2.21 – 2.11 (m, 1H), 2.08 (s, 3H).	1.75 [405.1]
25	"A177"	 N-[2-(3-Fluorophenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.07 – 7.98 (m, 3H), 7.94 (d, J = 8.1 Hz, 1H), 7.67 (t, J = 11.7 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.39 (s, 1H), 7.32 (dd, J = 14.4, 7.6 Hz, 1H), 7.12 – 6.95 (m, 3H), 3.88 (t, J = 6.7 Hz, 2H), 3.32 – 3.08 (m, 2H), 2.79 (t, J = 7.2 Hz, 2H), 2.47 (m, 1H), 2.09 (dt, J = 12.9, 7.9 Hz, 1H).	1.80 [386.1]

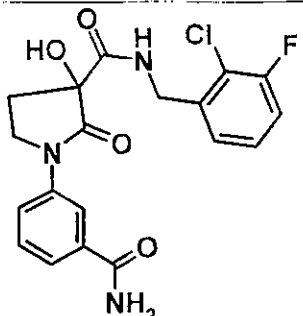
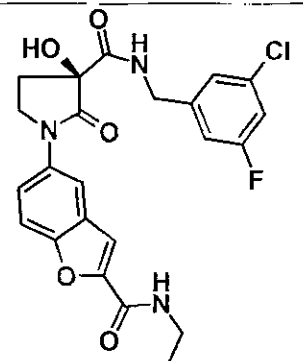
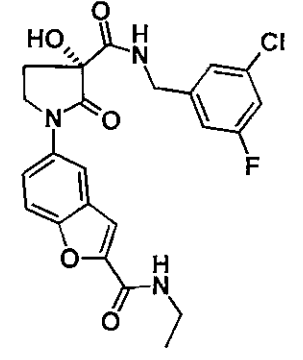
5	"A178"	 N-(3,5-Difluorobenzyl)-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.70 (t, $J = 6.3$ Hz, 1H), 8.13 (s, 1H), 8.06 – 8.03 (m, 1H), 3.01 (s, 1H), 7.95 (dd, $J = 8.2$, 1.4 Hz, 1H), 7.68 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 8.0$ Hz, 1H), 7.38 (s, 1H), 7.09 – 7.01 (m, 1H), 6.99 (d, $J = 6.6$ Hz, 2H), 6.78 (s, 1H), 4.40 (dd, $J = 15.8$, 6.7 Hz, 1H), 4.27 (dd, $J = 15.8$, 6.0 Hz, 1H), 3.91 (t, $J = 6.9$ Hz, 2H), 2.66 – 2.57 (m, 1H), 2.16 (dt, $J = 13.0$, 7.5 Hz, 1H).	1.77 [390.1]
15	"A179"	 N-[2-(2-Fluorophenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	* 8.15 (s, 1H), 7.96 (dd, $J = 3.2$, 1.4 Hz, 1H), 7.74 (d, $J = 7.8$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 7.32 (t, $J = 7.6$ Hz, 1H), 7.26 (dd, $J = 14.3$, 6.6 Hz, 1H), 7.12 (dd, $J = 14.9$, 7.5 Hz, 2H), 4.00 – 3.86 (m, 2H), 3.48 (m, 1H), 3.43 – 3.32 (m, 1H), 2.93 – 2.80 (m, 2H), 2.54 (m, 1H), 2.17 (dt, $J = 12.9$, 8.1 Hz, 1H).	1.77 [390.1]
25	"A180"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-piperidin-4-yl-1H-pyrazol-4-yl)pyrrolidine-3-carboxamide		1.57 [436.1]

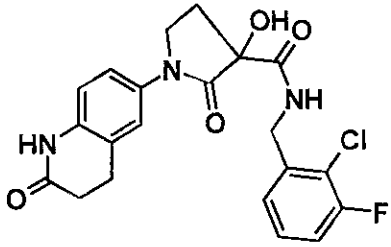
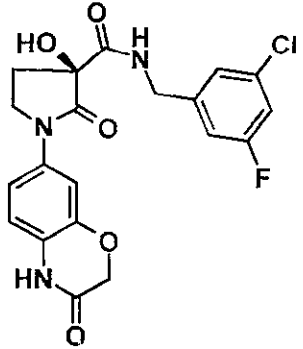
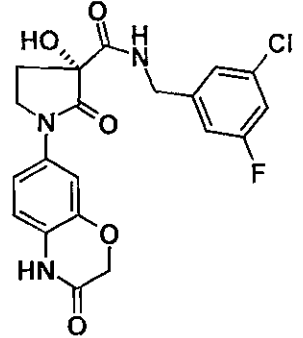
5	"A181"		2.11 [407.1]	
10		N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(4-methoxybenzyl)-2-oxopyrrolidine-3-carboxamide		
15	"A182"		2.11 [407.1]	
20		N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(4-methoxybenzyl)-2-oxopyrrolidine-3-carboxamide		
25	"A183"		10.06 (s, 1H), 7.96 (t, $J = 5.9$ Hz, 1H), 7.48 (s, 1H), 7.43 (dd, $J = 8.6, 2.3$ Hz, 1H), 7.32 (dd, $J = 14.3, 7.7$ Hz, 1H), 7.09 – 6.97 (m, 3H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.55 (s, 1H), 3.81 – 3.73 (m, 2H), 3.40 (dd, $J = 12.9, 6.7$ Hz, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.78 (t, $J = 7.3$ Hz, 2H), 2.48 – 2.39 (m, 3H), 2.04 (dt, $J = 12.9, 7.8$ Hz, 1H).	1.72 [412.2]
30		N-[2-(3-Fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide		

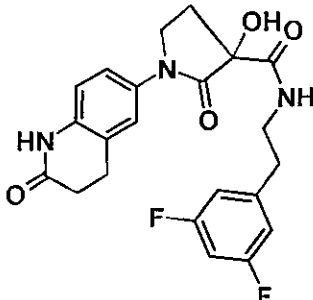
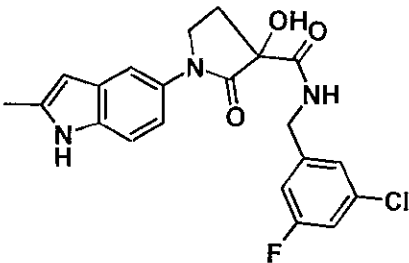
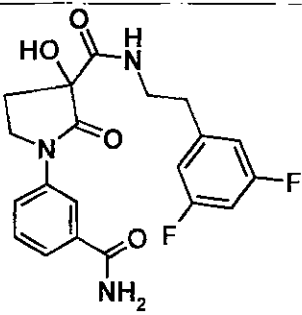
5	"A184"	 N-[2-(2-Fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	¹ H NMR (400 MHz, DMSO) δ 10.06 (s, 1H), 8.02 (t, J = 5.8 Hz, 1H), 7.48 (s, 1H), 7.43 (dd, J = 8.6, 2.3 Hz, 1H), 7.27 (dt, J = 7.7, 6.7 Hz, 2H), 7.18 – 7.08 (m, 2H), 6.86 (d, J = 8.6 Hz, 1H), 3.77 (t, J = 6.8 Hz, 2H), 3.26 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.84 – 2.72 (m, 2H), 2.44 (m, 3H), 2.10 – 1.97 (m, 1H).	1.72 [412.2]
15	"A185"	 N-(3,5-Difluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	10.06 (d, J = 6.0 Hz, 1H), 8.65 (q, J = 6.3 Hz, 1H), 7.48 (d, J = 1.9 Hz, 1H), 7.43 (dd, J = 8.6, 2.3 Hz, 1H), 7.05 (ddd, J = 13.2, 6.6, 3.1 Hz, 1H), 6.99 (d, J = 6.8 Hz, 2H), 6.87 (d, J = 8.6 Hz, 1H), 6.69 (s, 1H), 4.40 (dd, J = 15.7, 6.6 Hz, 1H), 4.26 (dd, J = 15.8, 6.0 Hz, 1H), 3.81 (t, J = 6.8 Hz, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.62 – 2.54 (m, 1H), 2.47 – 2.39 (m, 2H), 2.11 (dt, J = 13.0, 7.6 Hz, 1H).	1.70 [416.1]
25	"A186"	 N-(2-Chloro-3-fluorobenzyl)-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.50 (s, 1H), 8.65 (dd, J = 5.6, 4.1 Hz, 2H), 8.08 (d, J = 8.9 Hz, 2H), 7.42 – 7.25 (m, 2H), 7.21 (d, J = 7.5 Hz, 1H), 3.82 (s, 1H), 4.45 (dd, J = 16.2, 5.7 Hz, 1H), 4.36 (dd, J = 16.1, 5.3 Hz, 1H), 3.88 (m, 2H), 2.70 – 2.58 (m, 1H), 2.18 (dt, J = 13.0, 7.6 Hz, 1H), 2.08 (s, 3H).	1.80 [421.0]

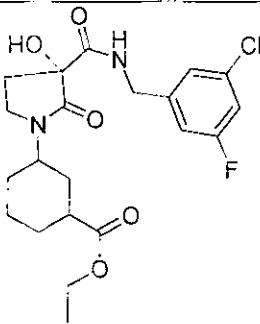
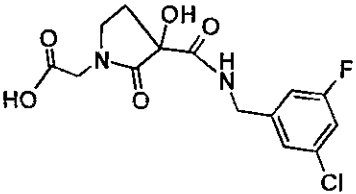
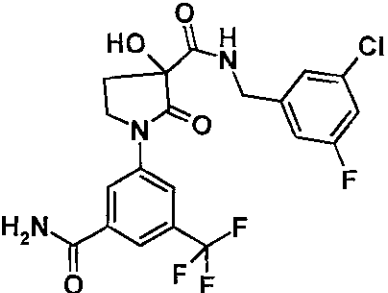
5	"A187"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenyl-carbamoylmethylpyrrolidine-3-carboxamide	9.89 (s, 1H), 8.75 (t, $J = 6.3$ Hz, 1H), 7.58 (d, $J = 7.7$ Hz, 2H), 7.28 (dd, $J = 12.9, 4.6$ Hz, 2H), 7.27 – 7.24 (m, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 7.06 (t, $J = 7.4$ Hz, 1H), 6.63 (s, 1H), 4.41 (dd, $J = 15.6, 6.6$ Hz, 1H), 4.26 (dd, $J = 15.6, 6.0$ Hz, 1H), 3.56 – 3.43 (m, 2H), 2.49 – 2.43 (m, 1H), 2.14 – 2.03 (m, 1H).	2.18 [420.0]
10				
15	"A188"	 N-[2-(3,5-Difluorophenyl)ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.49 (s, 1H), 8.63 (dd, $J = 2.4, 1.0$ Hz, 1H), 8.13 – 8.05 (m, 2H), 8.02 (d, $J = 6.1$ Hz, 1H), 7.01 (ddt, $J = 9.0, 6.7, 3.3$ Hz, 1H), 6.94 (dt, $J = 6.2, 3.1$ Hz, 2H), 6.62 (s, 1H), 3.87 – 3.79 (m, 2H), 3.44 – 3.31 (m, 2H), 2.80 (t, $J = 7.0$ Hz, 2H), 2.46 (m, 1H), 2.08 (s, 3H).	1.80 [419.1]
20				
25				
30	"A189"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(1H-indazol-5-yl)-2-oxopyrrolidine-3-carboxamide		1.94 [403.0]
35				

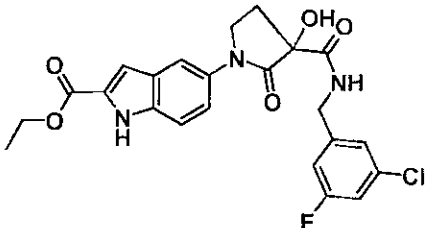
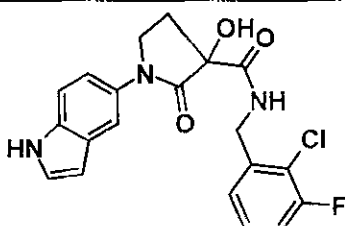
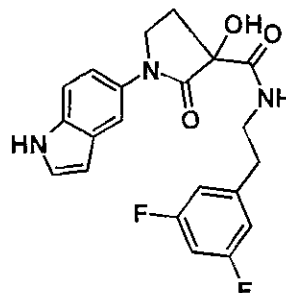
5	"A190"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(1H-indazol-5-yl)-2-oxopyrrolidine-3-carboxamide	1.94 [403.0]
10	"A191"	 N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(S)-3-hydroxy-1-(1H-indazol-5-yl)-2-oxopyrrolidine-3-carboxamide	2.01 [417.0]
15	"A192"	 N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(R)-3-hydroxy-1-(1H-indazol-5-yl)-2-oxopyrrolidine-3-carboxamide	2.01 [417.1]
20			
25			
30			

5	"A193"	 N-(2-Chloro-3-fluorobenzyl)-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.66 (t, $J = 6.3$ Hz, 1H), 8.05 (t, $J = 1.8$ Hz, 1H), 8.00 (s, 1H), 7.97 – 7.91 (m, 1H), 7.68 (d, $J = 7.8$ Hz, 1H), 7.48 (t, $J = 8.0$ Hz, 1H), 7.43 – 7.33 (m, 2H), 7.32 – 7.25 (m, 1H), 7.22 (d, $J = 7.7$ Hz, 1H), 6.80 (s, 1H), 4.45 (dd, $J = 16.2, 6.5$ Hz, 1H), 4.36 (dd, $J = 16.2, 6.0$ Hz, 1H), 2.64 (dt, $J = 11.8, 5.7$ Hz, 1H), 2.38 (m, 2H), 2.17 (dt, $J = 13.0, 7.6$ Hz, 1H).	1.82 [406.0]
15	"A194"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-ethylcarbamoylbenzofuran-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		2.17 [474.1]
20				
25				
30	"A195"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(2-ethylcarbamoylbenzofuran-		2.17 [474.1]
35				

	5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		
"A196"	 N-(2-Chloro-3-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 7.49 (d, $J = 2.2$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.35 (tt, $J = 10.9, 5.5$ Hz, 1H), 7.29 (dd, $J = 12.6, 4.7$ Hz, 1H), 7.22 (d, $J = 7.6$ Hz, 1H), 6.88 (d, $J = 8.6$ Hz, 1H), 4.45 (d, $J = 16.2$ Hz, 1H), 4.36 (d, $J = 16.2$ Hz, 1H), 3.87 – 3.74 (m, 3H), 2.89 (dd, $J = 9.5, 5.6$ Hz, 2H), 2.63 – 2.54 (m, 1H), 2.48 – 2.40 (m, 2H), 2.14 (dt, $J = 13.0, 7.6$ Hz, 1H).	1.87 [432.0]
"A197"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide		2.08 [434.0]
"A198"			2.08 [434.0]

	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide			
5	"A199"	 N-[2-(3,5-Difluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	^{xx} 10.06 (s, 1H), 7.99 (t, <i>J</i> = 6.0 Hz, 1H), 7.48 (d, <i>J</i> = 2.2 Hz, 1H), 7.42 (dd, <i>J</i> = 8.6, 2.4 Hz, 1H), 7.03 (tt, <i>J</i> = 9.5, 2.3 Hz, 1H), 6.99 – 6.93 (m, 2H), 5.86 (d, <i>J</i> = 8.6 Hz, 1H), 6.55 (s, 1H), 3.76 (dd, <i>J</i> = 14.4, 8.5 Hz, 2H), 3.44 – 3.36 (m, 2H), 2.88 (dd, <i>J</i> = 10.1, 4.9 Hz, 2H), 2.79 (t, <i>J</i> = 7.0 Hz, 2H), 2.48 – 2.39 (m, 3H), 2.04 (dt, <i>J</i> = 12.8, 7.8 Hz, 1H).	
20	"A200"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	^{xx} 10.91 (s, 1H), 8.65 (t, <i>J</i> = 5.4 Hz, 1H), 7.57 (d, <i>J</i> = 1.8 Hz, 1H), 7.30 (dd, <i>J</i> = 8.7, 2.0 Hz, 1H), 7.27 – 7.20 (m, 3H), 7.11 (t, <i>J</i> = 11.6 Hz, 1H), 6.64 (s, 1H), 6.12 (s, 1H), 4.40 (dd, <i>J</i> = 15.7, 6.8 Hz, 1H), 4.26 (dd, <i>J</i> = 15.7, 6.0 Hz, 1H), 3.86 (dd, <i>J</i> = 14.7, 8.5 Hz, 2H), 2.62 – 2.54 (m, 1H), 2.37 (s, 3H), 2.12 (dt, <i>J</i> = 12.9, 7.5 Hz, 1H).	
35	"A201"		^{xx} 8.04 (dd, <i>J</i> = 12.8, 7.1 Hz, 3H), 7.98 – 7.92 (m, 1H), 7.70 (t, <i>J</i> = 10.4 Hz, 1H), 7.49 (t, <i>J</i> = 7.9 Hz, 1H), 7.40 (s, 1H), 7.07 – 7.00 (m, 1H), 6.97 (d, <i>J</i> = 6.8 Hz, 2H), 6.66 (s, 1H),	1.83 [404.1]

5	N-[2-(3,5-Difluorophenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.88 (dd, $J = 7.3, 6.1$ Hz, 2H), 3.50 – 3.38 (m, 3H), 2.80 (dd, $J = 16.6, 9.7$ Hz, 2H), 2.49 – 2.44 (m, 1H), 2.10 (dt, $J = 12.9, 7.8$ Hz, 1H).	
10	"A202"		2.23 [441.1]
15	Ethyl 3-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-cyclohexanecarboxylate	7.20 (d, $J = 1.2$ Hz, 1H), 7.09 (t, $J = 7.9$ Hz, 2H), 4.47 (d, $J = 15.9$ Hz, 1H), 4.33 (d, $J = 15.8$ Hz, 1H), 4.12 – 4.04 (m, 2H), 3.89 (dt, $J = 11.7, 9.9$ Hz, 1H), 3.43 (q, $J = 7.1$ Hz, 2H), 2.56 – 2.41 (m, 2H), 2.07 (m, 1H), 2.00 – 1.82 (m, 3H), 1.69 (m, 1H), 1.65 – 1.53 (m, 1H), 1.54 – 1.38 (m, 2H), 1.32 – 1.23 (m, 1H), 1.21 (t, $J = 7.1$ Hz, 3H).	
20	"A203"		1.70 [345.0]
25	[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-acetic acid		
30	"A204"		2.14 [474.0]
35	N-(3-Chloro-5-fluorobenzyl)-1-(3-carbamoyl-5-trifluoromethyl-		

	phenyl)-3-hydroxy-2-oxo- pyrrolidine-3-carboxamide			
5	"A205"	 Ethyl 5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indol-2-carboxylate	8.71 (s, 1H), 7.82 (d, $J = 1.9$ Hz, 1H), 7.64 (dd, $J = 9.0$, 2.1 Hz, 1H), 7.47 (d, $J = 9.0$ Hz, 1H), 7.26 (dt, $J = 8.7$, 2.1 Hz, 1H), 7.22 (s, 1H), 7.16 (d, $J = 0.5$ Hz, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 4.40 (d, $J = 15.7$ Hz, 1H), 4.35 (q, $J = 7.1$ Hz, 2H), 4.27 (d, $J = 15.7$ Hz, 1H), 3.90 (dd, $J = 14.6$, 8.4 Hz, 2H), 2.66 – 2.57 (m, 1H), 2.15 (dt, $J = 12.9$, 7.5 Hz, 1H), 1.35 (t, $J = 7.1$ Hz, 3H).	2.28 [474.1]
10				
15				
20	"A206"	 N-(2-Chloro-3-fluorobenzyl)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	11.10 (s, 1H), 8.61 (t, $J = 6.3$ Hz, 1H), 7.71 (s, 1H), 7.43 – 7.37 (m, 2H), 7.35 (dt, $J = 11.0$, 4.2 Hz, 2H), 7.32 – 7.27 (m, 1H), 7.25 (d, $J = 7.6$ Hz, 1H), 6.70 (s, 1H), 6.46 – 6.41 (m, 1H), 4.46 (dd, $J = 16.2$, 6.5 Hz, 1H), 4.36 (dd, $J = 16.2$, 6.0 Hz, 1H), 3.94 – 3.83 (m, 2H), 2.64 (m, 1H), 2.21 – 2.12 (m, 1H).	2.07 [402.0]
25				
30	"A207"	 N-[2-(3,5-Difluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	11.12 (d, $J = 37.6$ Hz, 1H), 7.98 (t, $J = 6.0$ Hz, 1H), 7.72 – 7.67 (m, 1H), 7.43 – 7.37 (m, 2H), 7.37 – 7.33 (m, 1H), 7.03 (tt, $J = 9.5$, 2.3 Hz, 1H), 6.99 – 6.94 (m, 2H), 6.52 (s, 1H), 6.46 – 6.41 (m, 1H), 3.88 –	2.08 [400.1]
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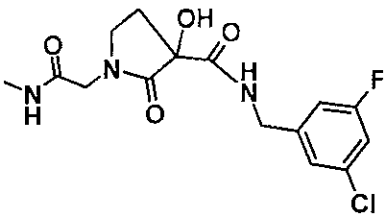
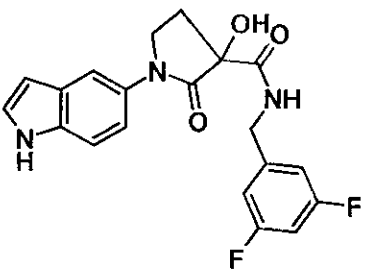
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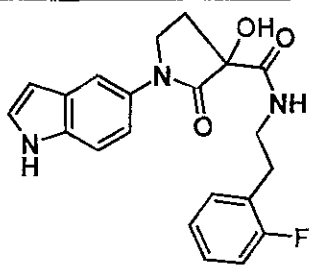
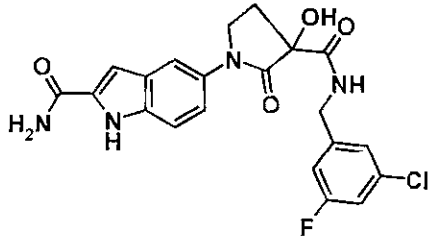
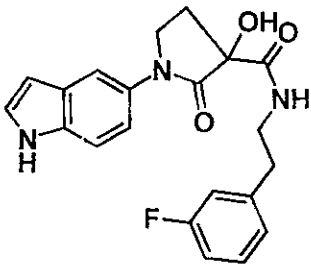
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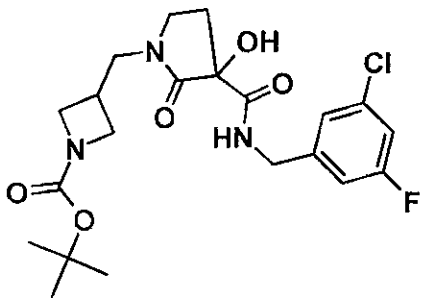
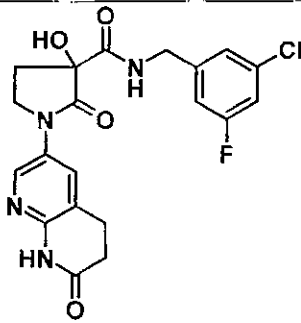
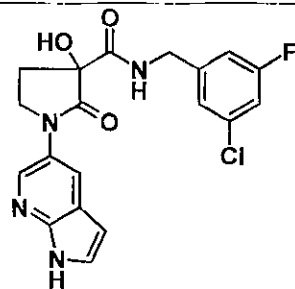
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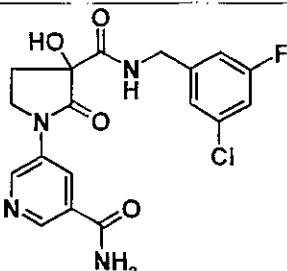
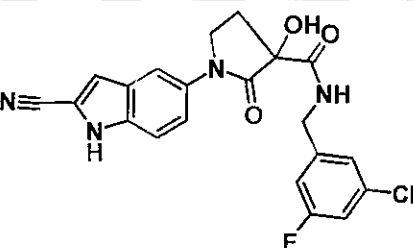
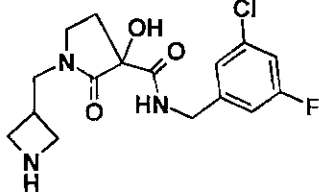
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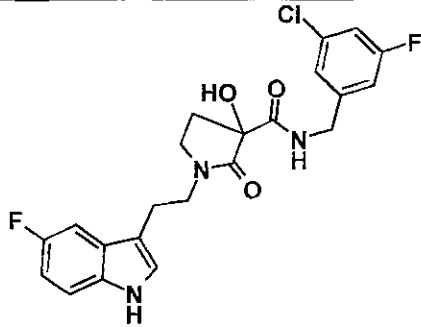
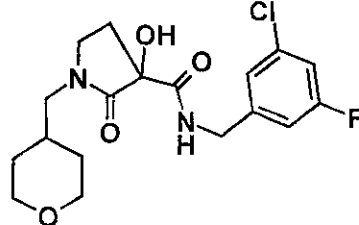
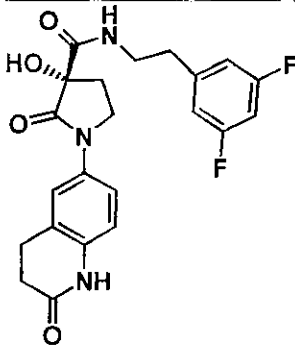
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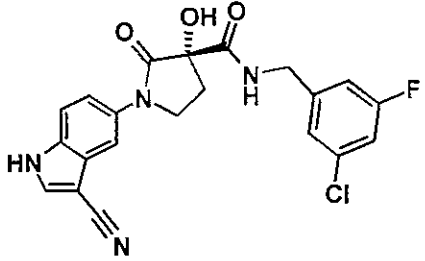
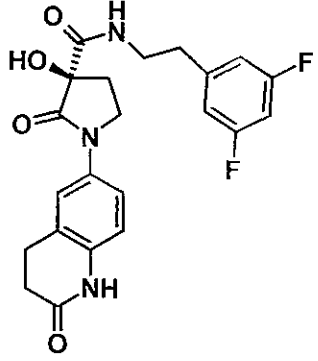
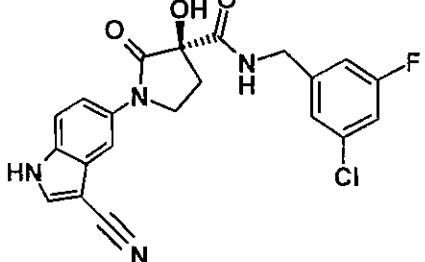
	3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	3.80 (m, 2H), 3.44 – 3.37 (m, 1H), 3.37 – 3.31 (m, 1H), 2.80 (t, $J = 7.0$ Hz, 2H), 2.48 – 2.44 (m, 1H), 2.07 (dt, $J = 12.8, 7.7$ Hz, 1H).	
"A208"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-methylcarbamoyl-methyl-2-oxopyrrolidine-3-carboxamide	¹³ C 8.69 (t, $J = 6.3$ Hz, 1H), 7.81 (d, $J = 4.5$ Hz, 1H), 7.26 (dt, $J = 8.8, 2.0$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.6$ Hz, 1H), 6.55 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.47 – 3.35 (m, 2H), 2.59 (d, $J = 4.6$ Hz, 3H), 2.43 (ddd, $J = 12.8, 7.5, 3.3$ Hz, 1H), 2.11 – 1.97 (m, 1H).	1.74 [358.0]
"A209"	 N-(3,5-Difluorobenzyl)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	¹³ C 11.10 (s, 1H), 8.65 (t, $J = 6.4$ Hz, 1H), 7.72 – 7.68 (m, 1H), 7.44 – 7.37 (m, 2H), 7.36 (t, $J = 2.7$ Hz, 1H), 7.08 – 7.02 (m, 1H), 7.02 – 6.95 (m, 2H), 6.66 (s, 1H), 6.47 – 6.39 (m, 1H), 4.42 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.27 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.93 – 3.83 (m, 2H), 2.62 (ddd, $J = 12.0, 6.9, 4.8$ Hz, 1H), 2.14 (dt, $J = 12.9, 7.5$ Hz, 1H).	2.00 [386.1]

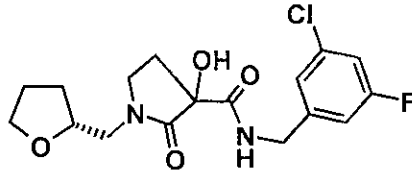
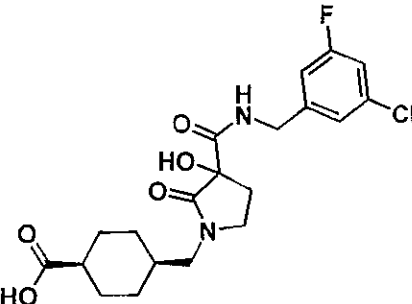
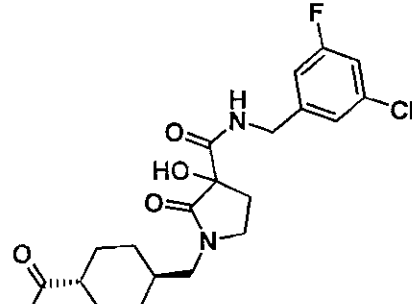
5	"A210"	 N-[2-(2-Fluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	11.08 (s, 1H), 7.98 (dd, $J = 15.2, 9.2$ Hz, 1H), 7.70 (s, 1H), 7.43 – 7.37 (m, 2H), 7.36 – 7.34 (m, 1H), 7.30 (dd, $J = 8.4, 6.7$ Hz, 1H), 7.28 – 7.22 (m, 1H), 7.15 (d, $J = 7.1$ Hz, 1H), 7.12 (ddd, $J = 4.5, 3.8, 1.2$ Hz, 1H), 6.67 – 6.22 (m, 2H), 3.90 – 3.77 (m, 2H), 3.40 (m, 1H), 3.34 – 3.29 (m, 1H), 2.86 – 2.76 (m, 2H), 2.49 – 2.42 (m, 1H), 2.07 (dt, $J = 12.8, 7.9$ Hz, 1H).	2.01 [382.1]
15	"A211"	 5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	11.54 (s, 1H), 8.67 (t, $J = 6.4$ Hz, 1H), 7.94 (s, 1H), 7.77 (d, $J = 2.0$ Hz, 1H), 7.54 (dd, $J = 8.9, 2.1$ Hz, 1H), 7.42 (d, $J = 8.9$ Hz, 1H), 7.33 (s, 1H), 7.28 – 7.23 (m, 1H), 7.22 (s, 1H), 7.16 – 7.08 (m, 2H), 6.67 (s, 1H), 4.40 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.94 – 3.85 (m, 2H), 2.61 (dt, $J = 11.9, 5.8$ Hz, 1H), 2.14 (dt, $J = 12.9, 7.5$ Hz, 1H).	1.91 [445.0]
30	"A212"	 N-[2-(3-Fluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	11.08 (s, 1H), 7.94 (t, $J = 5.9$ Hz, 1H), 7.70 (s, 1H), 7.44 – 7.36 (m, 2H), 7.33 (dt, $J = 14.2, 5.2$ Hz, 2H), 7.11 – 6.95 (m, 3H), 6.50 (s, 1H), 6.43 (s, 1H), 3.85 (m, 2H), 3.46 – 3.29 (m, 2H), 2.79 (t, $J = 7.2$ Hz, 2H), 2.49 – 2.37 (m, 1H), 2.07 (dt, $J = 12.8, 7.9$ Hz, 1H).	2.01 [382.1]
35				

5	"A213"	 tert-Butyl 3-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl-methyl]-azetidine-1-carboxylate	2.18 [400.1]	
15	"A214"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)pyrrolidine-3-carboxamide	10.51 (s, 1H), 8.74 (t, $J = 6.3$ Hz, 1H), 8.40 (d, $J = 2.5$ Hz, 1H), 7.94 (d, $J = 2.1$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.1$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd, $J = 15.6, 6.5$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.84 (t, $J = 5.9$ Hz, 2H), 2.90 (t, $J = 7.6$ Hz, 2H), 2.63 – 2.55 (m, 1H), 2.18 – 2.09 (m, 1H).	3.18 [433]
25	"A215"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)-pyrrolidine-3-carboxamide	11.70 (s, 1H), 8.74 (t, $J = 6.4$ Hz, 1H), 8.49 (d, $J = 2.4$ Hz, 1H), 8.16 (d, $J = 2.4$ Hz, 1H), 7.53 – 7.48 (m, 1H), 7.27 (dt, $J = 8.8, 2.0$ Hz, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 6.77 (s, 1H), 6.46 (dd, $J = 3.3, 1.8$ Hz, 1H), 4.40 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.26 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.96 – 3.85 (m, 2H), 2.68 – 2.57 (m, 1H), 2.16 (dt, $J = 12.9, 7.5$ Hz, 1H).	3.2 [403]
35				

5	"A216"	 5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-nicotinamide	9.10 (d, $J = 2.0$ Hz, 1H), 8.83 (s, 1H), 8.79 (t, $J = 6.3$ Hz, 1H), 8.44 (s, 1H), 8.23 (s, 1H), 7.67 (s, 1H), 7.28 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.88 (s, 1H), 4.38 (dd, $J = 15.7, 6.6$ Hz, 1H), 4.25 (dd, $J = 15.6, 6.0$ Hz, 1H), 3.94 (m, 2H), 2.68 – 2.58 (m, 1H), 2.23 – 2.13 (m, 1H).	2.89 [407]
15	"A217"	 N-(3-Chloro-5-fluorobenzyl)-1-(2-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.69 (t, $J = 6.3$ Hz, 1H), 7.86 (d, $J = 1.8$ Hz, 1H), 7.78 – 7.74 (m, 1H), 7.50 (d, $J = 9.0$ Hz, 1H), 7.38 (d, $J = 0.7$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 6.72 (s, 1H), 4.40 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.26 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.96 – 3.82 (m, 2H), 2.66 – 2.57 (m, 1H), 2.22 – 2.09 (m, 1H).	2.17 [427.0]
25	"A218"	 N-(3-Chloro-5-fluorobenzyl)-1-azetidin-3-ylmethyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.60 (t, $J = 6.4$ Hz, 1H), 8.37 (s, 1H), 7.31 – 7.24 (m, 1H), 7.23 – 7.18 (m, 1H), 7.10 (d, $J = 9.0$ Hz, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.29 – 4.17 (m, 2H), 3.88 – 3.73 (m, 5H), 3.64 – 3.46 (m, 1), 3.06 – 2.91 (m, 3H), 2.48 – 2.40 (m, 1H), 2.05 – 1.90 (m, 1H).	1.39 [356.1]

5	"A219"	 N-(3-Chloro-5-fluorobenzyl)-1-[2-(5-fluoro-1H-indol-3-yl)ethyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide	2.25 [448.1]
15	"A220"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(tetrahydropyran-4-ylmethyl)pyrrolidine-3-carboxamide	1.86 [385.1]
25	"A221"	 N-[2-(3,5-Difluorophenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide	1.87 [430.1]

"A222" 5 10	 N-(3-Chloro-5-fluorobenzyl)-(S)- 1-(3-cyano-1H-indol-5-yl)-3- hydroxy-2-oxopyrrolidine-3- carboxamide	2.07 [427.0]
"A223" 15 20	 N-[2-(3,5-Difluorophenyl)ethyl]- (R)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	1.88 [430.1]
"A224" 25 30	 N-(3-Chloro-5-fluorobenzyl)-(R)- 1-(3-cyano-1H-indol-5-yl)-3- hydroxy-2-oxopyrrolidine-3- carboxamide	2.07 [427.0]

5	"A225"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-[(R)-1-(tetrahydrofuran-2-yl)methyl]-pyrrolidine-3-carboxamide	1.89 [371.1]	
10	"A226"	 4-[3-(3-Chloro-5-fluorobenzyl)-carbamoyl]-3-hydroxy-2-oxo-pyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid	** 12.01 (s, 1H), 8.53 (t, $J = 6.4$ Hz, 1H), 7.24 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.18 (s, 1H), 7.10 – 7.06 (m, 1H), 6.40 (s, 1H), 4.41 – 4.32 (m, 1H), 4.23 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.33 (ddd, $J = 12.3, 8.6, 5.3$ Hz, 2H), 3.19 (dd, $J = 13.4, 8.4$ Hz, 1H), 3.00 (dd, $J = 13.4, 7.1$ Hz, 1H), 2.48 – 2.38 (m, 2H), 1.95 (ddd, $J = 12.9, 8.5, 6.7$ Hz, 1H), 1.89 – 1.78 (m, 2H), 1.73 (dt, $J = 16.1, 6.2$ Hz, 1H), 1.54 – 1.38 (m, 4H), 1.22 – 1.04 (m, 2H).	1.98 [427.2]
20				
25	"A227"	 4-[3-(3-Chloro-5-fluorobenzyl)-carbamoyl]-3-hydroxy-2-oxo-pyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid	** 11.94 (s, 1H), 8.54 (t, $J = 6.4$ Hz, 1H), 7.24 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.18 (s, 1H), 7.11 – 7.05 (m, 1H), 6.41 (s, 1H), 4.37 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.22 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.42 – 3.30 (m, 2H), 3.12 (dd, $J = 13.4, 7.9$ Hz, 1H), 2.98 (dd, $J = 13.4, 6.8$ Hz, 1H), 2.45 (ddd, $J = 11.6, 7.6, 3.8$ Hz,	1.89 [427.1]
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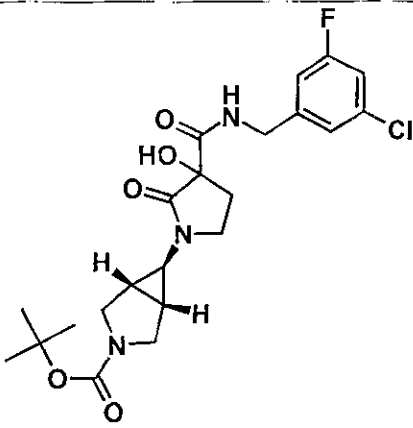
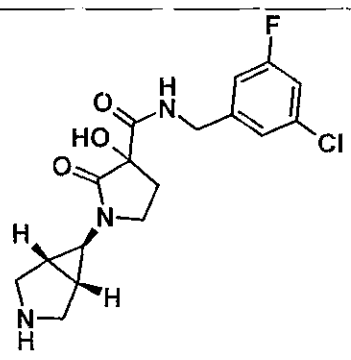
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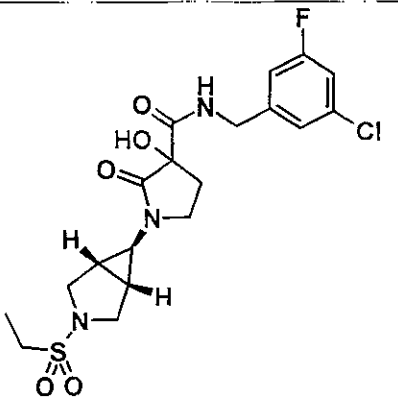
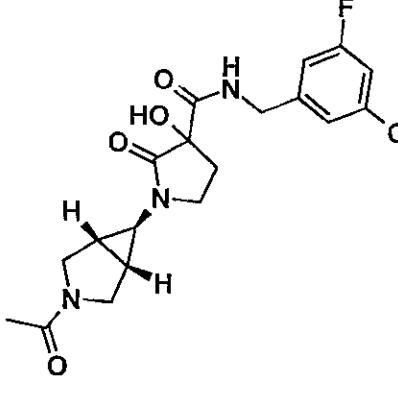
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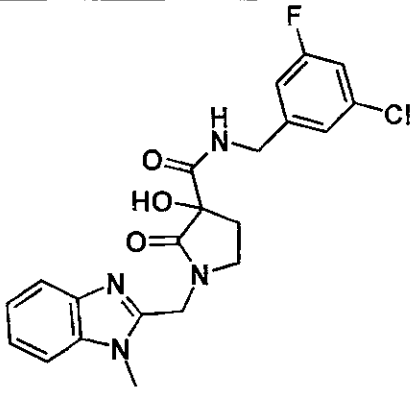
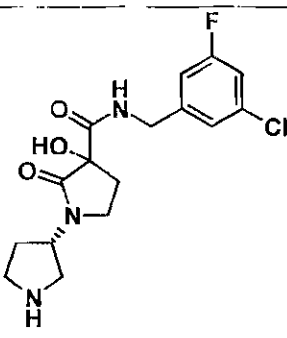
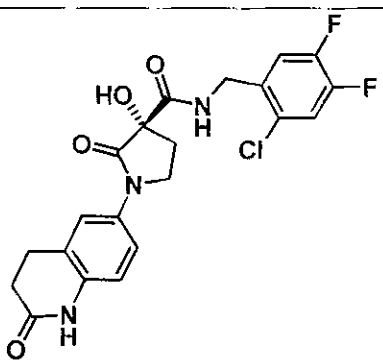
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		1H), 2.10 (tt, $J = 12.0, 3.4$ Hz, 1H), 2.01 – 1.91 (m, 1H), 1.91 – 1.78 (m, 2H), 1.68 (d, $J = 12.5$ Hz, 2H), 1.57 (dq, $J = 15.2, 7.6, 3.7$ Hz, 1H), 1.34 – 1.16 (m, 2H), 1.00 – 0.79 (m, 2H).	
"A228"	 tert-Butyl (1S,5R,6S)-6-[3-(3-chloro-5-fluorobenzyl-carbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-3-azabicyclo-[3.1.0]hexane-3-carboxylate	** 8.60 (dt, $J = 12.7, 6.1$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.47 (s, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.23 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.58 (s, 1H), 3.55 – 3.48 (m, 2H), 3.40 – 3.32 (m, 2H), 3.27 (m, 1H), 2.42 (ddd, $J = 12.3, 7.1, 4.9$ Hz, 1H), 2.34 (m, 1H), 1.99 – 1.87 (m, 3H), 1.39 (s, 9H).	2.23 [412.0]
"A229"	 N-(3-Chloro-5-fluorobenzyl)-1-(1S,5R,6S)-3-azabicyclo-[3.1.0]hex-6-yl-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	** 8.56 (t, $J = 6.3$ Hz, 1H), 8.24 (s, 1H), 7.27 (dt, $J = 8.8, 2.0$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.3$ Hz, 1H), 4.37 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.23 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.30 – 3.23 (m, 2H), 3.07 (m, 2H), 2.90 (m, 2H), 2.66 – 2.61 (m, 1H), 2.45 – 2.39 (m, 1H), 1.98 – 1.89 (m, 1H), 1.89 – 1.78 (m, 2H).	1.42 [368.0]

"A230"	 N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-ethanesulfonyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.56 (t, $J = 6.4$ Hz, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.18 (d, $J = 8.0$ Hz, 1H), 7.08 (d, $J = 9.4$ Hz, 1H), 6.47 (s, 1H), 4.35 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.22 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.49 – 3.39 (m, 4H), 3.09 (q, $J = 7.3$ Hz, 2H), 2.56 (t, $J = 2.3$ Hz, 1H), 2.42 (ddd, $J = 12.4, 7.1, 4.9$ Hz, 1H), 2.05 – 2.01 (m, 1H), 2.01 – 1.96 (m, 1H), 1.92 (ddd, $J = 17.4, 10.0, 5.5$ Hz, 1H), 1.18 (t, $J = 7.3$ Hz, 4H).	1.93 [460.0]
"A231"	 N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-acetyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.57 (t, $J = 6.3$ Hz, 1H), 7.96 (s, 1H), 7.31 – 7.23 (m, 2H), 7.19 (s, 1H), 7.09 (t, $J = 7.1$ Hz, 1H), 4.36 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.28 – 4.19 (m, 2H), 3.67 – 3.57 (m, 4H), 3.34 – 3.26 (m, 3H), 2.46 – 2.34 (m, 2H), 2.08 – 2.05 (m, 1H), 2.05 – 2.00 (m, 1H), 2.00 – 1.92 (m, 2H), 1.90 (s, 3H).	1.75 [410.1]

5	"A232"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-methyl-1H-benzimidazol-2-ylmethyl)-2-oxopyrrolidine-3-carboxamide	8.69 (t, $J = 6.3$ Hz, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.52 (d, $J = 7.9$ Hz, 1H), 7.28 – 7.22 (m, 2H), 7.21 – 7.17 (m, 2H), 7.12 – 7.07 (m, 1H), 4.84 (d, $J = 15.3$ Hz, 1H), 4.67 (d, $J = 15.3$ Hz, 1H), 4.39 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.71 (s, 3H), 3.37 (m, 2H), 3.26 – 3.17 (m, 2H), 2.44 (ddd, $J = 12.0, 8.0, 3.8$ Hz, 1H), 2.00 (ddd, $J = 13.1, 8.7, 6.4$ Hz, 1H).	1.78 [431.1]
15	"A233"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-[1,3']bipyrrolidiny-3-carboxamide	9.29 (s, 1H), 8.63 (q, $J = 6.1$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.21 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.59 (s, 1H), 4.66 – 4.51 (m, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.10 (br. s, 1H), 3.53 – 3.37 (m, 3H), 3.25 – 3.11 (m, 4H), 2.49 – 2.41 (m, 1H), 2.12 (m, 1H), 2.07 – 1.95 (m, 2H).	1.40 [356.1]
20	"A234"	 N-(2-Chloro-4,5-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)-pyrrolidine-3-carboxamide	10.07 (s, 1H), 8.70 (t, $J = 3.3$ Hz, 1H), 7.70 (dd, $J = 10.3, 7.3$ Hz, 1H), 7.48 (d, $J = 2.1$ Hz, 1H), 7.44 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.40 (dd, $J = 11.7, 8.6$ Hz, 1H), 6.87 (d, $J = 8.6$ Hz, 1H), 6.77 (s, 1H), 4.40 (dd, $J = 16.2, 6.7$ Hz, 1H), 4.22 (dd, $J = 16.2, 5.8$ Hz, 1H), 3.88 – 3.72	1.93 [450.0]

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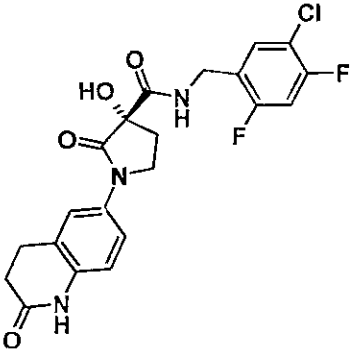
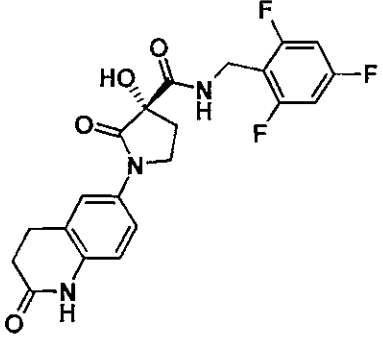
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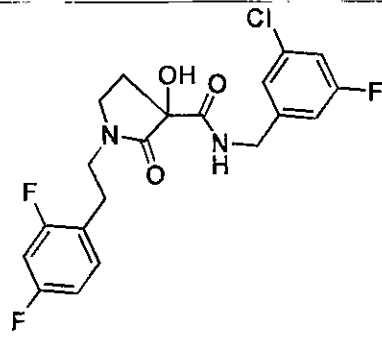
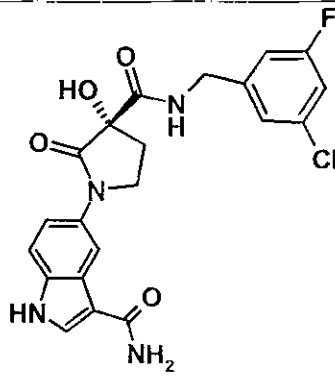
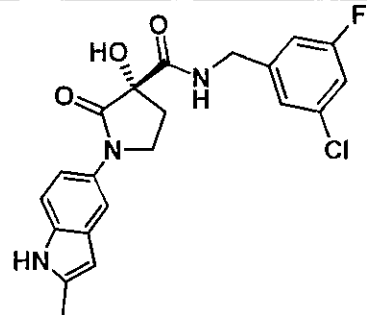
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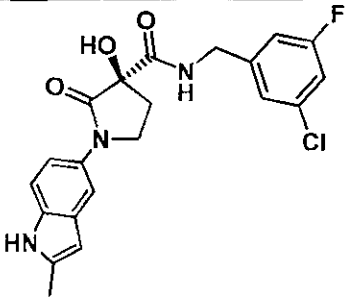
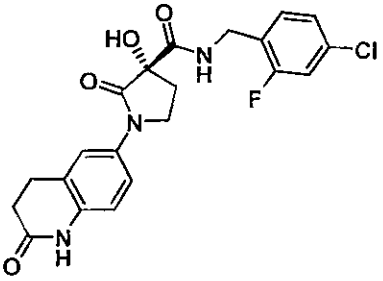
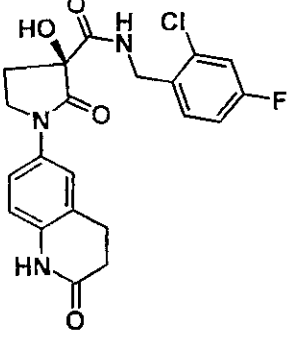
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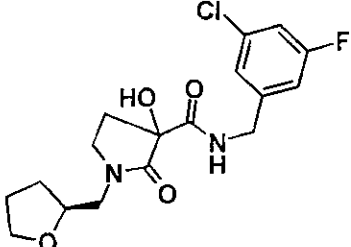
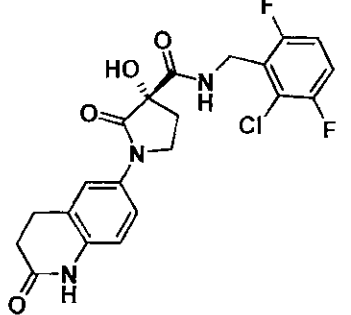
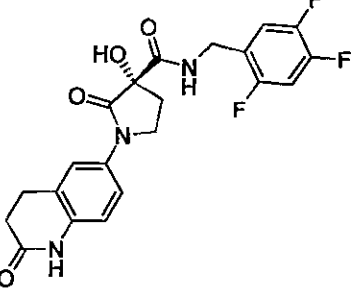
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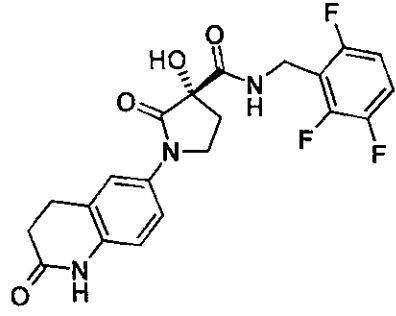
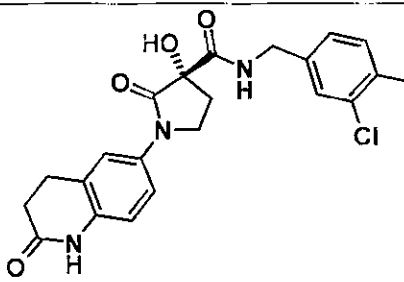
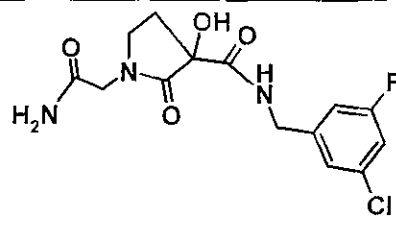
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	1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	(m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.62 (ddd, $J = 12.4, 7.0, 5.0$ Hz, 1H), 2.44 (dd, $J = 8.3, 5.8$ Hz, 2H), 2.12 (dt, $J = 13.0, 7.4$ Hz, 1H).	
"A235"	 N-(5-Chloro-2,4-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	¹³ C 10.06 (s, 1H), 8.62 (t, $J = 3.2$ Hz, 1H), 7.54 (t, $J = 8.0$ Hz, 1H), 7.50 – 7.45 (m, 2H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.70 (s, 1H), 4.37 (dd, $J = 15.6, 6.5$ Hz, 1H), 4.25 (dd, $J = 15.6, 5.8$ Hz, 1H), 3.87 – 3.74 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.57 (ddd, $J = 11.8, 7.0, 4.7$ Hz, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.10 (dt, $J = 12.9, 7.6$ Hz, 1H).	1.92 [450.0]
"A236"	 N-(2,4,6-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	¹³ C 10.06 (s, 1H), 8.20 (t, $J = 5.7$ Hz, 1H), 7.47 (d, $J = 2.1$ Hz, 1H), 7.41 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.20 – 7.09 (m, 2H), 6.85 (d, $J = 8.6$ Hz, 1H), 6.55 (s, 1H), 4.35 (dd, $J = 14.5, 5.8$ Hz, 1H), 4.30 (dd, $J = 14.5, 5.6$ Hz, 1H), 3.88 – 3.67 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.47 – 2.38 (m, 2H), 2.05 (dt, $J = 12.8, 8.4$ Hz, 1H).	1.78 [434.1]

5	"A237"	 N-(3-Chloro-5-fluorobenzyl)-1-[2-(2,4-Difluorophenyl)ethyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide	2.31 [427.0]
15	"A238"	 5-[(S)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-3-carboxamide	1.90 [445.0]
25	"A239"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	2.19 [416.0]

"A240"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide		2.19 [416.1]
"A241"	 N-(4-Chloro-2-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.54 (t, $J = 5.2$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.39 – 7.34 (m, 2H), 7.25 (dd, $J = 8.3, 1.9$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.66 (s, 1H), 4.35 (dd, $J = 15.6, 6.4$ Hz, 1H), 4.29 (dd, $J = 15.6, 6.1$ Hz, 1H), 3.88 – 3.75 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.56 (ddd, $J = 12.6, 6.8, 4.8$ Hz, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.10 (dt, $J = 12.9, 7.7$ Hz, 1H).	1.91 [432.0]
"A242"	 N-(2-Chloro-4-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.07 (s, 1H), 8.57 (t, $J = 6.3$ Hz, 1H), 7.48 (d, $J = 2.1$ Hz, 1H), 7.46 – 7.37 (m, 3H), 7.20 (td, $J = 8.6, 2.6$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.72 (s, 1H), 4.38 (dd, $J = 15.9, 6.5$ Hz, 1H), 4.29 (dd, $J = 15.9, 6.0$ Hz, 1H), 3.90 – 3.63 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.67 –	1.88 [432.1]

	1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	2.55 (m, 1H), 2.44 (dd, $J = 8.3$, 6.8 Hz, 2H), 2.19 – 2.03 (m, 1H).	
5	"A243"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-[(S)-1-(tetrahydrofuran-2-yl)methyl]-pyrrolidine-3-carboxamide	1.89 [371.1]
15	"A244"	 N-(2-Chloro-3,6-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.85 [450.0]
25	"A245"	 N-(2,4,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.83 [434.1]

		1H), 2.45 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.12 (dt, $J = 13.0, 7.5$ Hz, 1H).	
"A246"	 N-(2,3,6-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.07 (s, 1H), 8.32 (t, $J = 5.7$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.47 – 7.40 (m, 2H), 7.11 (tdd, $J = 9.2, 3.7, 2.1$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.57 (s, 1H), 4.44 (dd, $J = 14.5, 5.8$ Hz, 1H), 4.38 (dd, $J = 14.5, 5.6$ Hz, 1H), 3.88 – 3.68 (m, 2H), 2.89 (t, $J = 7.5$ Hz, 2H), 2.46 (td, $J = 8.8, 5.6$ Hz, 2H), 2.15 – 1.97 (m, 1H).	1.77 [434.1]
"A247"	 N-(3-Chloro-4-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.61 (t, $J = 6.4$ Hz, 1H), 7.48 (d, $J = 2.4$ Hz, 1H), 7.48 – 7.45 (m, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.36 – 7.31 (m, 1H), 7.29 – 7.25 (m, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.64 (s, 1H), 4.39 – 4.28 (m, 1H), 4.23 (dd, $J = 15.2, 6.1$ Hz, 1H), 3.84 – 3.72 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.60 – 2.51 (m, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.09 (dt, $J = 12.9, 7.7$ Hz, 1H).	1.89 [432.1]
"A248"	 N-(3-Chloro-5-fluorobenzyl)-1-carbamoylmethyl-3-hydroxy-2-	8.71 (t, $J = 6.3$ Hz, 1H), 7.33 (s, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (d, $J = 11.4$ Hz, 2H), 7.08 (d, $J = 9.1$ Hz, 1H), 6.57 (s, 1H), 4.37 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J =$	1.66 [344.0]

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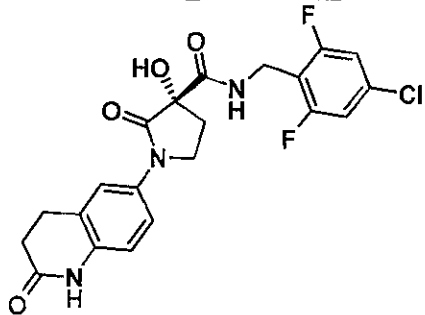
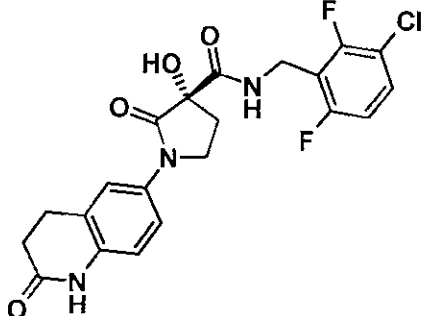
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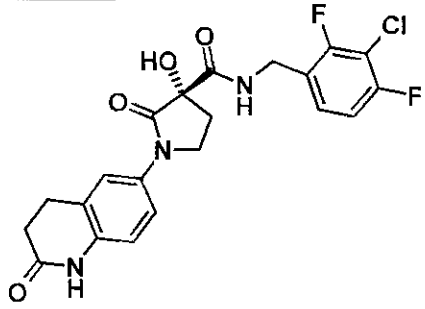
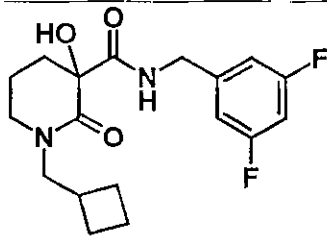
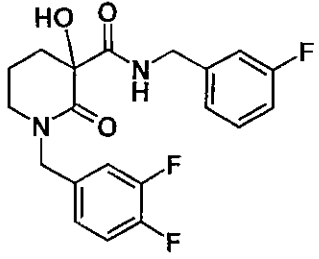
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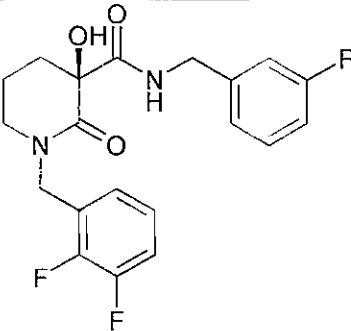
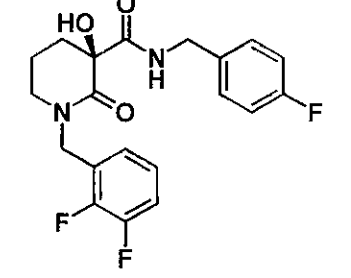
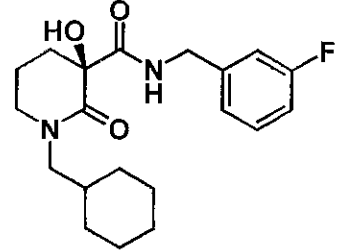
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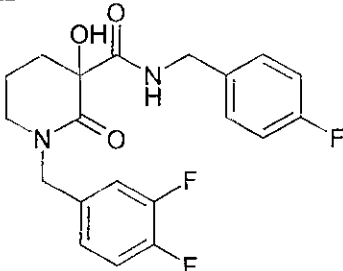
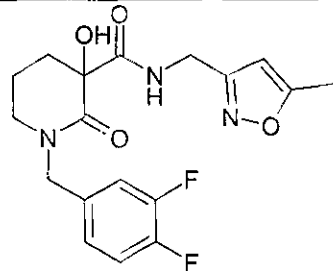
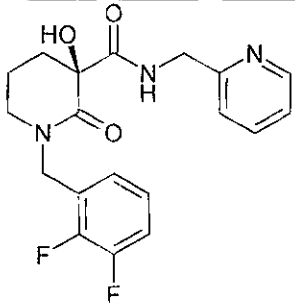
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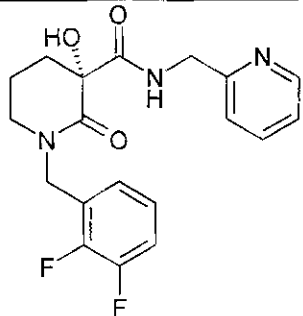
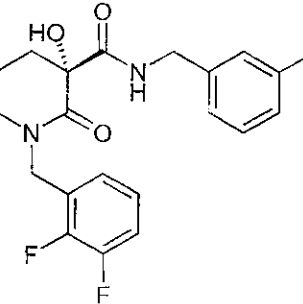
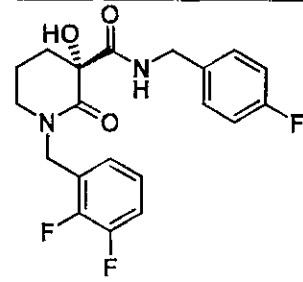
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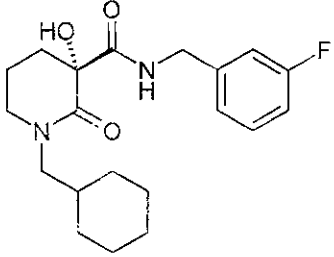
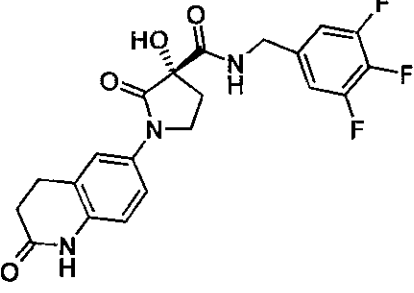
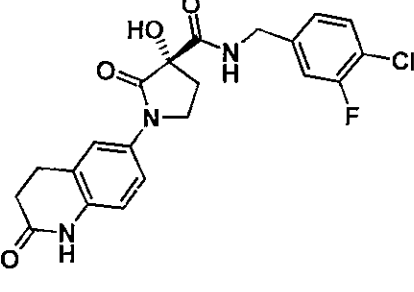
	oxopyrrolidine-3-carboxamide	15.7, 6.0 Hz, 1H), 3.89 (d, J = 16.8 Hz, 1H), 3.74 (d, J = 16.8 Hz, 1H), 3.42 (ddd, J = 14.9, 10.9, 5.4 Hz, 3H), 2.41 (ddd, J = 13.0, 7.2, 3.2 Hz, 1H), 2.05 (dt, J = 13.0, 8.2 Hz, 1H).	
"A249"	 N-(4-Chloro-2,6-difluorobenzyl)- (S)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.33 – 8.16 (m, 1H), 7.47 (d, J = 2.1 Hz, 1H), 7.41 (dd, J = 8.6, 2.4 Hz, 1H), 7.37 – 7.25 (m, 2H), 6.85 (d, J = 8.6 Hz, 1H), 6.55 (s, 1H), 4.36 (dd, J = 14.5, 5.8 Hz, 1H), 4.31 (dd, J = 14.5, 5.5 Hz, 1H), 3.85 – 3.70 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.45 (ddd, J = 15.1, 7.1, 4.4 Hz, 3H), 2.05 (dt, J = 12.9, 8.4 Hz, 1H).	1.92 [450.0]
"A250"	 N-(3-Chloro-2,6-difluorobenzyl)- (S)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.31 (t, J = 5.7 Hz, 1H), 7.57 (td, J = 8.7, 5.7 Hz, 1H), 7.47 (d, J = 2.2 Hz, 1H), 7.41 (dd, J = 8.6, 2.4 Hz, 1H), 7.14 (td, J = 9.0, 1.5 Hz, 1H), 6.85 (d, J = 8.6 Hz, 1H), 6.55 (s, 1H), 4.42 (dd, J = 14.5, 5.8 Hz, 1H), 4.37 (dd, J = 14.5, 5.6 Hz, 1H), 3.86 – 3.68 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.45 (td, J = 8.9, 5.6 Hz, 2H), 2.16 – 1.97 (m, 1H).	1.88 [450.1]

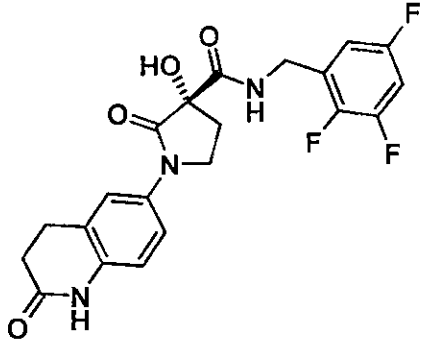
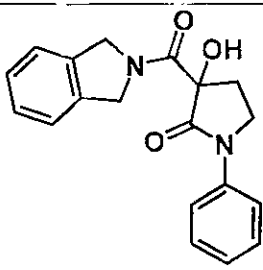
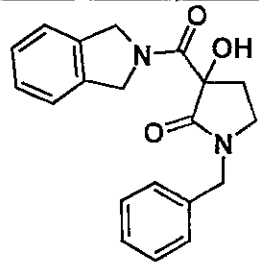
5	"A251"	 N-(3-Chloro-2,4-difluorobenzyl)- (S)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	10.06 (s, 1H), 8.60 (t, $J = 6.2$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.40 – 7.34 (m, 1H), 7.29 (td, $J = 8.8, 1.5$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.67 (s, 1H), 4.38 (dd, $J = 15.4, 6.3$ Hz, 1H), 4.31 (dd, $J = 15.4, 6.0$ Hz, 1H), 3.88 – 3.69 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.56 (ddd, $J = 12.6, 6.8, 4.8$ Hz, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.10 (dt, $J = 12.9, 7.6$ Hz, 1H).	1.95 [450.0]
15	"A252"	 N-(3,5-Difluorobenzyl)-1- cyclobutylmethyl-3-hydroxy-2- oxopiperidine-3-carboxamide	8.49 (t, $J = 6.3$ Hz, 1H), 7.12 – 6.93 (m, 3H), 6.14 (s, 1H), 4.39 (dd, $J = 16.1, 7.1$ Hz, 1H), 4.20 (dd, $J = 16.1, 5.7$ Hz, 1H), 3.41 (dd, $J = 13.1, 7.4$ Hz, 1H), 3.25 (dd, $J = 13.1, 7.3$ Hz, 2H), 2.54 (m, 1H), 2.12 (m, 1H), 1.99 – 1.90 (m, 2H), 1.85 – 1.75 (m, 4H), 1.75 – 1.62 (m, 2H).	3.93 [353.2]
20	"A253"	 N-(3-Fluorobenzyl)-1-(3,4- difluorobenzyl)-3-hydroxy-2-oxo- piperidine-3-carboxamide	8.52 (t, $J = 6.3$ Hz, 1H), 7.35 (m, 3H), 7.16 – 7.09 (m, 3H), 7.07 – 6.98 (m, 1H), 6.37 (s, 1H), 4.61 (d, $J = 15.3$ Hz, 1H), 4.41 (d, $J = 15.3$ Hz, 1H), 4.39 (dd, $J = 15.6, 6.9$ Hz, 1H), 4.26 (dd, $J = 15.6, 5.9$ Hz, 1H), 3.25 (m, 2H), 2.24 – 2.12 (m, 1H), 1.86 (m, 3H).	4.23 [393]

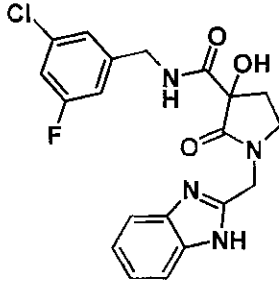
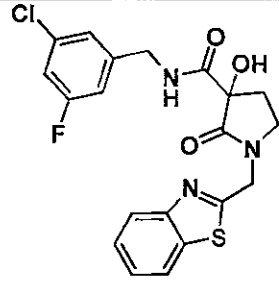
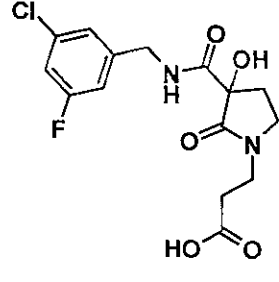
"A254"	 N-(3-Fluorobenzyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.51 (t, $J = 6.3$ Hz, 1H), 7.39 – 7.27 (m, 2H), 7.15 (m, 4H), 7.07 – 6.97 (m, 1H), 6.35 (s, 1H), 4.69 (d, $J = 15.7$ Hz, 1H), 4.52 (d, $J = 15.7$ Hz, 1H), 4.38 (dd, $J = 15.6, 6.8$ Hz, 1H), 4.26 (dd, $J = 15.6, 5.9$ Hz, 1H), 2.18 (m, 1H), 1.88 (m, 3H).	4.16 [393]
"A255"	 N-(4-Fluorobenzyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.44 (t, $J = 6.3$ Hz, 1H), 7.38 – 7.28 (m, 3H), 7.22 – 7.08 (m, 4H), 6.31 (s, 1H), 4.68 (d, $J = 15.7$ Hz, 1H), 4.51 (d, $J = 15.7$ Hz, 1H), 4.32 (dd, $J = 15.2, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.2, 6.0$ Hz, 1H), 2.22 – 2.15 (m, 1H), 1.85 (m, 3H), 1.23 (m, 2H), 0.84 (m, 1H).	4.13 [393]
"A256"	 N-(3-Fluorobenzyl)-(S)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide	8.40-8.39 (m, 1H), 7.31 (t, $J = 7.48$ Hz, 1H), 7.11 (m, 2H), 7.05-7.00 (m, 1H), 6.08 (s, 1H), 4.39-4.33 (m, 1H), 4.26-4.20 (m, 1H), 3.28-3.22 (m, 3H), 3.04-3.01 (m, 1H), 2.17 (m, 1H), 1.85-1.77 (m, 3H), 1.63-1.62 (m, 6H), 1.23-1.13 (m, 3H), 0.89-0.83 (m, 2H).	4.44 [363.3]

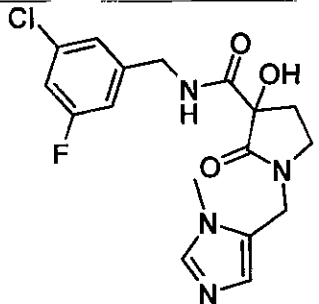
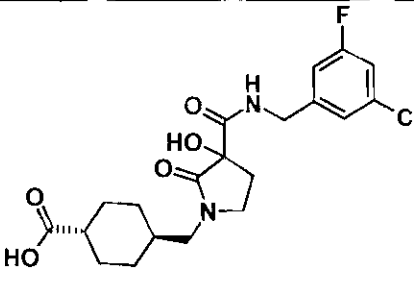
5	"A257"	 N-(4-Fluorobenzyl)-1-(3,4-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.45 (t, $J = 6.4$ Hz, 1H), 7.40 (dt, $J = 10.8, 8.5$ Hz, 1H), 7.31 (dt, $J = 5.5, 4.5$ Hz, 3H), 7.11 (dd, $J = 12.3, 5.5$ Hz, 3H), 6.32 (s, 1H), 4.61 (d, $J = 15.3$ Hz, 1H), 4.40 (d, $J = 15.3$ Hz, 1H), 4.33 (dd, $J = 15.0, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.2, 6.0$ Hz, 1H), 3.25 (t, $J = 8.7$ Hz, 2H), 2.15 (d, $J = 8.5$ Hz, 1H), 1.84 (d, $J = 3.2$ Hz, 3H).	4.19 [393.2]
15	"A258"	 N-(5-Methylisoxazol-3-ylmethyl)-1-(3,4-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.49 (t, $J = 6.1$ Hz, 1H), 7.40 (dt, $J = 10.7, 8.5$ Hz, 1H), 7.35 – 7.28 (m, 1H), 7.13 (s, 1H), 6.32 (s, 1H), 6.12 (s, 1H), 4.61 (d, $J = 15.3$ Hz, 1H), 4.39 (d, $J = 15.3$ Hz, 1H), 4.28 (m, 2H), 3.24 (d, $J = 5.2$ Hz, 2H), 2.35 (s, 3H), 2.13 (m, 1H), 1.90 – 1.78 (m, 3H).	3.45 [380]
25	"A259"	 N-(Pyridin-2-ylmethyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.53 (t, $J = 5.9$ Hz, 1H), 8.49 (d, $J = 4.1$ Hz, 1H), 7.73 (td, $J = 7.7, 1.8$ Hz, 1H), 7.40 – 7.29 (m, 2H), 7.24 (dd, $J = 7.0, 5.3$ Hz, 1H), 7.21 – 7.11 (m, 2H), 6.40 (s, 1H), 4.69 (d, $J = 15.7$ Hz, 1H), 4.52 (d, $J = 15.7$ Hz, 1H), 4.44 (dd, $J = 16.4, 6.2$ Hz, 1H), 4.35 (dd, $J = 16.4, 5.8$ Hz, 1H), 3.30 (m, 1H), 2.52 (m, 1H), 2.21 (m, 1H), 1.89 (m, 3H).	2.57 [376]
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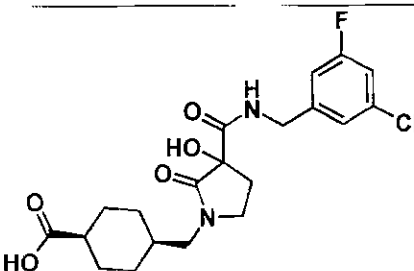
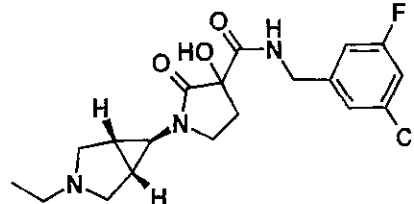
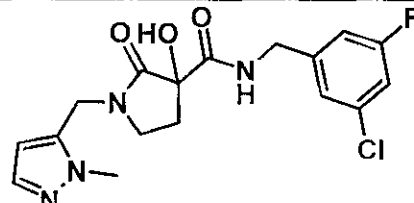
"A260"	 N-(Pyridin-2-ylmethyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.53 (t, $J = 6.0$ Hz, 1H), 8.49 (ddd, $J = 4.8, 1.7, 0.9$ Hz, 1H), 7.73 (td, $J = 7.7, 1.8$ Hz, 1H), 7.40 – 7.29 (m, 2H), 7.24 (dd, $J = 7.0, 5.3$ Hz, 1H), 7.22 – 7.10 (m, 2H), 6.40 (s, 1H), 4.69 (d, $J = 15.6$ Hz, 1H), 4.52 (d, $J = 15.5$ Hz, 1H), 4.44 (dd, $J = 16.4, 6.2$ Hz, 1H), 4.35 (dd, $J = 16.4, 5.7$ Hz, 1H), 3.30 (m, 1H), 2.52 (m, 1H), 2.29 – 2.16 (m, 1H), 1.90 (m, 3H).	2.57 [376.2]
"A261"	 N-(3-Fluorobenzyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.51 (t, $J = 6.2$ Hz, 1H), 7.33 (dt, $J = 8.1, 6.3$ Hz, 2H), 7.15 (ddd, $J = 24.5, 12.2, 8.4$ Hz, 4H), 7.03 (t, $J = 9.1$ Hz, 1H), 5.35 (s, 1H), 4.69 (d, $J = 15.6$ Hz, 1H), 4.52 (d, $J = 15.6$ Hz, 1H), 4.38 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.38 – 3.33 (m, 1H), 2.52 (m, 1H), 2.19 (m, 1H), 1.88 (m, 3H).	4.16 [393]
"A262"	 N-(4-Fluorobenzyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	3.45 (d, $J = 6.3$ Hz, 1H), 7.38 – 7.28 (m, 3H), 7.14 (dt, $J = 17.8, 7.0$ Hz, 4H), 6.31 (s, 1H), 4.68 (d, $J = 15.7$ Hz, 1H), 4.51 (d, $J = 15.7$ Hz, 1H), 4.32 (dd, $J = 15.1, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.1, 6.1$ Hz, 1H), 2.52 (m, 2H), 2.23 – 2.11 (m, 1H), 1.87 (m, 3H).	4.13 [393.2]

"A263"	 N-(3-Fluorobenzyl)-(R)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide	5 8.40-8.39 (m, 1H), 7.31 (t, J = 7.48 Hz, 1H), 7.11-7.11 (m, 2H), 7.05-7.00 (m, 1H), 6.08 (s, 1H), 4.39-4.33 (m, 1H), 4.26-4.20 (m, 1H), 3.28-3.22 (m, 3H), 3.04-3.01 (m, 1H), 2.17-2.17 (m, 1H), 1.85-1.77 (m, 3H), 1.63-1.62 (m, 6H), 1.23-1.13 (m, 3H), 0.89-0.83 (m, 2H).	4.44 [363.3]
"A264"	 N-(3,4,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	15 10.07 (s, 1H), 8.69 (t, J = 6.4 Hz, 1H), 7.48 (d, J = 2.1 Hz, 1H), 7.43 (dd, J = 8.6, 2.4 Hz, 1H), 7.28 – 7.11 (m, 2H), 6.87 (d, J = 8.6 Hz, 1H), 6.70 (s, 1H), 4.37 (dd, J = 15.7, 6.7 Hz, 1H), 4.22 (dd, J = 15.7, 6.0 Hz, 1H), 3.92 – 3.69 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.62 – 2.55 (m, 1H), 2.44 (dd, J = 8.3, 6.8 Hz, 2H), 2.10 (dt, J = 13.0, 7.5 Hz, 1H).	1.87 [434.1]
"A265"	 N-(4-Chloro-3-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	30 10.07 (s, 1H), 8.64 (t, J = 6.4 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.48 (d, J = 2.2 Hz, 1H), 7.43 (dd, J = 8.6, 2.4 Hz, 1H), 7.29 (dd, J = 10.5, 1.8 Hz, 1H), 7.14 (dd, J = 8.3, 1.3 Hz, 1H), 6.86 (d, J = 8.6 Hz, 1H), 6.67 (s, 1H), 4.36 (dd, J = 15.5, 6.7 Hz, 1H), 4.25 (dd, J = 15.6, 6.1 Hz, 1H), 3.85 – 3.69 (m, 2H),	1.90 [432.0]

		2.88 (t, $J = 7.5$ Hz, 2H), 2.57 (dt, $J = 11.8, 5.6$ Hz, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.15 – 1.99 (m, 1H).	
5	"A266"	 N-(2,3,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.07 (s, 1H), 8.68 (t, $J = 6.2$ Hz, 1H), 7.47 (t, $J = 7.0$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.3$ Hz, 1H), 7.41 – 7.35 (m, 1H), 7.10 – 6.97 (m, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.72 (s, 1H), 4.45 (dd, $J = 15.9, 6.6$ Hz, 1H), 4.32 (dd, $J = 15.9, 5.8$ Hz, 1H), 3.92 – 3.67 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.62 – 2.53 (m, 1H), 2.46 – 2.37 (m, 2H), 2.11 (dt, $J = 13.0, 7.5$ Hz, 1H). 1.83 [434.1]
20	"A267"	 3-(1,3-Dihydroisoindole-2-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one	¹H (300 MHz, DMSO-d_6/TFA-d_1) 7.75 (2 H, m), 7.30 (7 H, m), 4.81 (4 H, m), 3.88 (2 H, m), 2.81 (1 H, ddd, J 12.8, 6.5, 2.8), 2.25 (1 H, m). 2.04 [323.0]
30	"A268"	 1-Benzyl-3-(1,3-dihydroisoindole-2-carbonyl)-3-hydroxy-pyrrolidin-2-one	* 7.33 (9 H, m), 4.74 (6 H, m), 3.48 (2 H, m), 2.75 (1 H, m), 2.12 (1 H, m). 2.04 [337.0]
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"A269"	 N-(3-Chloro-5-fluorobenzyl)-1-(1H-benzimidazol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	7.83 (2 H, dd, J 6.2, 3.1), 7.58 (2 H, dd, J 6.2, 3.2), 7.23 (1 H, s), 7.13 (2 H, dt, J 16.1, 4.9), 5.06 (2 H, s), 4.48 (1 H, d, J 15.6), 4.33 (1 H, d, J 15.6), 3.65 (2 H, m), 2.63 (1 H, m), 2.25 (1 H, m).	1.72 [417.0]
"A270"	 N-(3-Chloro-5-fluorobenzyl)-1-benzothiazol-2-ylmethyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.65 (1 H, t, J 6.3), 8.08 (1 H, dd, J 8.0, 0.6), 7.99 (1 H, d, J 7.6), 7.52 (1 H, m), 7.45 (1 H, td, J 7.7, 1.2), 7.28 (1 H, ddd, J 12.3, 8.7, 4.9), 7.22 (1 H, s), 7.12 (1 H, dd, J 9.6, 0.7), 6.64 (1 H, s), 4.88 (2 H, s), 4.40 (1 H, dd, J 15.7, 6.7), 4.26 (1 H, dd, J 15.7, 6.0), 3.51 (2 H, m), 2.54 (1 H, m), 2.05 (1 H, dt, J 13.1, 7.0).	2.16 [434.0]
"A271"	 3-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-propionic acid	¹H NMR (500 MHz, DMSO-d₆ / TFA-d₄) 7.20 (2 H, m), 7.11 (1 H, d, J 9.4), 4.41 (1 H, d, J 15.7), 4.28 (1 H, d, J 15.7), 3.48 (2 H, t, J 7.2), 3.42 (2 H, m), 2.48 (3 H, dt, J 7.3, 6.0), 2.01 (1 H, m).	1.67 [359.0]

"A272"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(3-methyl-3H-imidazol-4-ylmethyl)-2-oxopyrrolidine-3-carboxamide	9.10 (1 H, s), 7.67 (1 H, s), 7.20 (2 H, m), 7.10 (1 H, d, J 10.0), 4.83 (1 H, d, J 15.8), 4.52 (1 H, d, J 15.9), 4.44 (1 H, d, J 15.8), 4.28 (1 H, d, J 15.8), 3.78 (3 H, s), 3.33 (2 H, m), 2.49 (1 H, m), 2.10 (1 H, m).	1.37 [381.0]
"A273"	 4-[3-(3-Chloro-5-fluorobenzylcarbonyl)-3-hydroxy-2-oxopyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid	** 11.94 (s, 1H), 8.54 (t, J = 6.4 Hz, 1H), 7.24 (dt, J = 8.7, 2.1 Hz, 1H), 7.18 (s, 1H), 7.11 - 7.06 (m, 1H), 6.41 (s, 1H), 4.37 (dd, J = 15.8, 6.8 Hz, 1H), 4.22 (dd, J = 15.8, 6.0 Hz, 1H), 3.41 - 3.30 (m, 2H), 3.12 (dd, J = 13.4, 7.9 Hz, 1H), 2.98 (dd, J = 13.4, 6.8 Hz, 1H), 2.45 (ddd, J = 11.6, 7.6, 3.8 Hz, 1H), 2.10 (tt, J = 12.0, 3.4 Hz, 1H), 1.95 (ddd, J = 12.9, 8.5, 6.7 Hz, 1H), 1.91 - 1.78 (m, 2H), 1.68 (d, J = 12.5 Hz, 2H), 1.57 (dq, J = 15.2, 7.6, 3.7 Hz, 1H), 1.24 (dq, J = 16.4, 13.0, 3.3 Hz, 2H), 0.90 (dh, J = 13.0, 3.3 Hz 2H).	1.89 [427.1]

"A274"	 4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl-methyl]cyclohexanecarboxylic acid	** 12.01 (s, 1H), 8.53 (t, $J = 6.4$ Hz, 1H), 7.24 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.18 (s, 1H), 7.09 – 7.04 (m, 1H), 6.40 (s, 1H), 4.36 (dd, $J = 15.8, 6.6$ Hz, 1H), 4.23 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.39 – 3.29 (m, 3H), 3.19 (dd, $J = 13.4, 8.4$ Hz, 1H), 3.00 (dd, $J = 13.4, 7.1$ Hz, 1H), 2.47 – 2.37 (m, 2H), 2.00 – 1.90 (m, 1H), 1.88 – 1.76 (m, 2H), 1.73 (dt, $J = 16.1, 6.2$ Hz, 1H), 1.52 – 1.38 (m, 4H), 1.23 – 1.10 (m, 2H).	1.98 [427.1]
"A275"	 N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-ethyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.54 (t, $J = 6.4$ Hz, 1H), 8.17 (s, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 9.1$ Hz, 1H), 4.36 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.22 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.28 – 3.21 (m, 2H), 3.05 (dd, $J = 8.9, 1.8$ Hz, 2H), 2.87 (d, $J = 14.1$ Hz, 1H), 2.44 – 2.34 (m, 4H), 2.33 – 2.27 (m, 2H), 1.93 – 1.86 (m, 1H), 1.81 – 1.74 (m, 2H), 0.98 (t, $J = 7.2$ Hz, 3H).	1.46 [396.1]
"A276"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-2H-pyrazol-3-ylmethyl)-2-oxopyrrolidine-3-carboxamide	** 8.63 (t, $J = 6.4$ Hz, 1H), 7.32 (d, $J = 1.8$ Hz, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (dd, $J = 9.7, 0.7$ Hz, 1H), 6.56 (s, 1H), 6.22 (d, $J = 1.8$ Hz, 1H), 4.60 (d, $J = 15.5$ Hz, 1H), 4.44 (d, $J = 15.5$ Hz, 1H).	1.84 [381.1]

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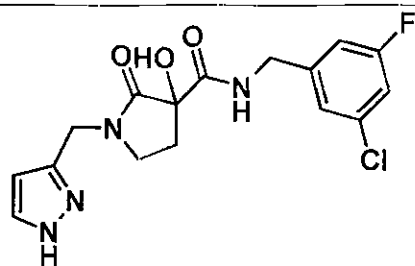
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carboxamide

1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.69 (s, 3H), 3.27 – 3.16 (m, 3H), 2.44 (ddd, $J = 12.8, 7.6, 4.0$ Hz, 1H), 1.97 (ddd, $J = 13.0, 8.6, 6.7$ Hz, 1H).

"A277"



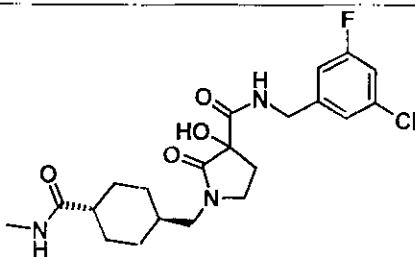
N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1H-pyrazol-3-ylmethyl)pyrrolidine-3-carboxamide

12.66 (s, 1H), 8.60 (t, $J = 6.0$ Hz, 1H), 8.57 – 8.48 (m, 1H), 8.16 (s, 1H), 7.64 (s, 1H), 7.33 – 7.24 (m, 2H), 7.20 (d, $J = 5.2$ Hz, 1H), 7.11 (d, $J = 9.7$ Hz, 2H), 6.50 (s, 1H), 6.13 (d, $J = 2.1$ Hz, 1H), 4.40 (s, 2H), 4.34 (dd, $J = 16.3, 6.4$ Hz, 2H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.57 (s, 2H), 2.43 (m, 1H), 2.02 – 1.90 (m, 1H).

1.78

[367.0]

"A278"

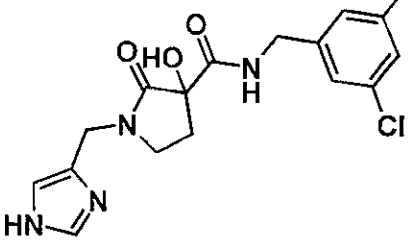
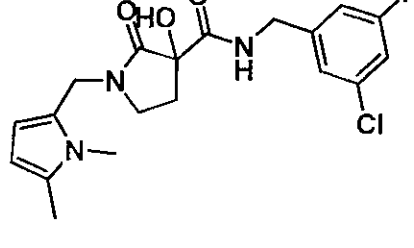
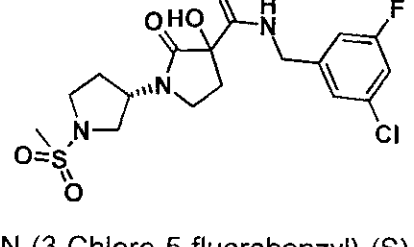


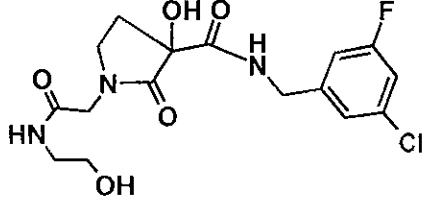
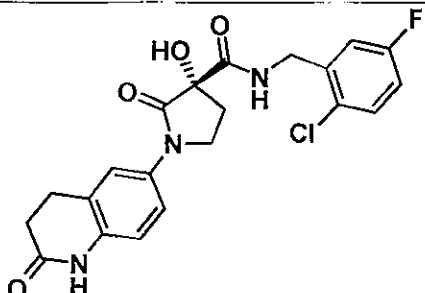
N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcarbamoylcyclohexylmethyl)-2-oxopyrrolidine-3-carboxamide

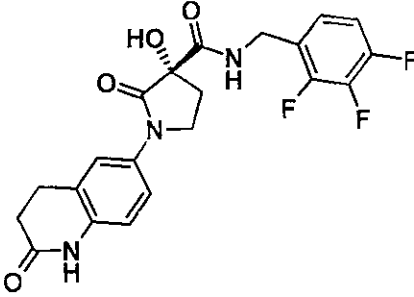
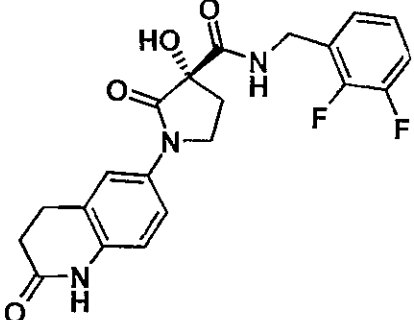
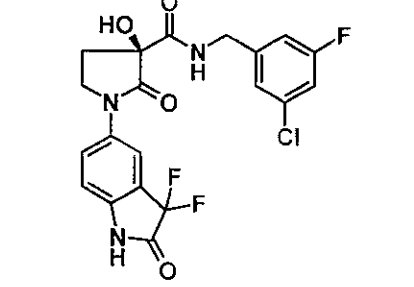
8.53 (t, $J = 6.4$ Hz, 1H), 7.58 (q, $J = 4.3$ Hz, 1H), 7.24 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.18 (s, 1H), 7.08 (d, $J = 9.1$ Hz, 1H), 6.40 (s, 1H), 4.37 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.22 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.39 – 3.29 (m, 2H), 3.11 (dd, $J = 13.4, 7.9$ Hz, 1H), 2.98 (dd, $J = 13.3, 6.8$ Hz, 1H), 2.53 (d, $J = 4.6$ Hz, 3H), 2.45 (ddd, $J = 11.8, 7.6, 3.9$ Hz, 1H), 2.05 – 1.91 (m, 2H), 1.69 (m, 4H), 1.62 – 1.49 (m, 1H), 1.29 (m, 4H), 0.96 – 0.77 (m, 2H).

1.80

[440.1]

"A279"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1H-imidazol-4-ylmethyl)-2-oxopyrrolidine-3-carboxamide	8.62 (t, $J = 6.4$ Hz, 1H), 8.15 (s, 1H), 7.58 (d, $J = 1.1$ Hz, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.21 (s, 1H), 7.11 (d, $J = 9.7$ Hz, 1H), 6.96 (s, 1H), 4.38 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.32 (s, 2H), 4.25 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.36 (dd, $J = 14.4, 8.2$ Hz, 4H), 2.43 (dt, $J = 12.1, 5.7$ Hz, 1H), 1.94 (dt, $J = 13.0, 7.4$ Hz, 1H).	1.40 [367.0]
"A280"	 N-(3-Chloro-5-fluorobenzyl)-1-(1,5-Dimethyl-1H-pyrrol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.59 (t, $J = 6.4$ Hz, 1H), 7.25 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.12 – 7.07 (m, 1H), 6.48 (s, 1H), 5.89 (d, $J = 3.4$ Hz, 1H), 5.67 (dd, $J = 3.3, 0.6$ Hz, 1H), 4.45 (d, $J = 15.1$ Hz, 1H), 4.37 (dd, $J = 15.8, 6.8$ Hz, 1H), 4.25 (d, $J = 15.1$ Hz, 1H), 4.23 (dd, $J = 15.8, 5.2$ Hz, 1H), 3.57 (s, 1H), 3.28 (d, $J = 4.5$ Hz, 5H), 3.20 – 3.08 (m, 2H), 2.44 – 2.36 (m, 1H), 2.12 (s, 3H), 1.91 (ddd, $J = 13.1, 8.6, 6.4$ Hz, 1H).	2.22 [394.1]
"A281"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1'-methanesulfonyl-2-oxo[1,3']bipyrrolidiny-3-carboxamide	** 8.58 (t, $J = 6.3$ Hz, 1H), 7.25 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 9.7$ Hz, 1H), 6.50 (d, $J = 1.1$ Hz, 1H), 4.60 – 4.53 (m, 1H), 4.36 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.26 – 4.20 (m, 1H), 3.48 – 3.35 (m, 4H), 3.26 (s, 2H), 3.18 (dd, $J =$	1.84 [434.0]

		10.2, 6.0 Hz, 1H), 2.93 (d, J = 4.2 Hz, 3H), 2.47 – 2.40 (m, 1H), 2.15 – 1.83 (m, 6H).	
5	"A282"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[(2-hydroxyethyl)carbamoyl]methyl]-2-oxo-pyrrolidine-3-carboxamide	1.65 [388.0]
10		8.70 (t, J = 6.3 Hz, 1H), 7.93 (t, J = 5.5 Hz, 1H), 7.27 (dt, J = 8.7, 2.1 Hz, 1H), 7.20 (s, 1H), 7.09 (d, J = 9.6 Hz, 1H), 6.61 (br. s, 1H), 4.68 (br. s, 1H), 4.38 (dd, J = 15.7, 6.7 Hz, 1H), 4.24 (dd, J = 15.7, 6.0 Hz, 1H), 3.86 (s, 2H), 3.47 – 3.41 (m, 1H), 3.27 (br. m, 2H), 3.21 – 3.05 (m, 2H), 2.43 (ddd, J = 12.7, 7.5, 3.5 Hz, 1H), 2.08 – 1.97 (m, 1H).	
15	"A283"	 N-(2-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.87 [432.1]
20		10.07 (s, 1H), 8.68 (t, J = 6.3 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.44 (dd, J = 8.6, 2.4 Hz, 1H), 7.19 (dd, J = 9.8, 3.1 Hz, 1H), 7.14 (td, J = 8.4, 3.1 Hz, 1H), 6.87 (d, J = 8.6 Hz, 1H), 6.76 (s, 1H), 4.42 (dd, J = 16.5, 6.7 Hz, 1H), 4.26 (dd, J = 16.5, 5.8 Hz, 1H), 3.88 – 3.75 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 2.61 (dt, J = 6.9, 5.8 Hz, 1H), 2.44 (dd, J = 8.3, 6.8 Hz, 2H), 2.13 (dt, J = 13.0, 7.5 Hz, 1H).	
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"A284" 5 10	 N-(2,3,4-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.59 (t, $J = 6.2$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.29 (qd, $J = 7.5, 3.8$ Hz, 1H), 7.19 (td, $J = 8.3, 2.1$ Hz, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.67 (s, 1H), 4.38 (dd, $J = 15.5, 6.3$ Hz, 1H), 4.31 (dd, $J = 15.4, 6.0$ Hz, 1H), 3.85 – 3.71 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.60 – 2.52 (m, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.10 (dt, $J = 12.9, 7.6$ Hz, 1H).	1.85 [434.1]
15 20 25	 N-(2,3-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.57 (t, $J = 6.3$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.43 (dd, $J = 8.6, 2.4$ Hz, 1H), 7.36 – 7.23 (m, 1H), 7.21 – 7.09 (m, 2H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.66 (s, 1H), 4.42 (dd, $J = 15.5, 6.4$ Hz, 1H), 4.35 (dd, $J = 15.5, 6.0$ Hz, 1H), 3.87 – 3.75 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.57 (ddd, $J = 12.6, 7.0, 4.5$ Hz, 1H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.10 (dt, $J = 12.9, 7.7$ Hz, 1H).	1.78 [416.1]
30 35	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	11.24 (s, 1H), 8.75 (t, $J = 6.4$ Hz, 1H), 8.02 (d, $J = 1.7$ Hz, 1H), 7.79 (dd, $J = 8.6, 2.0$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 7.04 (d, $J = 8.6$ Hz, 1H), 6.79 (s, 1H), 4.38 (dd,	3.94 [452]

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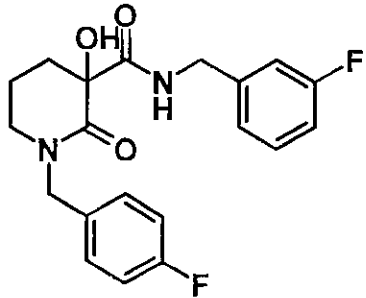
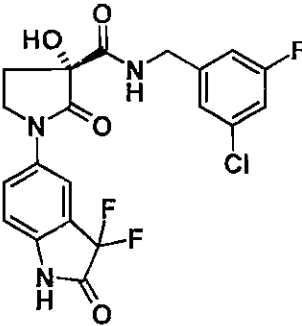
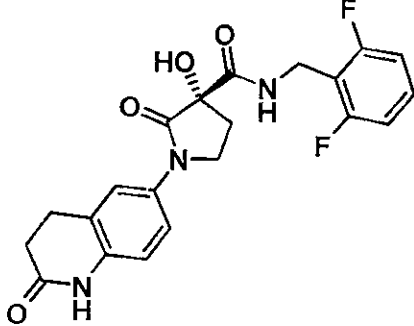
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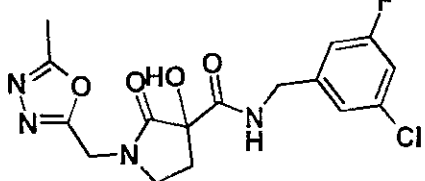
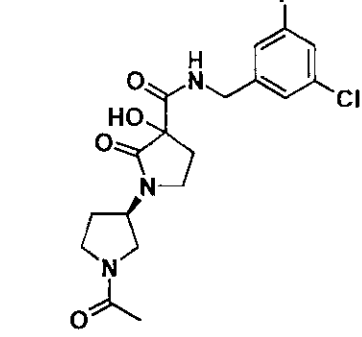
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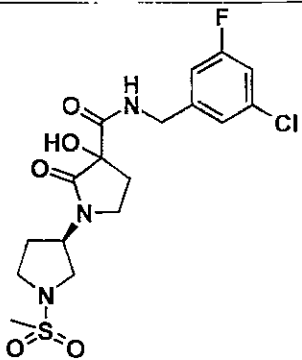
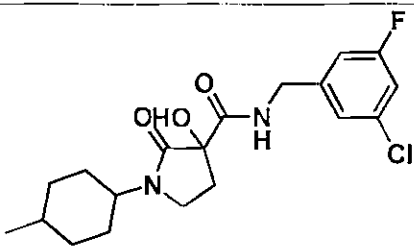
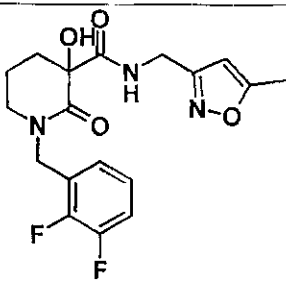
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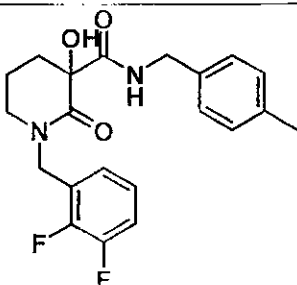
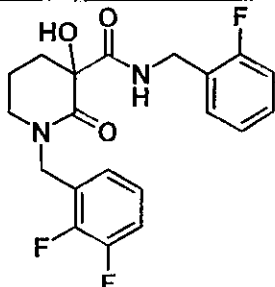
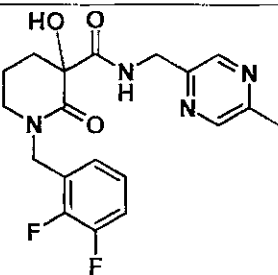
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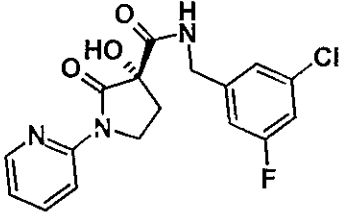
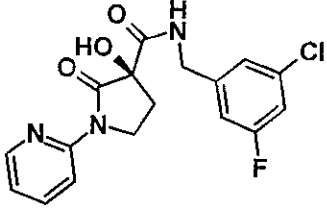
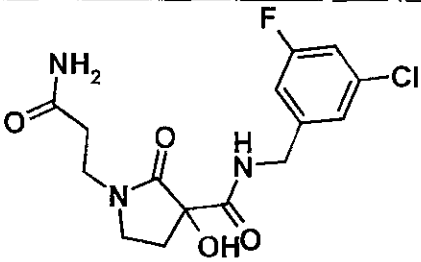
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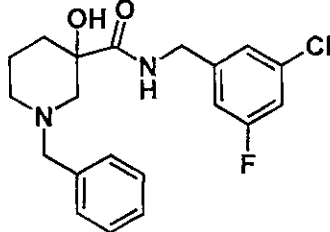
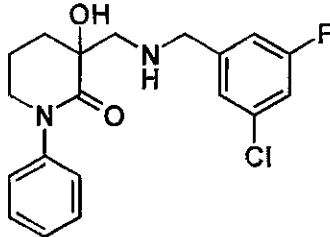
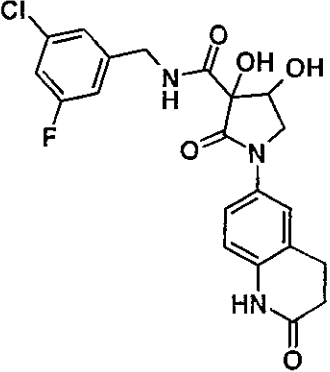
	1-(3,3-difluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	$J = 15.8, 6.8 \text{ Hz, 1H}$), 4.24 (dd, $J = 15.8, 6.0 \text{ Hz, 1H}$), 3.86 (t, $J = 7.1 \text{ Hz, 2H}$), 2.63 – 2.54 (m, 1H), 2.12 (dt, $J = 12.9, 7.7 \text{ Hz, 1H}$).	
"A287"	 N-(3-Fluorobenzyl)-1-(4-fluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.50 (t, $J = 6.3 \text{ Hz, 1H}$), 7.37 – 7.28 (m, 3H), 7.19 – 7.10 (m, 4H), 7.03 (td, $J = 8.3, 2.2 \text{ Hz, 1H}$), 6.32 (s, 1H), 4.58 (d, $J = 14.9 \text{ Hz, 1H}$), 4.44 (d, $J = 14.9 \text{ Hz, 1H}$), 4.38 (dd, $J = 15.6, 6.8 \text{ Hz, 1H}$), 4.26 (dd, $J = 15.6, 5.9 \text{ Hz, 1H}$), 3.23 (m, 2H), 2.16 (m, 1H), 1.84 (m, 3H).	4.03 [375]
"A288"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3,3-difluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	11.24 (s, 1H), 8.75 (t, $J = 6.3 \text{ Hz, 1H}$), 8.03 (s, 1H), 7.80 (dd, $J = 8.6, 1.9 \text{ Hz, 1H}$), 7.27 (dt, $J = 8.8, 2.1 \text{ Hz, 1H}$), 7.20 (s, 1H), 7.10 (d, $J = 9.5 \text{ Hz, 1H}$), 7.04 (d, $J = 8.6 \text{ Hz, 1H}$), 6.79 (s, 1H), 4.38 (dd, $J = 15.7, 6.7 \text{ Hz, 1H}$), 4.24 (dd, $J = 15.7, 6.1 \text{ Hz, 1H}$), 3.86 (m, 2H), 2.62 – 2.52 (m, 1H), 2.12 (dt, $J = 13.1, 7.6 \text{ Hz, 1H}$).	3.94 [452]
"A289"		10.06 (s, 1H), 8.11 (t, $J = 5.7 \text{ Hz, 1H}$), 7.47 (d, $J = 2.2 \text{ Hz, 1H}$), 7.41 (dd, $J = 8.6, 2.5 \text{ Hz, 1H}$), 7.38 (td, $J = 8.4, 4.2 \text{ Hz, 1H}$), 7.12 – 7.00 (m, 2H), 6.85 (d, $J = 8.6 \text{ Hz, 1H}$), 6.56 (s, 1H), 4.42 (dd, $J = 14.4, 5.9$	1.72 [416.1]

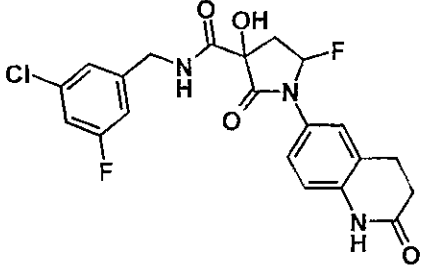
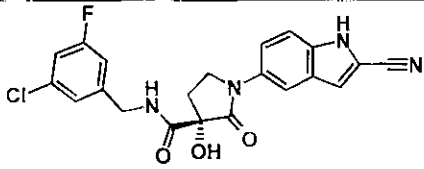
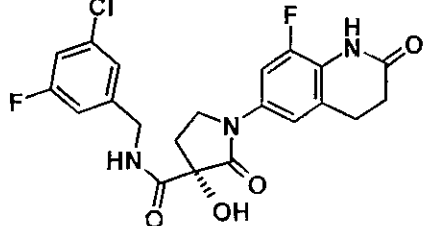
	N-(2,6-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	Hz, 1H), 4.36 (dd, $J = 14.4, 5.6$ Hz, 1H), 3.84 – 3.70 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.12 – 2.01 (m, 1H).	
"A290"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-2-oxo-pyrrolidine-3-carboxamide	8.62 (t, $J = 6.3$ Hz, 1H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.09 (t, $J = 9.5$ Hz, 1H), 6.60 (s, 1H), 4.72 (d, $J = 16.0$ Hz, 1H), 4.62 (d, $J = 16.0$ Hz, 1H), 4.37 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.57 (s, 1H), 3.49 – 3.36 (m, 2H), 2.47 (s, 3H), 2.01 (ddd, $J = 13.3, 8.3, 6.2$ Hz, 1H).	1.77 [398.1]
"A291"	 N-(3-chloro-5-fluorobenzyl)-(R)-1'-acetyl-3-hydroxy-2-oxo-[1,3']bipyrrolidinyl-3-carboxamide	8.59 (t, $J = 5.1$ Hz, 1H), 7.26 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.51 (dd, $J = 5.3, 4.7$ Hz, 1H), 4.60 – 4.43 (m, 1H), 4.36 (dd, $J = 15.6, 6.7$ Hz, 1H), 4.23 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.66 – 3.53 (m, 1H), 3.53 – 3.42 (m, 2H), 3.42 – 3.33 (m, 2H), 3.26 (m, 1H), 2.44 (m, 1H), 2.16 – 2.05 (m, 1H), 2.05 – 1.96 (m, 2H), 1.94 (s, $J = 2.9$ Hz, 3H), 1.93 – 1.89 (m, 1H).	1.71 [398.1]

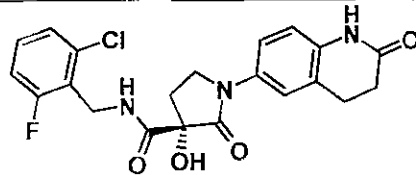
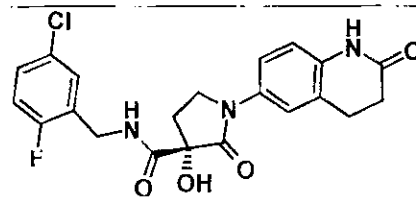
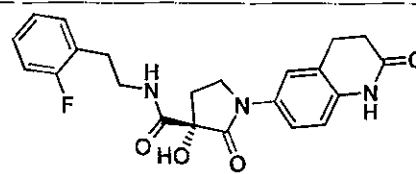
"A292"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1'-methanesulfonyl-2-oxo[1,3']bipyrrolidiny-3-carboxamide	** 8.58 (t, $J = 6.3$ Hz, 1H), 7.25 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 9.7$ Hz, 1H), 6.50 (d, $J = 1.0$ Hz, 1H), 4.57 (p, $J = 7.1$ Hz, 1H), 4.36 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.23 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.57 (s, 3H), 3.48 – 3.35 (m, 4H), 3.30 – 3.29 (m, 1H), 3.21 (m, 1H), 2.93 (d, $J = 4.2$ Hz, 3H), 2.49 – 2.40 (m, 1H), 2.15 – 2.08 (m, 1H), 2.01 (m, 1H).	1.85 [434.0]
"A293"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcyclohexyl)-2-oxopyrrolidine-3-carboxamide	** 8.51 (t, $J = 6.3$ Hz, 1H), 7.25 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.19 (s, 1H), 7.09 (d, $J = 9.6$ Hz, 1H), 6.39 (s, 1H), 4.36 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.22 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.73 – 3.60 (m, 1H), 3.39 – 3.32 (m, 1H), 2.42 (dq, $J = 7.4, 4.3$ Hz, 1H), 1.92 (tt, $J = 14.8, 6.4$ Hz, 1H), 1.77 – 1.67 (m, 2H), 1.61 – 1.41 (m, 4H), 1.36 – 1.26 (m, 1H), 1.10 – 0.92 (m, 2H), 0.87 (d, $J = 6.5$ Hz, 3H).	
"A294"	 N-(5-Methylisoxazol-3-ylmethyl)-1-(2,3-Difluorobenzyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.47 (t, $J = 6.2$ Hz, 1H), 7.34 (dd, $J = 17.5, 9.2$ Hz, 1H), 7.22 – 7.10 (m, 2H), 6.31 (s, 1H), 6.10 (s, 1H), 4.69 (d, $J = 15.7$ Hz, 1H), 4.50 (d, $J = 15.7$ Hz, 1H), 4.27 (d, $J = 6.3$ Hz, 2H), 3.27 (s, 2H), 2.34 (s, 3H), 2.22 – 2.09 (m, 1H), 1.94 – 1.80 (m,	3.39 [380.2]

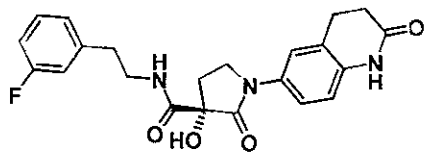
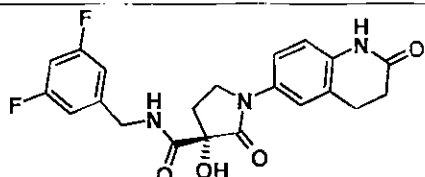
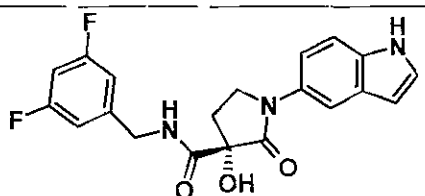
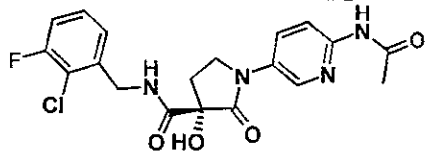
	hydroxy-2-oxopiperidine-3-carboxamide	3H).	
"A295"	 N-(4-Methylbenzyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.30 (t, $J = 6.1$ Hz, 1H), 7.38 – 7.29 (m, 1H), 7.20 – 7.06 (m, 6H), 6.27 (s, 1H), 4.69 (d, $J = 15.5$ Hz, 1H), 4.50 (d, $J = 15.6$ Hz, 1H), 4.25 (t, $J = 5.7$ Hz, 2H), 3.36 (m, 1H), 3.27 (m, 1H), 2.26 (s, 3H), 2.16 (m, 1H), 1.85 (m, 3H).	4.34 [389.2]
"A296"	 N-(2-Fluorobenzyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.41 (t, $J = 6.2$ Hz, 1H), 7.41 – 7.24 (m, 3H), 7.21 – 7.10 (m, 4H), 6.36 (s, 1H), 4.69 (d, $J = 15.7$ Hz, 1H), 4.52 (d, $J = 15.5$ Hz, 1H), 4.37 – 4.29 (m, 2H), 3.33 (s, 1H), 3.30 – 3.25 (m, 1H), 2.19 (d, $J = 8.1$ Hz, 1H), 1.92 – 1.82 (m, 3H).	4.11 [393.2]
"A297"	 N-(5-Methylpyrazin-2-ylmethyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide	8.61 (t, $J = 6.1$ Hz, 1H), 8.50 (s, 1H), 8.44 (s, 1H), 7.38 – 7.29 (m, 1H), 7.23 – 7.08 (m, 2H), 6.42 (s, 1H), 4.69 (d, $J = 15.6$ Hz, 1H), 4.51 (d, $J = 15.6$ Hz, 1H), 4.46 (dd, $J = 16.1, 6.1$ Hz, 1H), 4.35 (dd, $J = 16.1, 5.6$ Hz, 1H), 3.35 (m, 1H), 3.30 – 3.25 (m, 1H), 2.45 (s, 3H), 2.21 (m, 1H), 1.88 (m, 3H).	2.97 [391]

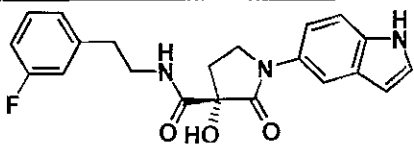
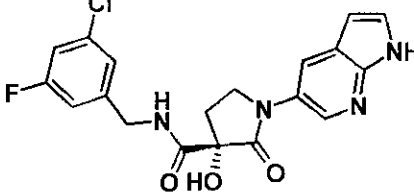
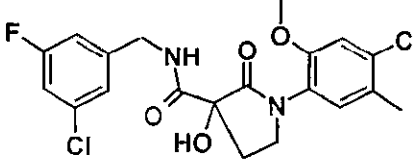
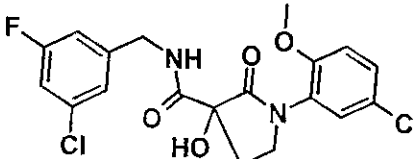
5	"A298"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-pyridin-2-ylpyrrolidine-3-carboxamide	8.77 (t, $J = 6.3$ Hz, 1H), 8.42 (dd, $J = 4.9, 1.0$ Hz, 1H), 8.29 (d, $J = 8.4$ Hz, 1H), 7.86 (ddd, $J = 8.6, 7.4, 1.9$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.24 – 7.17 (m, 2H), 7.10 (d, $J = 9.0$ Hz, 1H), 6.85 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.06 (ddd, $J = 10.6, 8.7, 3.9$ Hz, 1H), 3.94 (dt, $J = 10.6, 7.6$ Hz, 1H), 2.61 – 2.52 (m, 2H), 2.12 (dt, $J = 13.0, 8.6$ Hz, 1H).	3.49 [364]
15	"A299"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-pyridin-2-ylpyrrolidine-3-carboxamide	8.77 (t, $J = 6.4$ Hz, 1H), 8.42 (dd, $J = 4.9, 1.1$ Hz, 1H), 8.29 (d, $J = 8.5$ Hz, 1H), 7.86 (ddd, $J = 8.6, 7.4, 1.9$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.23 – 7.16 (m, 2H), 7.10 (d, $J = 9.0$ Hz, 1H), 6.85 (s, 1H), 4.38 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.06 (ddd, $J = 10.6, 8.8, 3.9$ Hz, 1H), 3.94 (dt, $J = 10.6, 7.6$ Hz, 1H), 2.56 (ddd, $J = 17.2, 8.5, 4.6$ Hz, 1H), 2.12 (dt, $J = 13.0, 8.6$ Hz, 1H).	3.49 [364]
20				
25				
30	"A300"	 N-(3-Chloro-5-fluorobenzyl)-1-(2-aminopropanoyl)pyrrolidine-3-carboxamide	* 7.21 (2 H, m), 7.11 (1 H, d, $J = 9.4$), 4.40 (1 H, d, $J = 15.8$), 4.27 (1 H, d, $J = 15.8$), 3.44 (4 H, m), 2.47 (1 H, dt, $J = 6.8, 5.7$), 2.34 (2 H, t, $J = 7.3$), 2.00 (1 H, m).	1.60 [358.0]
35				

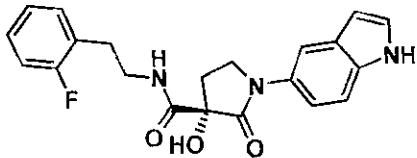
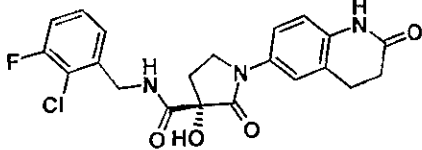
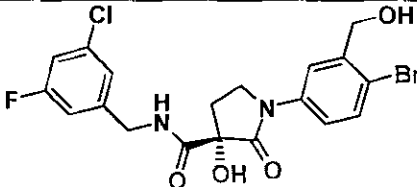
	(2-carbamoyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide		
"A301"	 N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypiperidine-3-carboxamide	3.56 [378.0]	
"A302"	 3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpiperidin-2-one		
"A303"	 N-(3-Chloro-5-fluorobenzyl)-3,4-dihydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide		

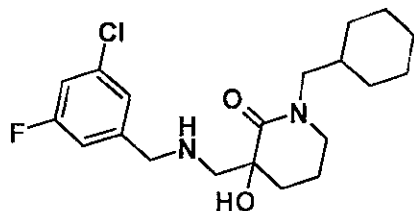
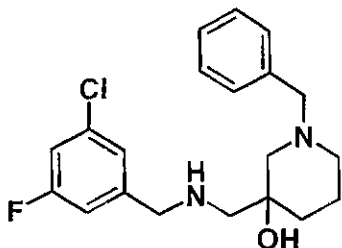
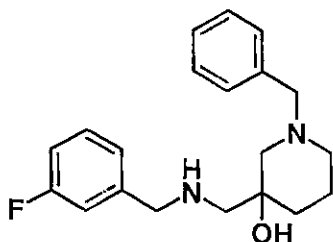
"A304"	 N-(3-Chloro-5-fluorobenzyl)-5-fluoro-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide		
"B1"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.68 (t, $J = 6.3$ Hz, 1H), 7.86 (d, $J = 1.7$ Hz, 1H), 7.78 – 7.74 (m, 1H), 7.50 (d, $J = 9.0$ Hz, 1H), 7.38 (d, $J = 0.7$ Hz, 1H), 7.26 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 6.72 (s, 1H), 4.40 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.26 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.96 – 3.82 (m, 2H), 2.67 – 2.57 (m, 1H), 2.22 – 2.09 (m, 1H).	
"B2"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(8-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.15 (s, 1H), 8.74 (s, 1H), 7.60 (dd, $J = 12.9, 1.9$ Hz, 1H), 7.33 – 7.24 (m, 2H), 7.20 (s, 1H), 7.09 (d, $J = 9.4$ Hz, 1H), 6.78 (s, 1H), 4.37 (d, $J = 15.6$ Hz, 1H), 4.23 (d, $J = 15.6$ Hz, 1H), 3.81 (m, 2H), 2.93 (t, $J = 7.4$ Hz, 2H), 2.63 – 2.53 (m, 1H), 2.18 – 2.04 (m, 1H).	

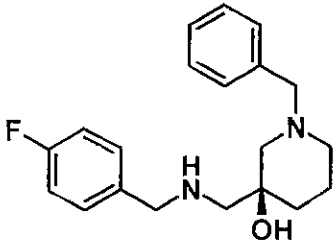
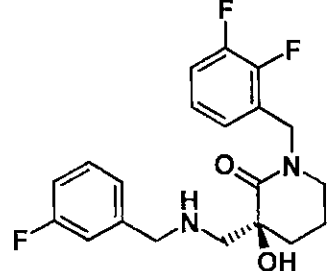
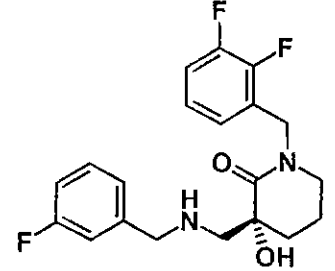
5	"B3"	 N-(2-Chloro-6-fluorobenzyl)- (S)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	10.06 (s, 1H), 7.97 (t, $J = 5.6$ Hz, 1H), 7.48 (d, $J = 2.2$ Hz, 1H), 7.42 (dd, $J = 8.6, 2.5$ Hz, 1H), 7.38 (dt, $J = 8.1, 4.0$ Hz, 1H), 7.33 (d, $J = 7.9$ Hz, 1H), 7.25 – 7.19 (m, 1H), 6.85 (d, J = 8.6 Hz, 1H), 6.58 (s, 1H), 4.51 (ddd, $J = 14.2, 5.8, 1.2$ Hz, 1H), 4.44 (ddd, $J = 14.4,$ 5.4, 1.0 Hz, 1H), 3.84 – 3.73 (m, 2H), 2.88 (t, $J = 7.5$ Hz, 2H), 2.44 (dd, $J = 8.3, 6.8$ Hz, 2H), 2.11 – 2.01 (m, 1H).	1.82 [432.1]
10				
15	"B4"	 N-(5-Chloro-2-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	10.06 (s, 1H), 8.61 (t, $J = 6.3$ Hz, 1H), 7.49 (d, $J = 2.2$ Hz, 1H), 7.44 (dd, $J = 8.6, 2.5$ Hz, 1H), 7.38 (dd, $J = 6.5, 2.7$ Hz, 1H), 7.36 – 7.32 (m, 1H), 7.24 – 7.19 (m, 1H), 6.86 (d, $J = 8.6$ Hz, 1H), 6.70 (s, 1H), 4.39 (dd, $J = 15.8, 6.6$ Hz, 1H), 4.28 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.86 – 3.76 (m, 2H), 2.91 – 2.85 (m, 2H), 2.57 (ddd, $J = 11.7, 7.0,$ 4.6 Hz, 1H), 2.44 (dd, $J = 8.3,$ 6.8 Hz, 2H), 2.11 (dt, $J = 12.9,$ 7.6 Hz, 1H).	1.87 [432.0]
20				
25				
30	"B5"	 N-[2-(2-Fluorophenyl)ethyl]-(S)- 3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)-		1.81 [412.1]
35				

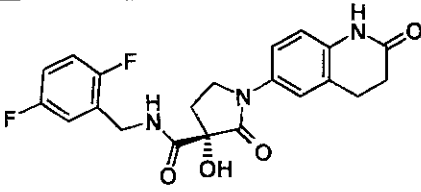
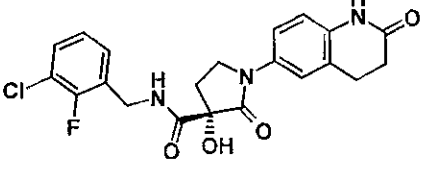
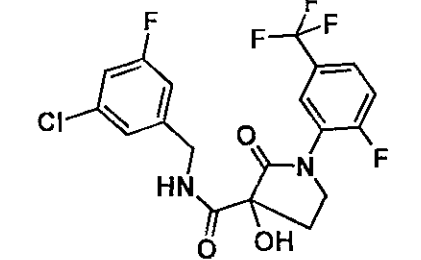
	pyrrolidine-3-carboxamide		
"B6"	 N-[2-(3-Fluorophenyl)ethyl]-(S)- 3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	1.82 [412.1]	
"B7"	 N-(3,5-Difluorobenzyl)-(S)-3- hydroxy-2-oxo-1-(2-oxo-1,2,3,4- tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	1.81 [416.1]	
"B8"	 N-(3,5-Difluorobenzyl)-(S)-3- hydroxy-1-(1H-indol-5-yl)-2-oxo- pyrrolidine-3-carboxamide	2.00 [386.1]	
"B9"	 N-(2-Chloro-3-fluorobenzyl)-(S)- 1-(6-acetylamino-3-pyridin-yl)-3- hydroxy-2-oxopyrrolidine-3- carboxamide	1.81 [421.1]	

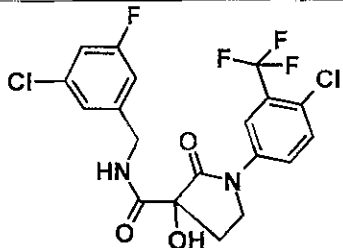
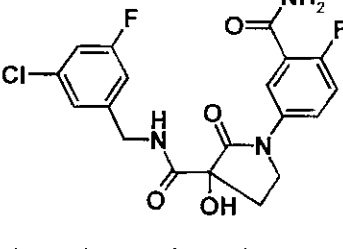
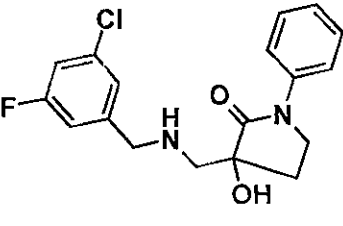
"B10" 5	 N-([2-(3-Fluorophenyl)ethyl]- (S)-3-hydroxy-1-(1H-indol-5-yl)- 2-oxopyrrolidine-3-carboxamide	2.01 [382.1]
"B11" 10 15	 N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(1H- pyrrolo[2,3-b]pyridin-5-yl)- pyrrolidine-3-carboxamide	
"B12" 20 25	 N-(3-Chloro-5-fluorobenzyl)-1- (4-chloro-2-methoxy-5-methyl- phenyl)-3-hydroxy-2-oxo- pyrrolidine-3-carboxamide	2.43 [441.0]
"B13" 30 35	 1-(5-Chloro-2-methoxyphenyl)- 3-hydroxy-2-oxopyrrolidine-3- carboxylic acid 3-chloro-5- fluorobenzylamide	2.31 [427.0]

5	"B14"	 (S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxylic acid [2-(2-fluorophenyl)ethyl]-amide	2.00 [382.1]
10	"B15"	 N-(2-Chloro-3-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.88 [432.1]
20	"B16"	 N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypiperidine-3-carboxamide	8.55 (t, $J = 6.2$ Hz, 1H), 7.32 – 7.25 (m, 5H), 7.25 – 7.19 (m, 1H), 7.11 (s, 1H), 7.01 (d, $J = 9.5$ Hz, 1H), 5.19 (s, 1H), 4.25 (d, $J = 6.3$ Hz, 2H), 3.49 (d, $J = 11.2$ Hz, 2H), 2.58 (d, $J = 10.7$ Hz, 1H), 2.41 (dd, $J = 23.0$, 11.2 Hz, 2H), 2.08 (s, 1H), 1.82 – 1.68 (m, 2H), 1.44 (dd, $J = 16.0$, 8.0 Hz, 2H).
30	"B17"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(4-bromo-3-hydroxymethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	3.74 (t, $J = 6.4$ Hz, 1H), 7.84 (s, 1H), 7.60 – 7.53 (m, 2H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.20 (s, 1H), 7.09 (d, $J = 9.1$ Hz, 1H), 6.80 (s, 1H), 5.51 (t, $J = 5.6$ Hz, 1H), 4.49 (d, $J = 5.6$ Hz, 2H), 4.37 (dd, $J = 15.6$, 6.8 Hz, 1H), 4.24 (dd, $J = 15.7$, 6.0 Hz, 1H), 3.85 (t, $J = 6.8$ Hz,
35			

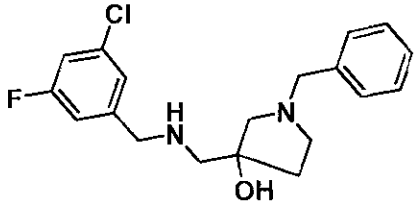
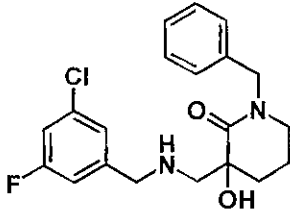
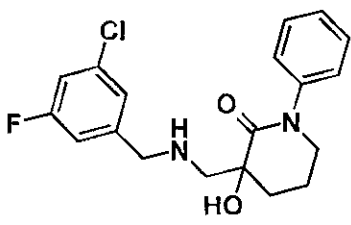
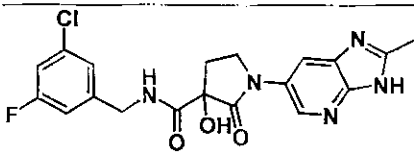
		2H), 2.63 – 2.54 (m, 1H), 2.19 – 2.07 (m, 1H).	
"B18"	 3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxy-piperidin-2-one	7.29 – 7.19 (m, 2H), 7.14 (d, J = 10.1 Hz, 1H), 4.94 (s, 1H), 3.77 – 3.61 (m, 2H), 3.26 (dd, J = 8.7, 4.3 Hz, 1H), 3.21 (dd, J = 9.1, 5.3 Hz, 2H), 2.93 (dd, J = 13.0, 6.7 Hz, 1H), 2.74 – 2.68 (m, 1H), 2.44 (d, J = 11.6 Hz, 1H), 2.13 (s, 1H), 2.00 (dd, J = 16.7, 6.2 Hz, 1H), 1.83 (d, J = 7.9 Hz, 1H), 1.69 – 1.49 (m, 8H), 1.10 (d, J = 8.6 Hz, 3H), 0.95 – 0.73 (m, 2H).	
"B19"	 1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-piperidin-3-ol	7.32 – 7.17 (m, 7H), 7.15 (d, J = 9.7 Hz, 1H), 4.21 (s, 1H), 3.71 (s, 2H), 3.46 (d, J = 13.4 Hz, 1H), 3.37 (d, J = 13.4 Hz, 1H), 2.40 (d, J = 10.8 Hz, 2H), 2.09 (d, J = 9.7 Hz, 1H), 2.02 (d, J = 9.8 Hz, 2H), 1.66 – 1.49 (m, 2H), 1.44 – 1.30 (m, 1H), 1.25 (dd, J = 15.0, 6.6 Hz, 1H).	
"B20"	 1-Benzyl-3-[(3-fluorobenzylamino)methyl]-piperidin-3-ol	7.36 – 7.30 (m, 1H), 7.29 – 7.24 (m, 4H), 7.23 – 7.18 (m, 1H), 7.16 – 7.09 (m, 2H), 7.06 – 6.98 (m, 1H), 4.20 (d, J = 12.6 Hz, 1H), 3.72 (s, 2H), 3.46 (d, J = 13.4 Hz, 1H), 3.38 (d, J = 13.4 Hz, 1H), 2.52 (d, J = 7.4 Hz, 1H), 2.35 (d, J = 28.1 Hz, 2H), 2.11 (s, 1H), 2.04 (d, J = 10.3 Hz, 1H), 1.58 (t, J = 12.7 Hz, 2H), 1.44 – 1.31 (m,	

		1H), 1.26 (dd, $J = 15.1, 6.5$ Hz, 1H).	
5	"B21"	 (S)-1-Benzyl-3-[(4-fluorobenzylamino)methyl]piperidin-3-ol	7.34 – 7.28 (m, 3H), 7.26 (d, $J = 3.9$ Hz, 3H), 7.22 (dd, $J = 13.6, 4.9$ Hz, 2H), 7.10 (t, $J = 8.9$ Hz, 2H), 4.19 (s, 1H), 3.67 (s, 2H), 3.45 (d, $J = 13.5$ Hz, 1H), 3.41 – 3.34 (m, 1H), 2.59 – 2.51 (m, 2H), 2.38 (d, $J = 10.7$ Hz, 2H), 2.11 (s, 1H), 2.03 (d, $J = 10.9$ Hz, 1H), 1.58 (s, 2H), 1.45 – 1.31 (m, 1H), 1.29 – 1.18 (m, 1H).
15	"B22"	 (S)-1-(2,3-Difluorobenzyl)-3-[(3-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one	
20			
25	"B23"	 (R)-1-(2,3-Difluorobenzyl)-3-[(3-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one	
30			

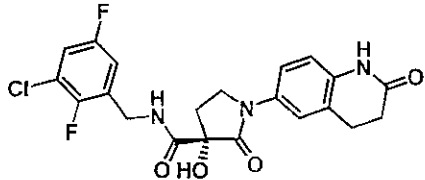
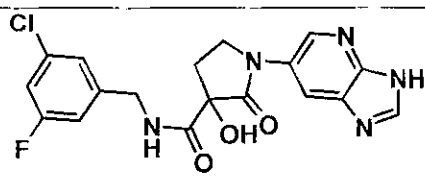
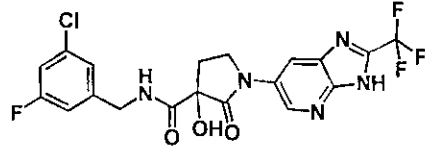
"B24"	 N-(2,5-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.60 (t, J=6.3, 1H), 7.48 (d, J=2.4, 1H), 7.43 (dd, J=8.6, 2.5, 1H), 7.21 (td, J=9.2, 4.5, 1H), 7.18 - 7.06 (m, 2H), 6.86 (d, J=8.6, 1H), 6.70 (s, 1H), 4.40 (dd, J=15.9, 6.6, 1H), 4.27 (dd, J=15.9, 5.9, 1H), 3.81 (dd, J=7.6, 5.9, 2H), 2.88 (t, J=7.5, 2H), 2.59 (dt, J=12.9, 5.8, 1H), 2.48 - 2.41 (m, 2H), 2.11 (dt, J=12.9, 7.6, 1H).	1.77 [416.1]
"B25"	 N-(3-Chloro-2-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	** 10.06 (s, 1H), 8.58 (t, J=6.3, 1H), 7.50 - 7.40 (m, 3H), 7.31 (t, J=6.4, 1H), 7.18 (t, J=8.1, 1H), 6.86 (d, J=8.6, 1H), 6.67 (s, 1H), 4.44 - 4.30 (m, 2H), 3.84 - 3.75 (m, 2H), 2.88 (t, J=7.5, 2H), 2.60 - 2.54 (m, 1H), 2.47 - 2.40 (m, 2H), 2.14 - 2.07 (m, 1H).	1.90 [432.1]
"B26"	 N-(3-Chloro-5-fluorobenzyl)-1-(2-Fluoro-5-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.73 (t, J=6.4, 1H), 7.86 (dd, J=6.7, 2.3, 1H), 7.81 - 7.73 (m, 1H), 7.60 (t, J=10.4, 3.7, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.21 (s, 1H), 7.13 - 7.08 (m, 1H), 6.81 (s, 1H), 4.41 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.92 - 3.82 (m, 2H), 2.65 (ddd, J=12.9, 7.0, 4.8, 1H), 2.26 - 2.17 (m, 1H).	2.39 [449.0]

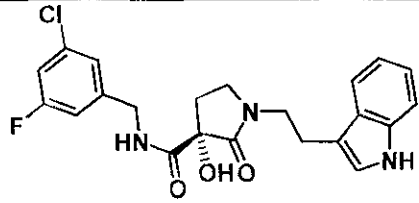
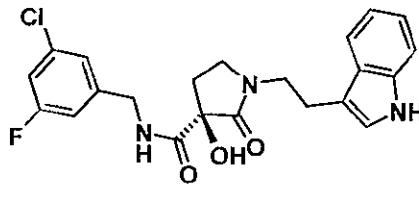
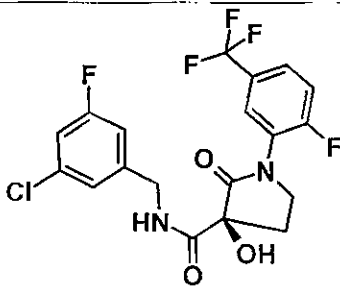
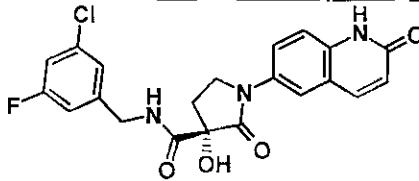
"B27"	 N-(3-Chloro-5-fluorobenzyl)-1-(4-Chloro-3-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.76 (t, J=6.4, 1H), 8.34 (d, J=2.7, 1H), 7.91 (dd, J=8.9, 2.7, 1H), 7.78 (d, J=8.9, 1H), 7.29 - 7.25 (m, 1H), 7.20 (s, 1H), 7.14 - 7.09 (m, 1H), 6.86 (s, 1H), 4.38 (dd, J=15.7, 6.7, 1H), 4.30 - 4.24 (m, 1H), 3.93 - 3.87 (m, 1H), 2.99 - 2.91 (m, 1H), 2.65 - 2.57 (m, 1H), 2.21 - 2.11 (m, 1H). (mit DMF + EE verunreinigt)
"B28"	 N-(3-Chloro-5-fluorobenzyl)-1-(3-carbamoyl-4-fluorophenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.76 (s, 1H), 7.91 (dd, J = 6.3, 2.9 Hz, 1H), 7.83 (ddd, J = 9.0, 4.3, 3.1 Hz, 1H), 7.76 (s, 1H), 7.70 (s, 1H), 7.37 - 7.30 (m, 1H), 7.27 (d, J = 8.7 Hz, 1H), 7.20 (s, 1H), 7.09 (d, J = 9.7 Hz, 1H), 6.83 (s, 1H), 4.37 (dd, J = 15.7, 6.2 Hz, 1H), 4.24 (dd, J = 15.6, 5.7 Hz, 1H), 3.86 (t, J = 6.7 Hz, 2H), 2.62 - 2.54 (m, 2H), 2.44 (s, 1H), 2.18 - 2.07 (m, 1H).
"B29"	 3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one	7.73 - 7.67 (m, 2H), 7.38 (t, J = 8.0 Hz, 2H), 7.26 - 7.20 (m, 2H), 7.13 (dd, J = 10.5, 4.2 Hz, 2H), 5.51 (s, 1H), 3.84 - 3.75 (m, 1H), 3.70 (dd, J = 15.4, 7.7 Hz, 3H), 2.71 - 2.62 (m, 2H), 2.41 (ddd, J = 12.7, 8.0, 4.9 Hz, 2H), 2.02 - 1.92 (m, 1H).

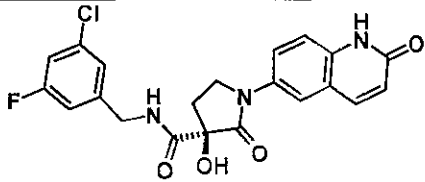
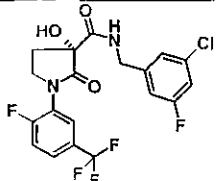
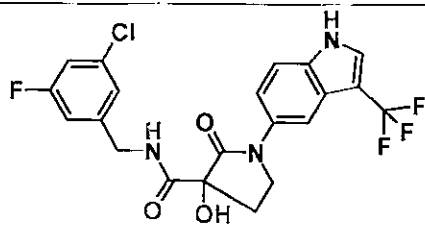
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"B30"	 1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-pyrrolidin-3-ol	7.33 – 7.12 (m, 8H), 4.60 (s, 1H), 3.73 (s, 2H), 3.52 (t, $J = 7.5$ Hz, 2H), 2.58 (dd, $J = 20.3$, 8.8 Hz, 2H), 2.46 (s, 2H), 2.34 (d, $J = 9.6$ Hz, 1H), 1.81 (dt, $J = 14.6$, 7.5 Hz, 1H), 1.70 – 1.53 (m, 1H).	
"B31"	 1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one	7.25 (dtd, $J = 10.3$, 8.1, 4.2 Hz, 7H), 7.17 (d, $J = 9.5$ Hz, 1H), 5.13 (s, 1H), 4.43 (d, $J = 14.9$ Hz, 1H), 3.71 (dd, $J = 27.5$, 11.9 Hz, 2H), 3.16 (dd, $J = 7.0$, 4.6 Hz, 2H), 2.80 (d, $J = 11.4$ Hz, 1H), 2.24 (s, 1H), 2.10 – 1.99 (m, 1H), 1.93 – 1.80 (m, 1H), 1.71 – 1.60 (m, 2H).	
"B32"	 3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpiperidin-2-one	7.39 – 7.33 (m, 2H), 7.29 – 7.20 (m, 5H), 7.18 (d, $J = 9.6$ Hz, 1H), 5.19 (s, 1H), 3.77 (d, $J = 14.9$ Hz, 1H), 3.72 (d, $J = 14.8$ Hz, 1H), 3.66 – 3.53 (m, 2H), 2.81 (d, $J = 11.8$ Hz, 1H), 2.54 (d, $J = 11.8$ Hz, 1H), 2.18 (dt, $J = 13.0$, 4.7 Hz, 1H), 2.10 – 1.95 (m, 1H), 1.86 – 1.70 (m, 2H).	
"B33"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-3H-imidazo[4,5-b]pyridin-6-yl)-2-	8.73 (t, $J = 6.4$ Hz, 1H), 8.55 (d, $J = 1.9$ Hz, 1H), 8.25 (d, $J = 2.1$ Hz, 1H), 7.27 (dt, $J = 8.8$, 2.1 Hz, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 6.80 (s, 1H), 4.41 (dd, $J = 15.7$, 6.7 Hz,	1.64 [418.1]

35

		oxopyrrolidine-3-carboxamide	1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.00 – 3.92 (m, 2H), 2.68 – 2.60 (m, 1H), 2.56 (s, 3H), 2.18 (dt, $J = 13.0, 7.5$ Hz, 1H).	
5	"B34"	 N-(3-Chloro-2,5-difluorobenzyl)- (S)-3-hydroxy-2-oxo-1-(2-oxo- 1,2,3,4-tetrahydroquinolin-6-yl)- pyrrolidine-3-carboxamide	** 10.07 (s, 1H), 8.68 (t, $J=6.3$, 1H), 7.53 – 7.45 (m, 2H), 7.43 (dd, $J=8.6, 2.5$, 1H), 7.17 (ddd, $J=8.7, 5.2, 3.2$, 1H), 6.86 (d, $J=8.6$, 1H), 6.72 (s, 1H), 4.44 (dd, $J=16.0, 6.6$, 1H), 4.30 (dd, $J=16.0, 5.9$, 1H), 3.87 – 3.75 (m, 2H), 2.88 (t, $J=7.5$, 2H), 2.59 (dt, $J=12.3, 5.9$, 1H), 2.47 – 2.40 (m, 2H), 2.11 (dt, $J=13.0, 7.6$, 1H).	1.96 [450.0]
10				
15				
20	"B35"	 N-(3-Chloro-5-fluorobenzyl)-3- hydroxy-1-(3H-imidazo[4,5-b]- pyridin-6-yl)-2-oxopyrrolidine-3- carboxamide	** 8.77 – 8.69 (m, 1H), 8.68 (d, $J = 2.3$ Hz, 1H), 8.55 (s, 1H), 8.37 (d, $J = 2.3$ Hz, 1H), 7.26 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 4.41 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.97 (dd, $J = 14.6, 8.3$ Hz, 2H), 2.70 – 2.61 (m, 1H), 2.19 (dt, $J = 13.0, 7.5$ Hz, 1H).	1.70 [404.0]
25				
30	"B36"	 N-(3-Chloro-5-fluorobenzyl)-3- hydroxy-2-oxo-1-(2- trifluoromethyl-3H-imidazo- [4,5-b]pyridin-6-yl)pyrrolidine-3-	** 8.89 (s, 1H), 8.75 (t, $J = 6.3$ Hz, 1H), 8.51 (d, $J = 1.9$ Hz, 1H), 7.27 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.11 (t, $J = 8.3$ Hz, 1H), 6.84 (s, 1H), 4.40 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.28 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.01	1.98 [472.0]
35				

	carboxamide	(s, 2H), 2.70 – 2.62 (m, 1H), 2.25 – 2.16 (m, 1H).	
5	 N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-1-[2-(1H-indol-3-yl)- ethyl]-2-oxopyrrolidine-3- carboxamide		
10			
15	 N-(3-Chloro-5-fluorobenzyl)-(R)- 3-hydroxy-1-[2-(1H-indol-3-yl)- ethyl]-2-oxopyrrolidine-3- carboxamide		
20			
25	 N-(3-Chloro-5-fluorobenzyl)-(S)- 1-(2-Fluoro-5-trifluoromethyl- phenyl)-3-hydroxy-2-oxo- pyrrolidine-3-carboxamide	** 8.72 (t, J=6.4, 1H), 7.86 (dd, J=6.7, 2.3, 1H), 7.81 - 7.73 (m, 1H), 7.60 (t, J=10.4, 8.7, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.21 (s, 1H), 7.13 - 7.08 (m, 1H), 6.81 (s, 1H), 4.41 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.92 - 3.82 (m, 2H), 2.65 (ddd, J=12.9, 7.0, 4.8, 1H), 2.25 - 2.17 (m, 1H).	2.39 [449.0]
30			
35	 N-(3-Chloro-5-fluorobenzyl)-(S)- 1-(2-Fluoro-5-trifluoromethyl- phenyl)-3-hydroxy-2-oxo- pyrrolidine-3-carboxamide	** 11.74 (s, 1H), 8.70 (t, J=6.4, 1H), 7.96 - 7.83 (m, 3H), 7.39 - 7.29 (m, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.23 -	2.07 [430.0]

5		N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide	7.17 (m, 1H), 7.17 - 7.05 (m, 1H), 6.75 (s, 1H), 6.57 - 6.45 (m, 1H), 4.39 (dd, J=15.7, 6.7, 1H), 4.26 (dd, J=15.7, 6.0, 1H), 3.95 - 3.84 (m, 2H), 2.61 (dt, J=12.9, 5.6, 1H), 2.15 (dt, J=12.9, 7.6, 1H).	
10	"B41"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide	** 11.75 (s, 1H), 8.71 (t, J=6.4, 1H), 7.94 - 7.86 (m, 3H), 7.33 (d, J=9.6, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.23 - 7.19 (m, 1H), 7.16 - 7.05 (m, 1H), 6.75 (s, 1H), 6.56 - 6.48 (m, 1H), 4.39 (dd, J=15.7, 6.7, 1H), 4.26 (dd, J=15.7, 6.0, 1H), 3.95 - 3.84 (m, 2H), 2.61 (dt, J=12.9, 5.7, 1H), 2.15 (dt, J=12.9, 7.6, 1H).	2.07 [430.0]
15				
20	"B42"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(2-Fluoro-5-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.72 (t, J=6.4, 1H), 7.86 (dd, J=6.8, 2.3, 1H), 7.81 - 7.73 (m, 1H), 7.61 (t, J=10.4, 3.7, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.21 (s, 1H), 7.14 - 7.08 (m, 1H), 6.81 (s, 1H), 4.41 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.92 - 3.82 (m, 2H), 2.65 (ddd, J=12.9, 7.0, 4.8, 1H), 2.26 - 2.17 (m, 1H).	2.39 [449.0]
25				
30				
35	"B43"		11.93 (s, 1H), 8.73 (t, J = 6.4 Hz, 1H), 7.99 (s, 1H), 7.86 (s, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.49 (dd, J = 8.9, 2.0 Hz, 1H), 7.27 (dt, J = 8.7, 2.1 Hz, 1H),	

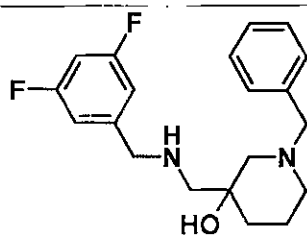
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N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-indol-5-yl)-pyrrolidine-3-carboxamide

7.21 (s, 1H), 7.11 (d, $J = 9.6$ Hz, 1H), 6.75 (s, 1H), 4.39 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.90 (t, $J = 6.8$ Hz, 2H), 2.64 – 2.56 (m, 1H), 2.19 – 2.08 (m, 1H).

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"B44"

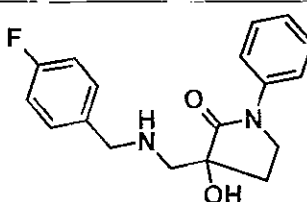


1-Benzyl-3-[(3,5-difluorobenzylamino)methyl]-piperidin-3-ol

7.30 – 7.17 (m, 3H), 7.03 (t, $J = 8.0$ Hz, 2H), 4.23 (s, 1H), 3.72 (s, 1H), 3.46 (d, $J = 13.4$ Hz, 1H), 3.38 (d, $J = 13.4$ Hz, 1H), 2.41 (d, $J = 11.2$ Hz, 1H), 2.08 (d, $J = 22.0$ Hz, 1H), 2.03 (d, $J = 9.6$ Hz, 1H), 1.59 (s, 1H), 1.37 (d, $J = 9.1$ Hz, 1H), 1.31 – 1.19 (m, 1H).

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"B45"



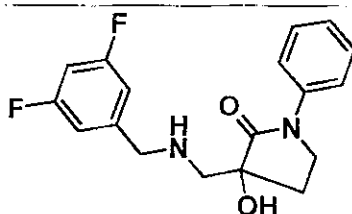
3-[(4-Fluorobenzylamino)-methyl]-3-hydroxy-1-phenylpyrrolidin-2-one

7.70 (t, $J = 1.6$ Hz, 1H), 7.68 (d, $J = 1.0$ Hz, 1H), 7.41 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.17 – 7.05 (m, 3H), 5.50 (s, 1H), 3.81 – 3.73 (m, 1H), 3.73 – 3.61 (m, 3H), 2.64 (q, $J = 11.9$ Hz, 2H), 2.40 (ddd, $J = 12.8, 8.0, 4.8$ Hz, 1H), 1.95 (ddd, $J = 13.0, 8.4, 6.1$ Hz, 1H).

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"B46"



3-[(3,5-Difluorobenzylamino)-methyl]-3-hydroxy-1-phenylpyrrolidin-2-one

7.71 (d, $J = 1.0$ Hz, 1H), 7.69 (s, 1H), 7.41 – 7.33 (m, 2H), 7.14 (t, $J = 7.4$ Hz, 1H), 7.08 – 6.96 (m, 3H), 5.52 (s, 1H), 3.84 – 3.75 (m, 1H), 3.72 (d, $J = 7.5$ Hz, 2H), 3.70 – 3.64 (m, 1H), 2.64 (q, $J = 12.0$ Hz, 2H), 2.41 (ddd, $J = 12.9, 8.0, 4.8$ Hz, 2H), 2.02 – 1.91 (m, 1H).

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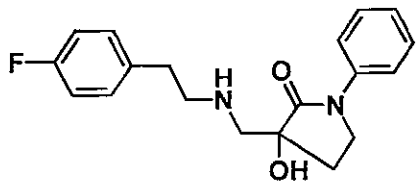
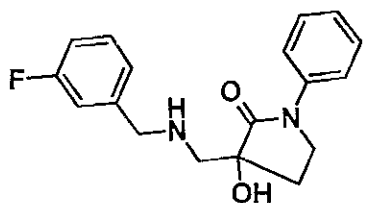
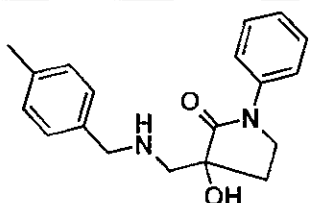
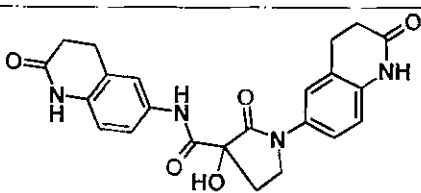
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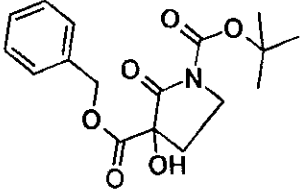
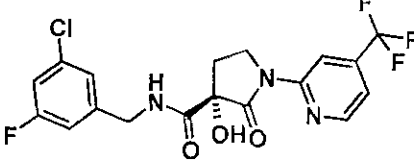
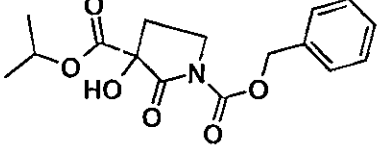
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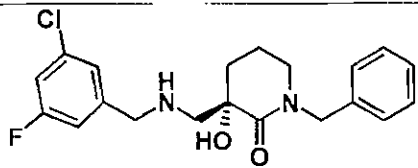
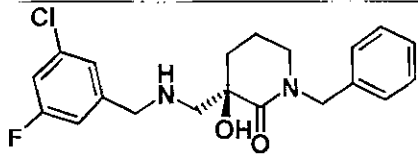
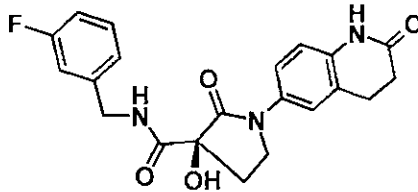
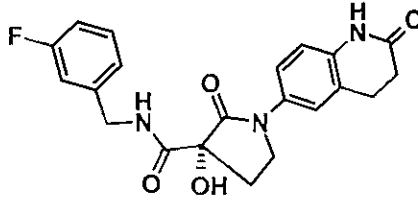
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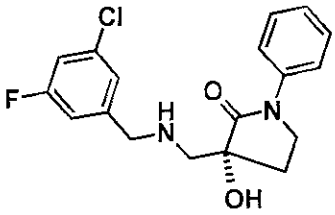
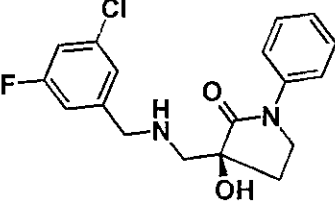
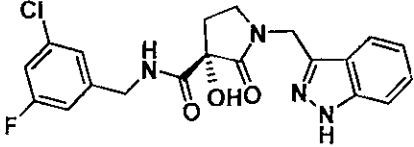
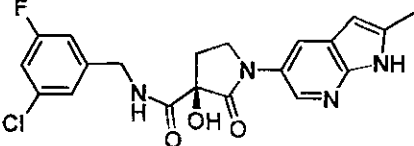
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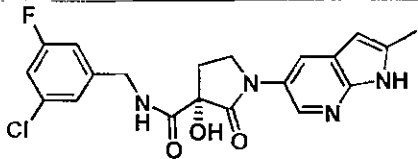
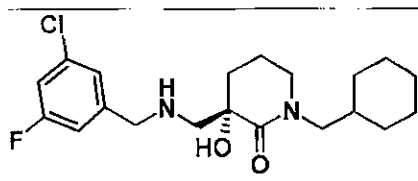
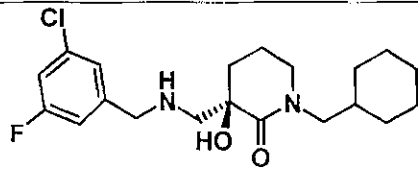
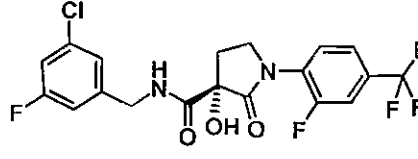
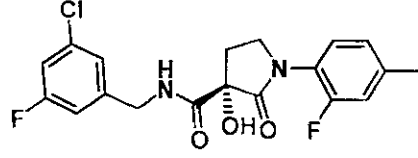
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"B47"	 3-[[2-(4-Fluorophenyl)-ethylamino]methyl]-3-hydroxy-1-phenylpyrrolidin-2-one	7.68 (d, $J = 7.8$ Hz, 2H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.17 (dt, $J = 15.1, 6.6$ Hz, 3H), 7.01 (t, $J = 8.9$ Hz, 2H), 5.51 (s, 1H), 3.75 (td, $J = 9.0, 4.6$ Hz, 1H), 3.66 (dd, $J = 15.2, 8.5$ Hz, 1H), 2.82 – 2.69 (m, 4H), 2.68 – 2.61 (m, 2H), 2.35 (ddd, $J = 12.8, 7.9, 4.6$ Hz, 1H), 1.99 – 1.88 (m, 1H).	
"B48"	 3-[(3-Fluorobenzylamino)-methyl]-3-hydroxy-1-phenylpyrrolidin-2-one	7.73 – 7.65 (m, 2H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.20 – 7.11 (m, 3H), 7.08 (d, $J = 7.8$ Hz, 2H), 5.48 (s, 1H), 3.81 – 3.73 (m, 1H), 3.73 – 3.66 (m, 1H), 3.64 (s, 2H), 2.64 (q, $J = 11.9$ Hz, 2H), 2.39 (ddd, $J = 12.7, 7.9, 4.8$ Hz, 1H), 1.99 – 1.90 (m, 1H).	
"B49"	 3-Hydroxy-3-[(4-methylbenzylamino)methyl]-1-phenylpyrrolidin-2-one	7.73 – 7.64 (m, 2H), 7.38 (t, $J = 8.0$ Hz, 2H), 7.21 – 7.10 (m, 3H), 7.08 (d, $J = 7.8$ Hz, 2H), 5.48 (s, 1H), 3.81 – 3.73 (m, 1H), 3.73 – 3.66 (m, 1H), 3.64 (s, 2H), 2.67 (d, $J = 11.9$ Hz, 1H), 2.62 (d, $J = 11.9$ Hz, 1H), 2.39 (ddd, $J = 12.7, 7.9, 4.8$ Hz, 1H), 2.25 (s, 3H), 1.99 – 1.89 (m, 1H).	
"B50"	 N-(2-Oxo-1,2,3,4-tetrahydro-		1.45 [435.1]

	quinolin-6-yl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide		
5 10	"B51"  3-Benzyl 1-tert-butyl 3-hydroxy-2-oxopyrrolidine-1,3-dicarboxylate	7.49 – 7.29 (m, 5H), 6.73 (d, J = 5.5 Hz, 1H), 5.20 (d, J = 10.3 Hz, 2H), 3.72 (ddd, J = 10.4, 8.5, 4.5 Hz, 1H), 3.61 (dt, J = 10.4, 7.5 Hz, 1H), 2.47 – 2.37 (m, 1H), 2.05 (ddd, J = 13.4, 8.4, 7.0 Hz, 1H), 1.46 (s, 9H).	
15 20 25	"B52"  N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(4-trifluoromethylpyridin-2-yl)pyrrolidine-3-carboxamide	* 8.80 (t, J = 6.4 Hz, 1H), 8.72 (d, J = 5.2 Hz, 1H), 8.62 (s, 1H), 7.59 (dd, J = 5.2, 1.0 Hz, 1H), 7.27 (dt, J = 8.8, 2.1 Hz, 1H), 7.20 (s, 1H), 7.13 – 7.07 (m, 1H), 6.94 (s, 1H), 4.39 (dd, J = 15.7, 6.7 Hz, 1H), 4.26 (dd, J = 15.7, 6.0 Hz, 1H), 4.15 – 4.09 (m, 1H), 3.98 (dt, J = 10.6, 7.6 Hz, 1H), 2.61 (ddd, J = 12.9, 7.9, 3.8 Hz, 1H), 2.18 (ddd, J = 13.1, 8.7, 7.3 Hz, 1H).	2.42 [432.0]
30 35	"B53"  1-Benzyl 3-isopropyl 3-hydroxy-2-oxopyrrolidine-1,3-dicarboxylate		2.10 [322.0]

5	"B54"	 (S)-1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one		
10	"B55"	 (R)-1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one		
15	"B56"	 N-(3-Fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.74 [398.1]	
25	"B57"	 N-(3-Fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	1.74 [398.1]	

5	"B58"	 (R)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one		
10	"B59"	 (S)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one		
20	"B60"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(1H-indazol-3-ylmethyl)-2-oxopyrrolidine-3-carboxamide		
30	"B61"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxopyrrolidine-3-carboxamide	2.01 [417.0]	
35				

5	"B62"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxo-pyrrolidine-3-carboxamide	2.01 [4.17.0]
10	"B63"	 (S)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxy-piperidin-2-one	
15	"B64"	 (R)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxy-piperidin-2-one	
20	"B65"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-fluoro-4-trifluoromethyl-phenyl)-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	2.43 [449.0]
25	"B66"	 3.65 (t, $J = 6.4$ Hz, 1H), 7.30 – 7.23 (m, 2H), 7.21 (s, 1H), 7.14 (d, $J = 11.8$ Hz, 1H), 7.10	2.26 [395.1]

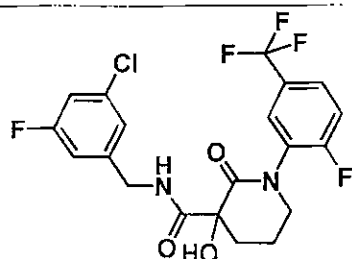
5

N-(3-Chloro-5-fluorobenzyl)-(S)-
1-(2-fluoro-4-methylphenyl)-3-
hydroxy-2-oxopyrrolidine-3-
carboxamide

(d, $J = 10.6$ Hz, 1H), 7.06 (d, $J = 8.1$ Hz, 1H), 6.71 (s, 1H), 4.40 (dd, $J = 15.9, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.84 – 3.64 (m, 2H), 2.62 (ddd, $J = 11.8, 9.3, 5.8$ Hz, 1H), 2.33 (s, 3H), 2.25 – 2.07 (m, 1H).

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"B67"



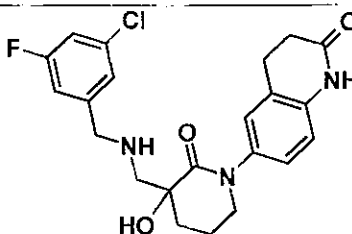
N-(3-Chloro-5-fluorobenzyl)-1-
(2-fluoro-5-trifluoromethyl-
phenyl)-3-hydroxy-2-oxo-
piperidine-3-carboxamide

8.64 (t, $J = 6.1$ Hz, 1H), 7.80 (t, $J = 9.1$ Hz, 2H), 7.56 (t, $J = 9.1$ Hz, 1H), 7.25 (d, $J = 8.7$ Hz, 1H), 7.21 (s, 1H), 7.11 (d, $J = 9.4$ Hz, 1H), 6.56 (s, 1H), 4.40 (dd, $J = 16.0, 6.8$ Hz, 1H), 4.23 (dd, $J = 15.9, 5.7$ Hz, 1H), 3.72 (d, $J = 8.4$ Hz, 1H), 3.61 (d, $J = 11.8$ Hz, 1H), 2.39 – 2.27 (m, 1H), 1.99 (m, 3H).

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"B68"



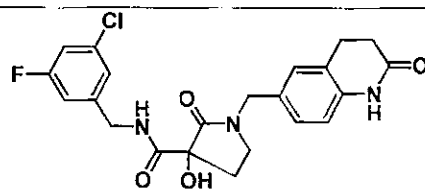
6-{3-[(3-Chloro-5-
fluorobenzylamino)methyl]-3-
hydroxy-2-oxopiperidin-1-yl}-3,4-
dihydro-1H-quinolin-2-one

10.10 (s, 1H), 7.25 (d, $J = 10.4$ Hz, 2H), 7.18 (d, $J = 9.9$ Hz, 1H), 7.03 (s, 1H), 6.99 (d, $J = 3.4$ Hz, 1H), 6.81 (d, $J = 8.3$ Hz, 1H), 5.15 (s, 1H), 3.74 (q, $J = 15.2$ Hz, 2H), 3.53 (s, 2H), 2.82 (dd, $J = 19.6, 12.0$ Hz, 3H), 2.14 (d, $J = 10.7$ Hz, 1H), 1.99 (s, 2H), 1.76 (s, 2H), 1.22 (s, 2H).

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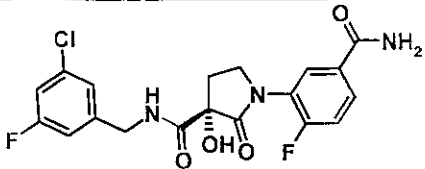
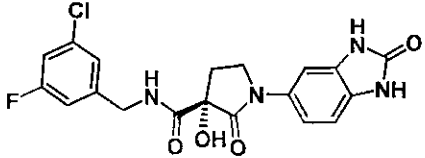
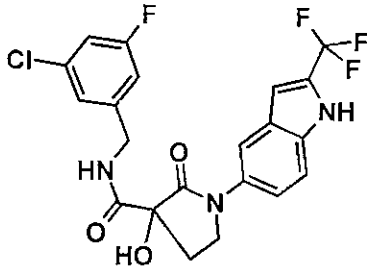
"B69"

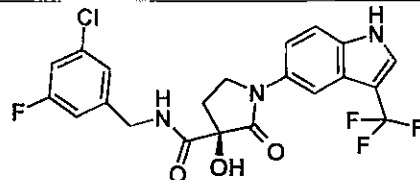
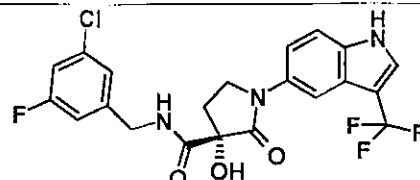
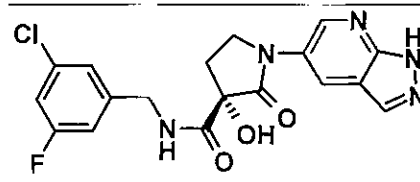
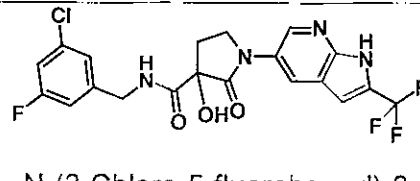


N-(3-Chloro-5-fluorobenzyl)-3-
hydroxy-2-oxo-1-(2-oxo-1,2,3,4-
tetrahydroquinolin-6-ylmethyl)-

10.06 (s, 1H), 8.65 (t, $J = 6.3$ Hz, 1H), 7.27 (d, $J = 8.7$ Hz, 1H), 7.21 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 7.03 (s, 1H), 7.00 (d, $J = 8.1$ Hz, 1H), 6.78 (d, $J = 8.0$ Hz, 1H), 6.56 (s, 1H), 4.38 (dd, $J = 15.4, 6.2$ Hz, 2H), 4.30

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		pyrrolidine-3-carboxamide	- 4.20 (m, 2H), 3.23 (dd, J = 12.5, 5.4 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 2.45 – 2.38 (m, 3H), 2.00 – 1.90 (m, 1H).	
5	"B70"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(5-carbamoyl-2-fluorophenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		1.87 [424.0]
10				
15	"B71"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)-pyrrolidine-3-carboxamide	* 10.60 (dd, J = 21.8, 6.3 Hz, 2H), 8.75 – 8.62 (m, 1H), 7.44 (t, J = 2.4 Hz, 1H), 7.26 (dt, J = 8.8, 2.1 Hz, 1H), 7.21 (d, J = 4.4 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.91 (dd, J = 12.7, 9.9 Hz, 1H), 6.68 (d, J = 3.7 Hz, 1H), 4.39 (dd, J = 15.7, 6.7 Hz, 1H), 4.26 (dd, J = 15.7, 6.0 Hz, 1H), 3.87 – 3.77 (m, 2H), 2.62 – 2.54 (m, 1H), 2.11 (dt, J = 12.9, 7.5 Hz, 1H).	1.82 [419.1]
20				
25				
30	"B72"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-indol-5-yl)-pyrrolidine-3-carboxamide	11.93 (s, 1H), 8.73 (t, J = 6.3 Hz, 1H), 7.99 (d, J = 1.2 Hz, 1H), 7.87 (s, 1H), 7.54 (d, J = 3.8 Hz, 1H), 7.50 (dd, J = 8.9, 1.9 Hz, 1H), 7.27 (dt, J = 8.8, 2.1 Hz, 1H), 7.22 (s, 1H), 7.11 (d, J = 9.6 Hz, 1H), 6.75 (s, 1H), 4.39 (dd, J = 15.8, 6.6 Hz, 1H), 4.25 (dd, J = 15.8, 5.9 Hz, 1H), 3.90 (t, J = 6.8 Hz, 2H),	2.41 [470.1]
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		2.65 – 2.55 (m, 1H), 2.14 (dt, J = 12.9, 7.5 Hz, 1H).	
5	"B73"  N-(3-Chloro-5-fluorobenzyl)-(R)- 3-hydroxy-2-oxo-1-(3-trifluoro- methyl-1H-indol-5-yl)pyrrolidine- 3-carboxamide		
10			
15	"B74"  N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(3-trifluoro- methyl-1H-indol-5-yl)pyrrolidine- 3-carboxamide	11.93 (s, 1H), 8.73 (t, J = 6.3 Hz, 1H), 7.99 (d, J = 1.3 Hz, 1H), 7.86 (s, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.50 (dd, J = 8.9, 1.9 Hz, 1H), 7.27 (dd, J = 8.7, 2.1 Hz, 1H), 7.22 (s, 1H), 7.11 (d, J = 9.5 Hz, 1H), 6.74 (s, 1H), 4.39 (dd, J = 15.8, 6.7 Hz, 1H), 4.25 (dd, J = 15.7, 6.0 Hz, 1H), 3.90 (t, J = 6.8 Hz, 2H), 2.65 – 2.56 (m, 1H), 2.14 (dt, J = 12.9, 7.5 Hz, 1H).	
20			
25	"B75"  N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(1H- pyrazolo[3,4-b]pyridin-5-yl)- pyrrolidine-3-carboxamide		
30			
35	"B76"  N-(3-Chloro-5-fluorobenzyl)-3-		

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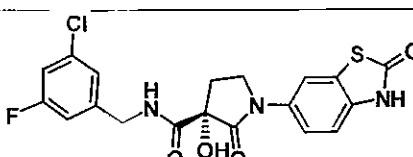
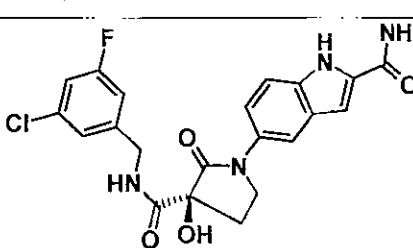
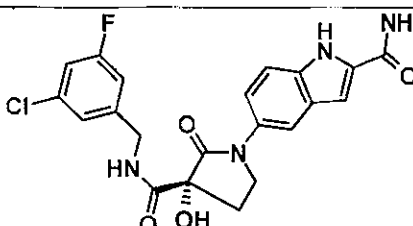
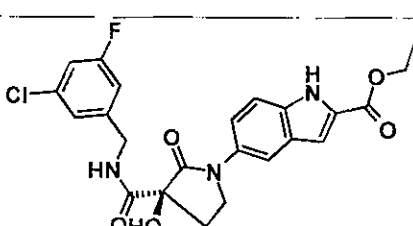
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	hydroxy-2-oxo-1-(2-trifluoro- methyl-1H-pyrrolo[2,3-b]pyridin- 5-yl)pyrrolidine-3-carboxamide		
"B77"	 N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(2-oxo-2,3- dihydrobenzothiazol-6-yl)- pyrrolidine-3-carboxamide	1.99 [436.0]	
"B78"	 5-[(S)-3-(3-Chloro-5- fluorobenzylcarbamoyl)-3- hydroxy-2-oxopyrrolidin-1-yl]- 1H-indole-2-carboxamide	1.91 [445.1]	
"B79"	 5-[(R)-3-(3-Chloro-5- fluorobenzylcarbamoyl)-3- hydroxy-2-oxopyrrolidin-1-yl]- 1H-indole-2-carboxamide	1.91 [445.1]	
"B80"	 Ethyl 5-[(S)-3-(3-chloro-5-	2.27 [474.0]	

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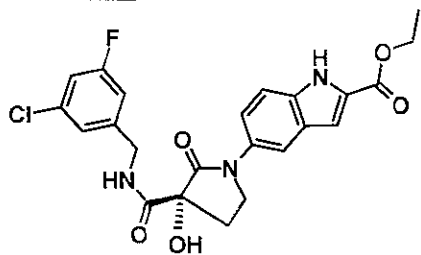
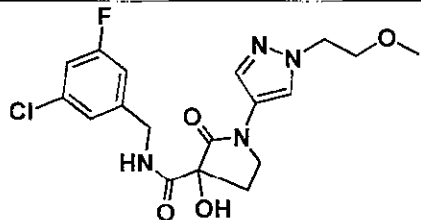
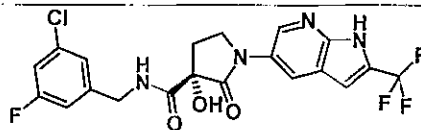
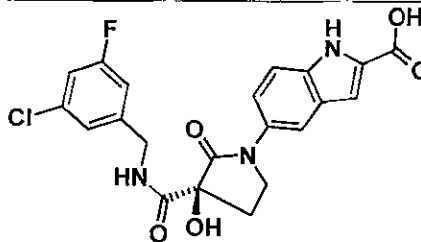
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	fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylate		
"B81"	 Ethyl 5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylate	2.27 [474.1]	
"B82"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxo-pyrrolidine-3-carboxamide	1.90 [411.1]	
"B83"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide	2.22 [471.0]	
"B84"	 12.94 (s, 1H), 11.78 (s, 1H), 8.68 (t, $J = 6.4$ Hz, 1H), 7.81 (d, $J = 1.9$ Hz, 1H), 7.62 (dd, $J = 9.0, 2.1$ Hz, 1H), 7.44 (d, $J =$	1.99 [446.0]	

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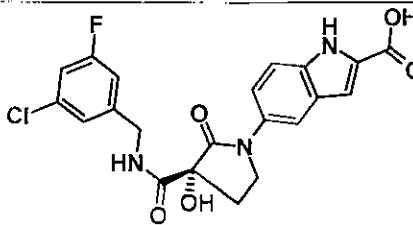
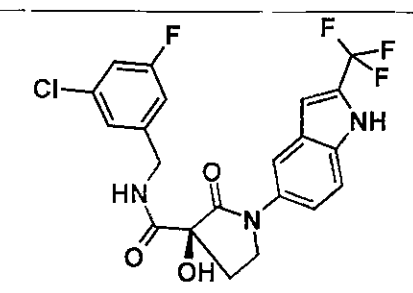
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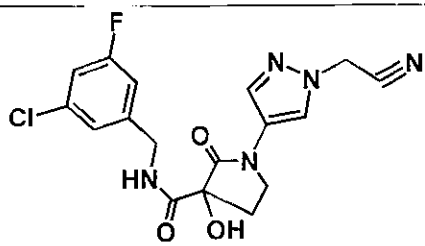
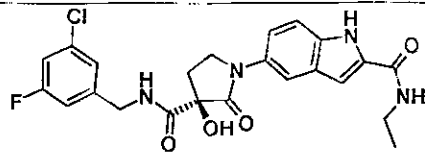
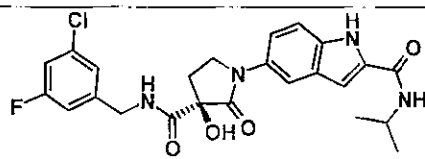
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	5-[(S)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylic acid	9.0 Hz, 1H), 7.26 (dt, $J = 8.7$, 2.1 Hz, 1H), 7.22 (s, 1H), 7.14 – 7.10 (m, 1H), 7.09 (d, $J = 1.5$ Hz, 1H), 6.69 (s, 1H), 4.40 (dd, $J = 15.7$, 6.7 Hz, 1H), 4.27 (dd, $J = 15.7$, 6.0 Hz, 1H), 3.89 (t, $J = 6.8$ Hz, 2H), 2.68 – 2.56 (m, 1H), 2.14 (dt, $J = 12.9$, 7.6 Hz, 1H).	
"B85"	 5-[(R)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylic acid	** ppm = 12.95 (s, 1H), 11.78 (s, 1H), 8.68 (t, $J=6.4$, 1H), 7.80 (d, $J=2.0$, 1H), 7.62 (dd, $J=9.0$, 2.1, 1H), 7.44 (d, $J=9.0$, 1H), 7.26 (dt, $J=8.8$, 2.2, 1H), 7.22 (s, 1H), 7.14 – 7.10 (m, 1H), 7.09 (d, $J=2.0$, 1H), 6.69 (s, 1H), 4.40 (dd, $J=15.7$, 6.8, 1H), 4.27 (dd, $J=15.7$, 6.0, 1H), 3.92 – 3.85 (m, 2H), 2.65 – 2.57 (m, 1H), 2.14 (dt, $J=12.8$, 7.6, 1H).	1.99 [446.0]
"B86"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-indol-5-yl)-pyrrolidine-3-carboxamide		2.36 [470.0]

5	"B87"	 N-(3-Chloro-5-fluorobenzyl)-1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	1.91 [392.0]	
10	"B88"	 N-Ethyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.59 - 11.55 (m, 1H), 8.71 - 8.64 (m, 1H), 8.46 (t, J=5.7, 1H), 7.80 - 7.75 (m, 1H), 7.52 (dd, J=8.9, 2.0, 1H), 7.42 (d, J=8.9, 1H), 7.28 - 7.24 (m, 1H), 7.22 (s, 1H), 7.14 - 7.10 (m, 1H), 7.10 - 7.07 (m, 1H), 6.68 (s, 1H), 4.41 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 3.93 - 3.86 (m, 2H), 3.35 - 3.30 (m, 2H), 2.65 - 2.58 (m, 1H), 2.14 (dt, J=12.9, 7.6, 1H), 1.15 (t, J=7.2, 3H).	2.04 [473.1]
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25	"B89"	 N-Isopropyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.57 - 11.53 (m, 1H), 8.68 (t, J=6.4, 1H), 8.22 (d, J=7.8, 1H), 7.79 - 7.76 (m, 1H), 7.51 (dd, J=8.9, 2.0, 1H), 7.42 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.16 - 7.09 (m, 2H), 6.68 (s, 1H), 4.41 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 4.17 - 4.07 (m, J=6.7, 1H), 3.93 - 3.86 (m, 2H), 2.65 - 2.57 (m, 1H), 2.14 (dt,	2.13 [487.1]
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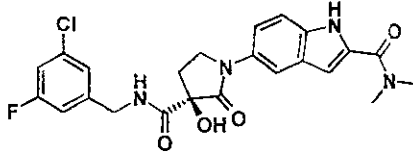
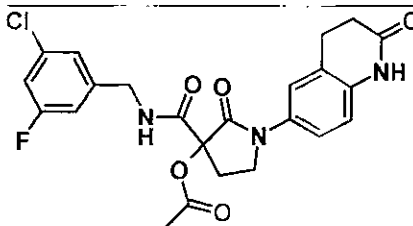
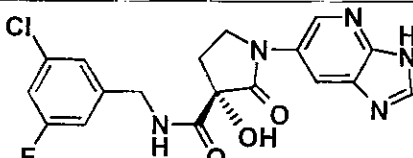
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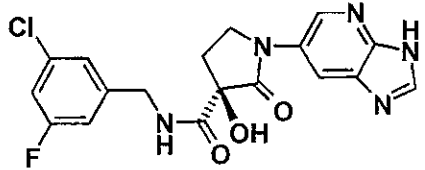
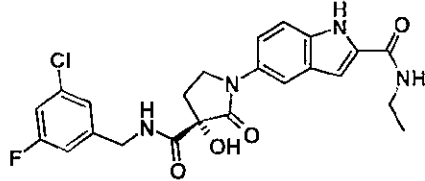
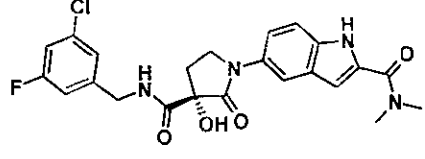
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		J=12.8, 7.5, 1H), 1.19 (d, J=6.6, 6H).	
"B90"	 N,N-Dimethyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.55 (s, 1H), 8.67 (t, J=6.4, 1H), 7.79 (d, J=2.0, 1H), 7.54 (dd, J=8.9, 2.1, 1H), 7.43 (d, J=8.8, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.23 - 7.20 (m, 1H), 7.15 - 7.09 (m, 1H), 3.88 (d, J=2.0, 1H), 6.69 (s, 1H), 4.40 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.93 - 3.85 (m, 2H), 3.28 - 2.93 (m, 6H), 2.65 - 2.57 (m, 1H), 2.19 - 2.09 (m, 1H).	2.04 [473.1]
"B91"	 3-(3-Chloro-5-fluorobenzyl-carbamoyl)-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidin-3-yl acetate	** 10.09 (s, 1H), 8.93 (t, J=6.2, 1H), 7.47 (d, J=2.5, 1H), 7.39 (dd, J=8.6, 2.5, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.19 - 7.16 (m, 1H), 7.07 - 7.03 (m, 1H), 6.87 (d, J=8.6, 1H), 4.42 - 4.26 (m, 2H), 3.89 - 3.81 (m, 2H), 2.92 - 2.85 (m, 3H), 2.47 - 2.42 (m, 2H), 2.40 - 2.32 (m, 1H), 2.19 (s, 3H).	2.11 [474.0]
"B92"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(3H-imidazo[4,5-b]pyridin-6-yl)-2-oxo-pyrrolidine-3-carboxamide	* 8.73 (t, J = 6.4 Hz, 1H), 8.68 (d, J = 2.3 Hz, 1H), 8.55 (s, 1H), 8.37 (d, J = 2.3 Hz, 1H), 7.26 (dt, J = 8.7, 2.1 Hz, 1H), 7.22 (s, 1H), 7.12 (d, J = 9.6 Hz, 1H), 4.41 (dd, J = 15.7, 6.7 Hz, 1H), 4.27 (dd, J = 15.7, 6.0 Hz, 1H), 3.97 (dd, J = 14.6, 8.3 Hz, 2H), 2.70 - 2.60 (m, 1H), 2.19 (dt, J = 13.0, 7.5 Hz, 1H).	1.70 [404.0]

5	"B93"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(3H-imidazo[4,5-b]pyridin-6-yl)-2-oxo-pyrrolidine-3-carboxamide		
10	"B94"	 N-Ethyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	11.57 (s, 1H), 8.68 (t, J=6.4, 1H), 8.47 (t, J=5.6, 1H), 7.77 (d, J=2.0, 1H), 7.52 (dd, J=8.9, 2.1, 1H), 7.42 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.23 (s, 1H), 7.14 - 7.10 (m, 1H), 7.09 (d, J=2.0, 1H), 6.68 (s, 1H), 4.40 (dd, J=15.8, 6.8, 1H), 4.26 (dd, J=15.8, 6.0, 1H), 3.93 - 3.85 (m, 2H), 3.35 - 3.31 (m, 2H), 2.61 (dt, J=12.2, 5.8, 1H), 2.14 (dt, J=12.8, 7.5, 1H), 1.15 (t, J=7.2, 3H).	2.05 [473.1]
25	"B95"	 N,N-Dimethyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	11.56 (s, 1H), 8.68 (t, J=6.4, 1H), 7.79 (d, J=2.0, 1H), 7.54 (dd, J=8.9, 2.1, 1H), 7.43 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.23 - 7.21 (m, 1H), 7.14 - 7.09 (m, 1H), 6.90 - 6.87 (m, 1H), 6.69 (s, 1H), 4.40 (dd, J=15.8, 6.7, 1H), 4.26 (dd, J=15.7, 6.0, 1H), 3.93 - 3.86 (m, 2H), 3.30 - 2.98 (m, 6H), 2.66 - 2.56 (m, 1H), 2.19 - 2.09 (m, 1H).	2.04 [473.1]

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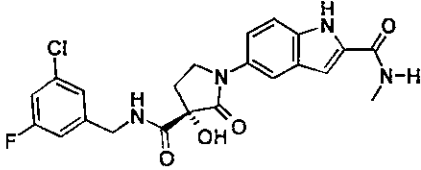
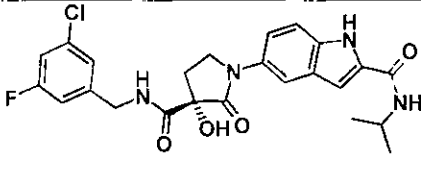
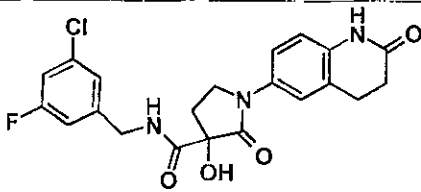
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"B96"	 N-Methyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.60 - 11.57 (m, 1H), 8.67 (t, J=6.4, 1H), 8.46 - 8.41 (m, 1H), 7.78 - 7.76 (m, 1H), 7.52 (dd, J=8.9, 2.1, 1H), 7.42 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.23 - 7.21 (m, 1H), 7.14 - 7.10 (m, 1H), 7.06 (d, J=2.0, 1H), 6.67 (s, 1H), 4.40 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 3.89 (t, J=6.8, 2H), 2.81 (d, J=4.5, 3H), 2.65 - 2.57 (m, 1H), 2.17 - 2.10 (m, 1H).	1.97 [459.0]
"B97"	 N-Isopropyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.56 - 11.53 (m, 1H), 8.67 (t, J=6.4, 1H), 8.21 (d, J=7.8, 1H), 7.78 (d, J=2.0, 1H), 7.51 (dd, J=8.9, 2.1, 1H), 7.44 - 7.40 (m, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.23 - 7.22 (m, 1H), 7.14 - 7.12 (m, 1H), 7.12 - 7.09 (m, 1H), 6.67 (s, 1H), 4.40 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 4.17 - 4.09 (m, 1H), 3.92 - 3.86 (m, 2H), 2.65 - 2.58 (m, 1H), 2.18 - 2.10 (m, 1H), 1.19 (d, J=6.6, 6H).	2.14 [487.1]
"B98"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-2-oxopyrrolidine	** 10.07 (s, 1H), 8.67 (t, J=6.4, 1H), 7.48 (d, J=2.4, 1H), 7.44 (dd, J=8.6, 2.5, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.23 - 7.19 (m, 1H), 7.13 - 7.07 (m, 1H), 6.86 (d, J=8.6, 1H), 6.69 (s, 1H), 4.39 (dd, J=15.7, 6.7,	

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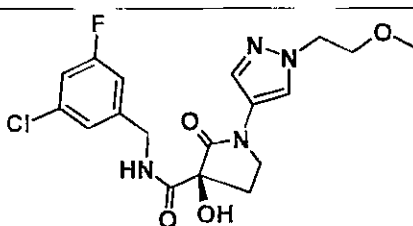
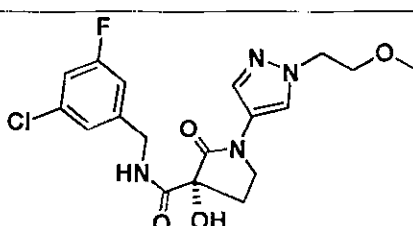
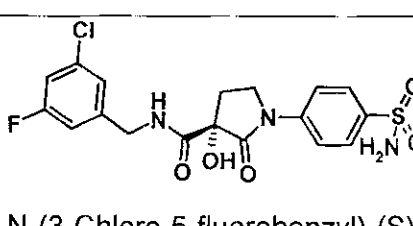
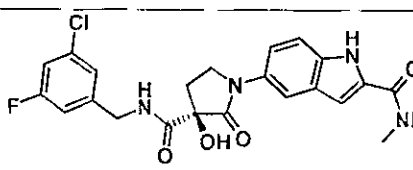
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	pyrrolidine-3-carboxamide	1H), 4.25 (dd, J=15.7, 6.0, 1H), 3.84 - 3.75 (m, 2H), 2.88 (t, J=7.5, 2H), 2.61 - 2.54 (m, 1H), 2.47 - 2.41 (m, 2H), 2.14 - 2.06 (m, 1H).	
"B99"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxo-pyrrolidine-3-carboxamide		1.90 [411.1]
"B100"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxo-pyrrolidine-3-carboxamide		1.90 [411.1]
"B101"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(4-sulfamoylphenyl)pyrrolidine-3-carboxamide		1.96 [442.0]
"B102"		** 11.59 (s, 1H), 8.67 (t, J=6.4, 1H), 8.44 (q, J=4.5, 1H), 7.77 (d, J=2.0, 1H), 7.52	1.97 [459.1]

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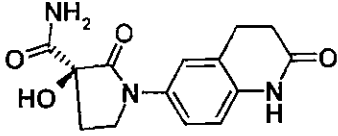
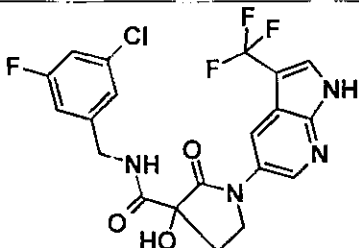
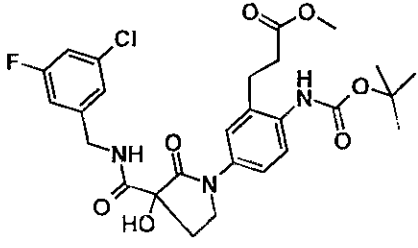
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	N-Methyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	(dd, J=8.9, 2.1, 1H), 7.42 (d, J=8.9, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.22 (s, 1H), 7.15 - 7.09 (m, 1H), 7.08 - 7.03 (m, 1H), 6.67 (s, 1H), 4.40 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.93 - 3.84 (m, 2H), 2.81 (d, J=4.5, 3H), 2.65 - 2.57 (m, 1H), 2.19 - 2.09 (m, 1H).	
"B103"	 (S)-3-Hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide	10.07 (s, 1H), 7.48 (d, J=2.4, 1H), 7.46 - 7.38 (m, 2H), 7.31 - 7.27 (m, 1H), 6.86 (d, J=8.6, 1H), 6.43 (s, 1H), 3.83 - 3.72 (m, 2H), 2.88 (t, J=7.5, 2H), 2.56 - 2.51 (m, 1H), 2.47 - 2.40 (m, 2H), 2.10 - 2.00 (m, 1H).	1.18 [290.1]
"B104"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide	12.61 (s, 1H), 8.78 (t, J = 6.4 Hz, 1H), 8.61 (d, J = 2.2 Hz, 1H), 8.34 (s, 1H), 8.21 (s, 1H), 7.27 (d, J = 8.8 Hz, 1H), 7.22 (s, 1H), 7.11 (d, J = 9.6 Hz, 1H), 6.82 (s, 1H), 4.39 (dd, J = 15.8, 6.7 Hz, 1H), 4.26 (dd, J = 15.8, 5.9 Hz, 1H), 3.97 (dd, J = 8.8, 5.4 Hz, 2H), 2.68 - 2.58 (m, 1H), 2.23 - 2.11 (m, 1H).	
"B105"	 Methyl 3-{2-tert-butoxy-1-[(3-chloro-5-fluorobenzyl)carbamoyl]-3-hydroxy-2-oxopyrrolidin-1-yl}propanoate	3.73 (t, J = 6.4 Hz, 1H), 8.61 (s, 1H), 7.53 (dd, J = 8.7, 2.5 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.26 (dd, J = 8.6, 3.8 Hz, 2H), 7.20 (s, 1H), 7.09 (d, J = 9.6 Hz, 1H), 6.75 (s, 1H), 4.37	

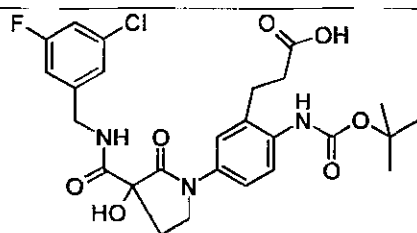
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carbonylamino-5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-phenyl}propionate

(dd, $J = 15.8, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.7, 5.9$ Hz, 1H), 3.82 (t, $J = 6.8$ Hz, 2H), 3.59 (s, 3H), 2.83 (t, $J = 7.8$ Hz, 2H), 2.63 – 2.53 (m, 4H), 2.16 – 2.05 (m, 1H), 1.44 (s, 9H).

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"B106"

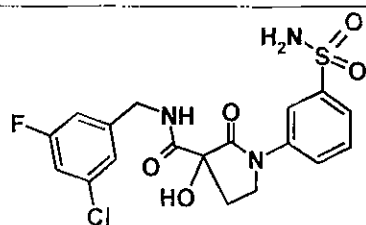


3-{2-tert-Butoxycarbonylamino-5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]phenyl}propionic acid

8.73 (t, $J = 6.5$ Hz, 1H), 7.48 (d, $J = 8.8$ Hz, 1H), 7.45 (s, 1H), 7.34 (d, $J = 8.7$ Hz, 1H), 7.27 (d, $J = 8.8$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.77 (s, 1H), 4.37 (dd, $J = 15.8, 6.7$ Hz, 1H), 4.24 (dd, $J = 15.8, 6.0$ Hz, 1H), 3.81 (t, $J = 6.7$ Hz, 2H), 2.73 (t, $J = 7.3$ Hz, 2H), 2.61 – 2.52 (m, 1H), 2.38 (t, $J = 6.9$ Hz, 2H), 2.14 – 2.04 (m, 1H), 1.44 (s, 9H).

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"B107"



N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-sulfamoylphenyl)pyrrolidine-3-carboxamide

** 8.77 – 8.68 (m, 1H), 8.23 (t, $J = 1.8$ Hz, 1H), 7.90 – 7.83 (m, 1H), 7.67 – 7.57 (m, 2H), 7.39 (s, 2H), 7.26 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.21 (s, 1H), 7.10 (d, $J = 9.0$ Hz, 1H), 6.82 (s, 1H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.1$ Hz, 1H), 3.89 (dd, $J = 14.2, 8.1$ Hz, 2H), 2.62 (dt, $J = 11.8, 5.7$ Hz, 1H), 2.17 (dt, $J = 13.0, 7.6$ Hz, 1H).

1.96
[442.0]

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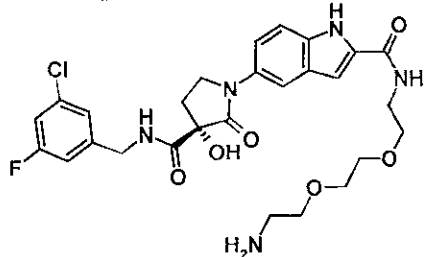
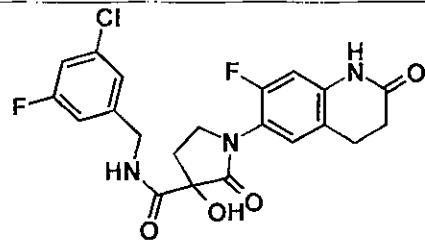
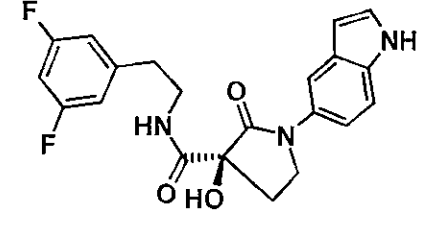
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"B108"	 N-({2-[2-(2-Aminoethoxy)ethoxy]ethyl})-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide	** 8.68 (t, J=6.4, 1H), 8.56 (t, J=5.7, 1H), 8.32 - 8.29 (m, 1H), 7.78 (d, J=2.1, 1H), 7.53 (dd, J=8.9, 2.1, 1H), 7.43 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.23 - 7.21 (m, 1H), 7.14 - 7.10 (m, 2H), 6.70 (s, 1H), 4.40 (dd, J=15.8, 6.8, 1H), 4.26 (dd, J=15.8, 6.0, 1H), 3.93 - 3.85 (m, 2H), 3.60 - 3.54 (m, 6H), 3.49 (t, J=5.5, 2H), 3.48 - 3.43 (m, 2H), 2.81 (t, J=5.4, 2H), 2.65 - 2.58 (m, 1H), 2.18 - 2.10 (m, 1H).	1.69 [576.2]
"B109"	 N-(3-Chloro-5-fluorobenzyl)-1-(7-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.24 (s, 1H), 8.71 (t, J = 6.5 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 7.20 (s, 1H), 7.18 (d, J = 3.1 Hz, 1H), 7.10 (d, J = 9.5 Hz, 1H), 6.75 (s, 1H), 6.72 (d, J = 11.5 Hz, 1H), 4.39 (dd, J = 15.8, 6.8 Hz, 1H), 4.24 (dd, J = 15.7, 5.8 Hz, 1H), 3.70 (dd, J = 12.9, 5.5 Hz, 2H), 2.85 (t, J = 7.5 Hz, 2H), 2.59 (d, J = 4.6 Hz, 1H), 2.45 (d, J = 7.2 Hz, 2H), 2.15 (dd, J = 13.7, 6.5 Hz, 1H).	
"B110"	 N-[2-(3,5-Difluorophenyl)ethyl]-(S)-3-hydroxy-1-(1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		2.07 [400.1]

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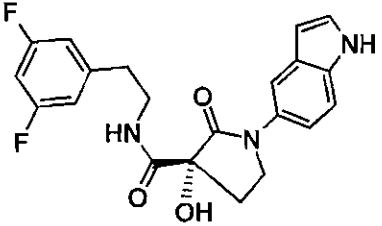
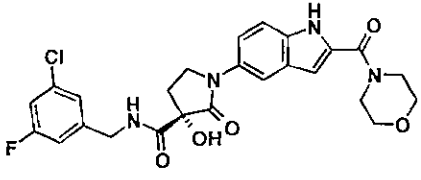
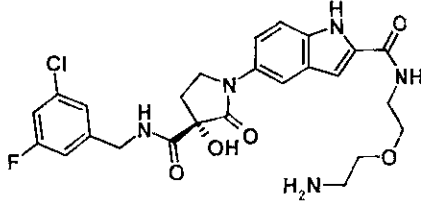
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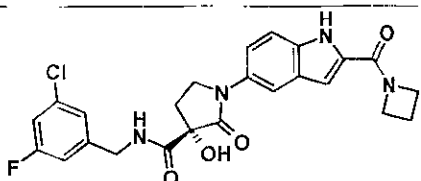
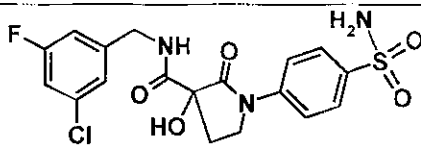
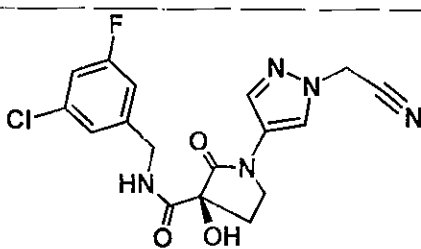
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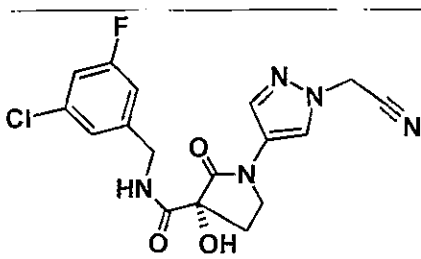
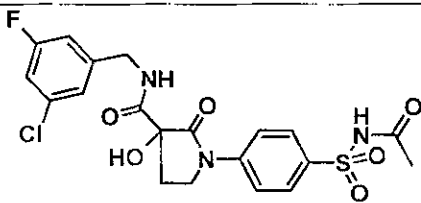
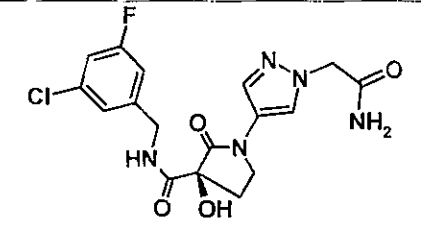
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	2-oxopyrrolidine-3-carboxamide		
"B111"	 N-[2-(3,5-Difluorophenyl)ethyl]- (R)-3-hydroxy-1-(1H-indol-5-yl)- 2-oxopyrrolidine-3-carboxamide		2.07 [400.1]
"B112"	 N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-1-[2-(morpholine-4- carbonyl)-1H-indol-5-yl]-2-oxo- pyrrolidine-3-carboxamide	** 11.65 - 11.59 (m, 1H), 8.68 (t, J=6.4, 1H), 7.79 (d, J=2.0, 1H), 7.55 (dd, J=8.9, 2.1, 1H), 7.43 (d, J=8.9, 1H), 7.27 (dt, J=8.8, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.14 - 7.09 (m, 1H), 6.84 - 6.81 (m, 1H), 6.69 (s, 1H), 4.40 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 3.91 - 3.85 (m, 2H), 3.76 (s, 4H), 3.69 - 3.63 (m, 4H), 2.65 - 2.58 (m, 1H), 2.18 - 2.10 (m, 1H).	2.01 [515.1]
"B113"	 N-[2-(2-Aminoethoxy)ethyl]-5- [(S)-3-(3-chloro-5- fluorobenzylcarbonyl)-3- hydroxy-2-oxopyrrolidin-1-yl]- 1H-indole-2-carboxamide	** 12.17 - 11.24 (m, 1H), 8.69 (t, J=6.4, 1H), 8.62 (t, J=5.6, 1H), 8.36 (s, 1H), 7.79 (d, J=2.0, 1H), 7.53 (dd, J=8.9, 2.1, 1H), 7.46 - 7.42 (m, 1H), 7.26 (dt, J=8.7, 2.3, 1H), 7.24 - 7.21 (m, 1H), 7.14 - 7.10 (m, 2H), 7.01 - 6.42 (m, 1H), 4.41 (dd, J=15.8, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 3.93 - 3.86 (m, 2H), 3.60 - 3.56 (m, 4H), 3.51 - 3.47 (m, 2H), 2.93	1.63 [532.1]

		- 2.88 (m, 2H), 2.65 - 2.57 (m, 1H), 2.15 (dt, J=12.8, 7.6, 1H).	
5	"B114"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-[2-(azetidine-1-carbonyl)-1H-indol-5-yl]-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	** 11.61 (s, 1H), 8.68 (t, J=6.4, 1H), 7.80 (d, J=2.0, 1H), 7.56 (dd, J=8.9, 2.1, 1H), 7.44 (d, J=8.9, 1H), 7.27 (dt, J=8.8, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.14 - 7.10 (m, 1H), 6.81 (d, J=1.7, 1H), 6.69 (s, 1H), 4.58 - 4.46 (m, 2H), 4.40 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 4.15 - 4.03 (m, 2H), 3.91 - 3.86 (m, 2H), 2.65 - 2.58 (m, 1H), 2.39 - 2.31 (m, 2H), 2.18 - 2.10 (m, 1H). 2.06 [485.1]
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20	"B115"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(4-sulfamoyl-phenyl)pyrrolidine-3-carboxamide	8.75 (t, J = 6.4 Hz, 1H), 7.93 - 7.87 (m, 2H), 7.86 - 7.81 (m, 2H), 7.30 (d, J = 11.8 Hz, 2H), 7.27 (dt, J = 8.8, 2.2 Hz, 1H), 7.21 (s, 1H), 7.10 (d, J = 9.7 Hz, 1H), 6.83 (s, 1H), 4.39 (dd, J = 15.8, 6.7 Hz, 1H), 4.26 (dd, J = 15.7, 6.0 Hz, 1H), 3.96 - 3.85 (m, 2H), 2.61 (ddd, J = 11.8, 6.9, 4.7 Hz, 1H), 2.16 (dt, J = 13.0, 7.6 Hz, 1H). 1.95 [442.0]
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35	"B116"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-[2-(1-cyano-1H-imidazol-2-yl)-2-oxo-1,3-dihydroisoxazol-5-yl]-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	1.91 [392.0]

		1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		
5	"B117"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		1.91 [392.0]
15	"B118"	 N-(3-Chloro-5-fluorobenzyl)-1-(4-acetylsulfamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.76 (t, $J = 6.3$ Hz, 1H), 7.89 (s, 4H), 7.27 (dt, $J = 8.8, 2.1$ Hz, 1H), 7.20 (s, 1H), 7.10 (d, $J = 9.6$ Hz, 1H), 6.90 (s, 1H), 4.38 (dd, $J = 15.6, 6.7$ Hz, 1H), 4.26 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.97 – 3.84 (m, 2H), 2.60 (ddd, $J = 11.9, 7.3, 4.4$ Hz, 1H), 2.18 (dt, $J = 12.9, 7.7$ Hz, 1H), 1.86 (d, $J = 8.5$ Hz, 3H).	2.01 [484.0]
25	"B119"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(1-carbamoylmethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.67 (t, $J = 6.4$ Hz, 1H), 3.04 (s, 1H), 7.67 (s, 1H), 7.42 (s, 1H), 7.26 (dt, $J = 8.7, 2.0$ Hz, 1H), 7.21 (s, 2H), 7.10 (d, $J = 9.5$ Hz, 1H), 6.68 (s, 1H), 4.75 (s, 2H), 4.38 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.25 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.77 – 3.64 (m, 2H), 2.67 – 2.57 (m, 1H), 2.15 (ddd, $J = 13.1, 8.5, 6.7$ Hz, 1H).	1.72 [410.1]

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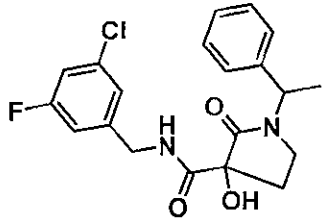
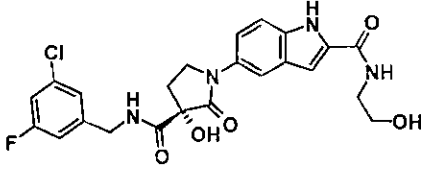
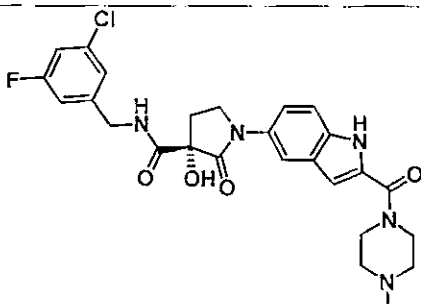
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"B120"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-phenylethyl)pyrrolidine-3-carboxamide	8.62 (t, $J = 6.2$ Hz, 1H), 7.39 – 7.24 (m, 6H), 7.20 (s, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.54 (d, $J = 15.9$ Hz, 1H), 5.29 – 5.14 (m, 1H), 4.36 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.23 (dd, $J = 15.8, 5.9$ Hz, 1H), 3.36 (dd, $J = 12.8, 4.0$ Hz, 1H), 2.99 (dd, $J = 16.0, 7.7$ Hz, 1H), 2.46 – 2.35 (m, 1H), 1.92 (ddd, $J = 28.5, 14.1, 7.4$ Hz, 1H), 1.47 (dd, $J = 19.9, 7.1$ Hz, 3H).	
"B121"	 N-(2-hydroxyethyl)-5-[(S)-3-(3-chloro-5-fluorobenzyl)-carbamoyl]-3-hydroxy-2-oxo-pyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.59 (s, 1H), 8.67 (t, $J = 6.4$ Hz, 1H), 8.45 (t, $J = 5.7$ Hz, 1H), 7.78 (d, $J = 1.9$ Hz, 1H), 7.52 (dd, $J = 8.9, 2.1$ Hz, 1H), 7.42 (d, $J = 8.9$ Hz, 1H), 7.26 (dt, $J = 8.7, 2.1$ Hz, 1H), 7.22 (s, 1H), 7.12 (dd, $J = 5.2, 3.6$ Hz, 2H), 6.68 (s, 1H), 4.74 (s, 1H), 4.41 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.93 – 3.84 (m, 2H), 3.53 (d, $J = 3.8$ Hz, 2H), 3.36 (q, $J = 6.1$ Hz, 2H), 2.67 – 2.56 (m, 1H), 2.14 (dt, $J = 12.9, 7.5$ Hz, 1H).	1.88 [489.1]
"B122"	 N-(2-hydroxyethyl)-5-[(S)-3-(3-chloro-5-fluorobenzyl)-carbamoyl]-3-hydroxy-2-oxo-pyrrolidin-1-yl]-1H-indole-2-carboxamide	** 11.59 (s, 1H), 8.67 (t, $J = 6.4$ Hz, 1H), 8.13 (s, 1H), 7.78 (d, $J = 1.9$ Hz, 1H), 7.54 (dd, $J = 8.9, 2.1$ Hz, 1H), 7.42 (d, $J = 8.9$ Hz, 1H), 7.29 – 7.23 (m, 1H), 7.22 (s, 1H), 7.12 (d, $J = 9.6$ Hz, 1H), 6.79 (d, $J = 1.6$	1.64 [528.2]

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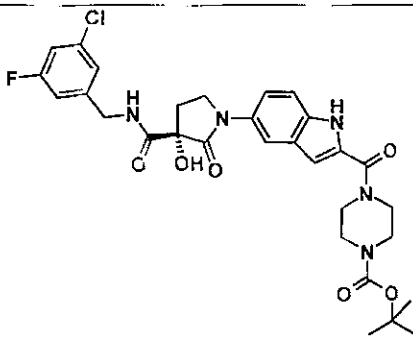
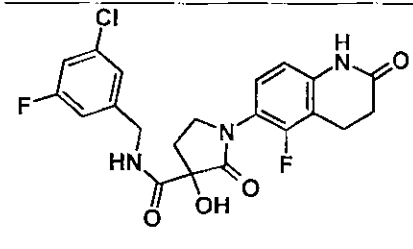
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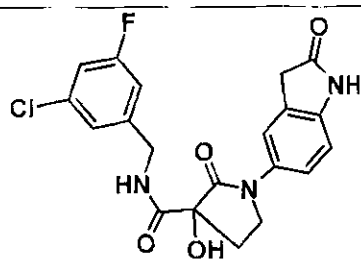
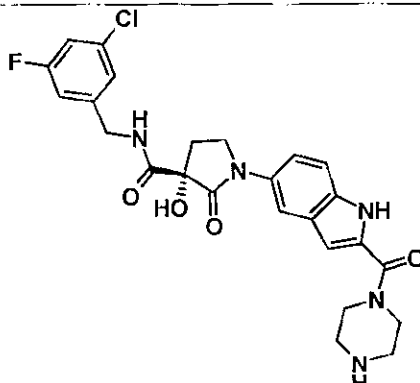
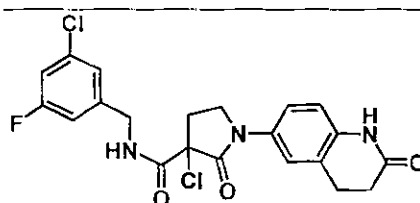
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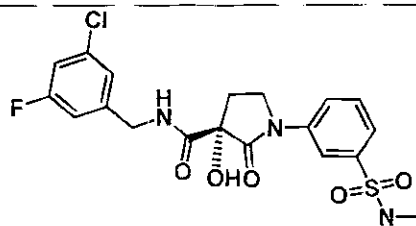
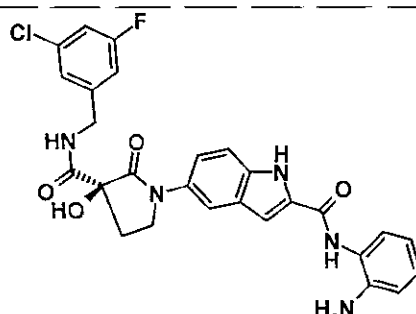
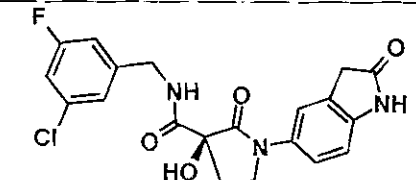
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	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(4-methylpiperazin-1-carbonyl)-1H-indol-5-yl]-2-oxopyrrolidine-3-carboxamide	Hz, 1H), 4.40 (dd, $J = 15.7, 6.8$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.88 (dt, $J = 9.3, 5.7$ Hz, 2H), 2.62 (dt, $J = 12.0, 5.7$ Hz, 1H), 2.44 – 2.35 (m, 4H), 2.23 (s, 3H), 2.19 – 2.08 (m, 1H).	
"B123"	 tert-Butyl 4-{5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indol-2-carbonyl}-piperazine-1-carboxylate	** 11.63 - 11.59 (m, 1H), 8.67 (t, $J=6.4$, 1H), 7.80 (d, $J=2.0$, 1H), 7.55 (dd, $J=8.9, 2.1$, 1H), 7.43 (d, $J=8.9$, 1H), 7.26 (dt, $J=8.7, 2.2$, 1H), 7.23 - 7.21 (m, 1H), 7.14 - 7.10 (m, 1H), 6.85 - 6.82 (m, 1H), 6.68 (s, 1H), 4.40 (dd, $J=15.7, 6.8$, 1H), 4.27 (dd, $J=15.8, 6.0$, 1H), 3.92 - 3.86 (m, 2H), 3.74 (s, 4H), 3.47 - 3.40 (m, 4H), 2.65 - 2.58 (m, 1H), 2.18 - 2.11 (m, 1H), 1.43 (s, 9H).	2.34 [558.0 + 514.9]
"B124"	 N-(3-Chloro-5-fluorobenzyl)-1-(5-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	10.34 (s, 1H), 8.69 (t, $J = 6.3$ Hz, 1H), 7.27 (dt, $J = 8.8, 2.2$ Hz, 1H), 7.20 (s, 1H), 7.15 (t, $J = 8.3$ Hz, 1H), 7.10 (d, $J = 9.7$ Hz, 1H), 6.74 (s, 1H), 6.71 (d, $J = 8.5$ Hz, 1H), 4.39 (dd, $J = 15.9, 6.6$ Hz, 1H), 4.24 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.69 (dd, $J = 12.1, 5.5$ Hz, 2H), 2.89 (t, $J = 7.6$ Hz, 2H), 2.60 (ddd, $J = 11.7, 7.1, 4.4$ Hz, 1H), 2.46 (s, 1H), 2.15 (dt, $J = 12.9, 7.5$ Hz, 1H).	

5	"B125"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-indol-5-yl)-pyrrolidine-3-carboxamide	1.87 [418.0]	
10	"B126"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-[2-(piperazin-1-carbonyl)-1H-indol-5-yl]-pyrrolidine-3-carboxamide	** 11.61 (s, 1H), 8.69 (t, $J = 6.4$ Hz, 1H), 8.20 (s, 1H), 7.80 (d, $J = 1.8$ Hz, 1H), 7.55 (dd, $J = 8.9, 2.0$ Hz, 1H), 7.44 (d, $J = 8.9$ Hz, 1H), 7.28 (dt, $J = 8.7, 2.0$ Hz, 1H), 7.24 (s, 1H), 7.13 (d, $J = 9.6$ Hz, 1H), 6.81 (d, $J = 1.5$ Hz, 1H), 4.42 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.28 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.96 – 3.84 (m, 2H), 3.70 (m, 4H), 2.85 (m, 4H), 2.63 (dt, $J = 12.3, 5.7$ Hz, 1H), 2.16 (dt, $J = 12.9, 7.6$ Hz, 1H).	1.64 [514.2]
15	"B127"	 N-(3-Chloro-5-fluorobenzyl)-3-chloro-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide		
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5	"B128"	 N-(3-Chloro-5-fluorobenzyl)-(S)- 1-(3-dimethylsulfamoylphenyl)- 3-hydroxy-2-oxopyrrolidine-3- carboxamide	2.20 [470.0]	
10	"B129"	 N-(2-Aminophenyl)-5-[(S)-3-(3- chloro-5-fluorobenzyl)- carbamoyl]-3-hydroxy-2-oxo- pyrrolidin-1-yl]-1H-indole-2- carboxamide	** 11.72 (s, 1H), 9.69 (s, 1H), 8.68 (t, J=6.4, 1H), 7.84 (d, J=2.0, 1H), 7.58 (dd, J=8.9, 2.1, 1H), 7.46 (d, J=8.9, 1H), 7.38 - 7.33 (m, 1H), 7.27 (dt, J=8.7, 2.2, 1H), 7.24 - 7.22 (m, 1H), 7.22 - 7.18 (m, 1H), 7.15 - 7.10 (m, 1H), 7.01 - 5.96 (m, 1H), 6.80 (dd, J=8.1, 1.4, 1H), 6.69 (s, 1H), 6.62 (td, J=7.5, 1.4, 1H), 4.93 (s, 2H), 4.41 (dd, J=15.7, 6.8, 1H), 4.27 (dd, J=15.8, 6.0, 1H), 3.94 - 3.89 (m, 2H), 2.62 (dt, J=12.8, 5.8, 1H), 2.15 (dt, J=12.8, 7.5, 1H).	2.06 [536.1]
30	"B130"	 N-(3-Chloro-5-fluorobenzyl)-(S)- 3-hydroxy-2-oxo-1-(2-oxo-2,3- dihydro-1H-indol-5-yl)- pyrrolidine-3-carboxamide		
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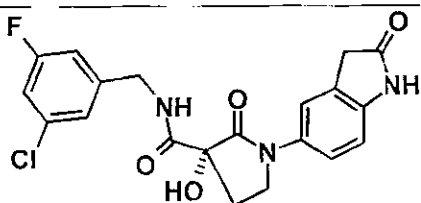
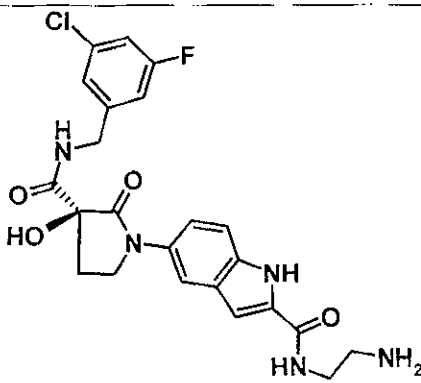
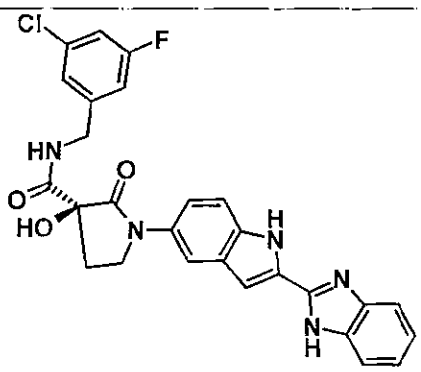
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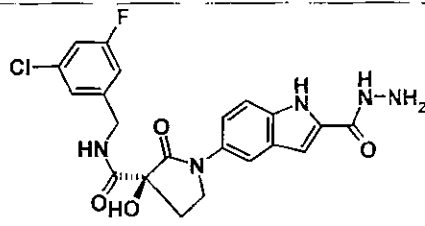
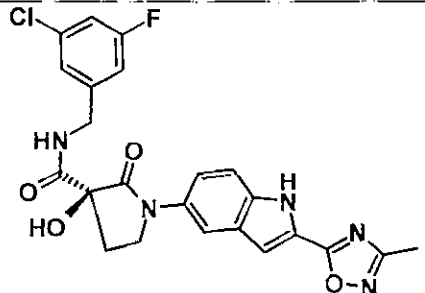
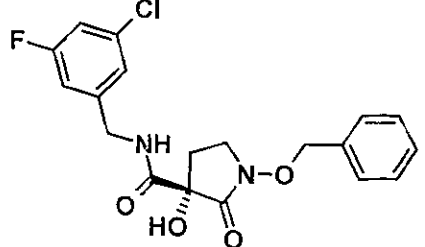
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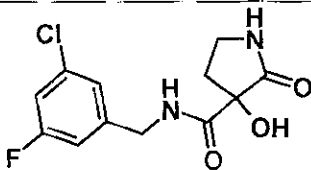
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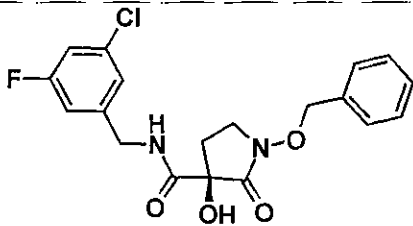
"B131"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-indol-5-yl)-pyrrolidine-3-carboxamide		
"B132"	 N-(2-Aminoethyl)-5-[(S)-3-(3-chloro-5-fluorobenzyl-carbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-1H-indole-2-carboxamide	11.71 (s, 1H), 8.82 (t, J=5.6, 1H), 8.70 (t, J=6.4, 1H), 8.30 (s, 2H), 7.80 (d, J=2.0, 1H), 7.54 (dd, J=8.9, 2.1, 1H), 7.44 (d, J=8.9, 1H), 7.27 (dt, J=8.8, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.15 - 7.09 (m, 2H), 4.41 (dd, J=15.8, 6.8, 1H), 4.26 (dd, J=15.8, 6.0, 1H), 3.94 - 3.85 (m, 2H), 3.47 (q, J=6.1, 2H), 2.93 (t, J=6.3, 2H), 2.61 (dt, J=12.8, 5.7, 1H), 2.14 (dt, J=12.9, 7.5, 1H).	1.59 [4.88.1]
"B133"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-[2-(1H-benzimidazol-2-yl)-1H-indol-5-yl]-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	** 12.95 (s, 1H), 12.01 (s, 1H), 8.69 (t, J=6.4, 1H), 7.82 (d, J=2.0, 1H), 7.71 - 7.54 (m, 2H), 7.53 (dd, J=8.8, 2.1, 1H), 7.46 (d, J=8.8, 1H), 7.27 (dt, J=8.8, 2.2, 1H), 7.25 - 7.19 (m, 4H), 7.16 - 7.11 (m, 1H), 6.87 - 6.52 (m, 1H), 4.42 (dd, J=15.8, 6.8, 1H), 4.28 (dd, J=15.8, 6.0, 1H), 3.94 - 3.89 (m, 2H), 2.67 - 2.60 (m, 1H), 2.16 (dt, J=12.8, 7.6, 1H).	1.97 [518.1]

5	"B134"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-hydrazinocarbonyl-1H-indol-5-yl)-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide	** 11.62 (s, 1H), 9.77 (s, 1H), 8.67 (t, J=6.4, 1H), 7.76 (d, J=2.0, 1H), 7.54 (dd, J=8.9, 2.1, 1H), 7.42 (d, J=8.9, 1H), 7.26 (dt, J=8.7, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.14 - 7.10 (m, 1H), 7.10 - 7.07 (m, 1H), 6.67 (s, 1H), 4.51 (s, 2H), 4.40 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.92 - 3.86 (m, 2H), 2.65 - 2.57 (m, 1H), 2.14 (dt, J=12.8, 7.6, 1H).	1.82 [460.1]
15	"B135"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-indol-5-yl]-2-oxopyrrolidine-3-carboxamide	** 12.34 (s, 1H), 8.69 (t, J=6.4, 1H), 7.88 (d, J=2.0, 1H), 7.70 (dd, J=9.0, 2.1, 1H), 7.50 (d, J=9.0, 1H), 7.38 (s, 1H), 7.26 (dt, J=8.8, 2.2, 1H), 7.24 - 7.21 (m, 1H), 7.14 - 7.10 (m, 1H), 6.72 (s, 1H), 4.40 (dd, J=15.7, 6.7, 1H), 4.27 (dd, J=15.7, 6.0, 1H), 3.94 - 3.88 (m, 2H), 2.62 (dt, J=12.8, 5.8, 1H), 2.44 (s, 3H), 2.16 (dt, J=12.7, 7.5, 1H).	2.21 [484.1]
30	"B136"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyloxy-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide		
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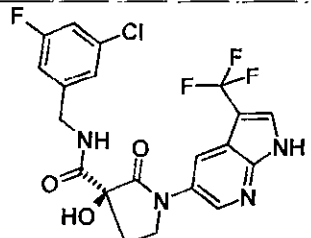
"B137"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	8.56 (t, J=6.4, 1H), 8.00 (s, 1H), 7.26 (m, 2H), 7.20 (s, 1H), 7.09 (m, 1H), 6.39 (s, 1H), 4.36 (dd, J=15.7, 6.7, 1H), 4.21 (dd, J=15.7, 6.0, 1H), 3.21 (m, 2H), 2.47 (m, 1H), 1.98 (m, 1H).	2.77 [287.0]
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"B138"	 N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyloxy-3-hydroxy-2-oxopyrrolidine-3-carboxamide		
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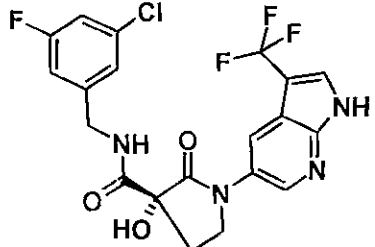
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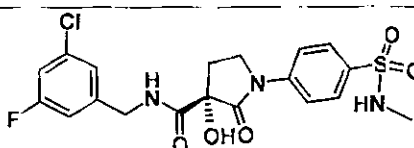
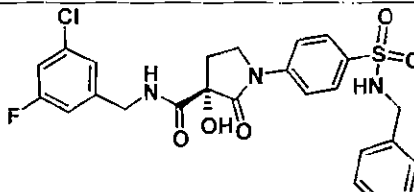
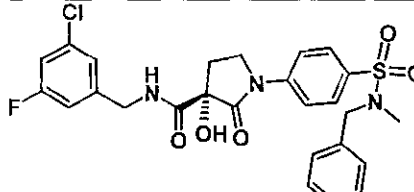
"B139"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide		
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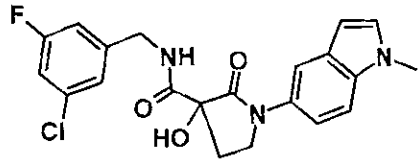
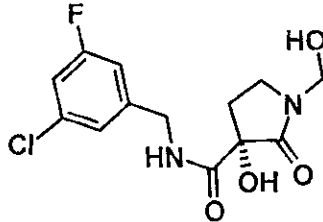
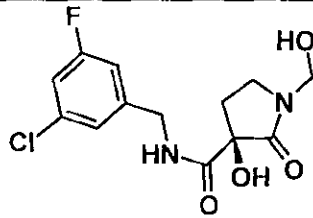
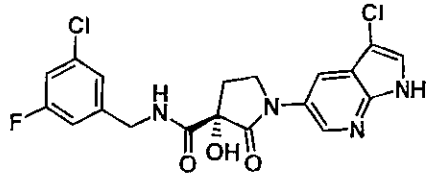
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"B140"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-		
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		carboxamide			
5	"B141"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(4-methylsulfamoylphenyl)-2-oxopyrrolidine-3-carboxamide	2.06 [456.0]		
10	"B142"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(4-benzylsulfamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.76 (t, $J = 6.4$ Hz, 1H), 8.09 (t, $J = 6.3$ Hz, 1H), 7.97 – 7.89 (m, 2H), 7.89 – 7.80 (m, 2H), 7.32 – 7.21 (m, 7H), 7.15 – 7.08 (m, 1H), 6.85 (s, 1H), 4.40 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 3.97 (d, $J = 6.3$ Hz, 2H), 3.95 – 3.90 (m, 2H), 2.63 (ddd, $J =$ 12.7, 6.9, 4.7 Hz, 1H), 2.18 (dt, $J = 13.0, 7.7$ Hz, 1H).	2.86 [532.1]	
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25	"B143"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-[4-(benzylmethylsulfamoyl)phenyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide	** 8.78 (t, $J = 6.4$ Hz, 1H), 8.04 – 7.99 (m, 2H), 7.92 – 7.88 (m, 2H), 7.42 – 7.35 (m, 2H), 7.32 (dd, $J = 7.4, 3.9$ Hz, 3H), 7.29 (ddd, $J = 8.8, 3.6,$ 2.0 Hz, 1H), 7.22 (s, 1H), 7.14 – 7.10 (m, 1H), 6.87 (s, 1H), 4.41 (dd, $J = 15.7, 6.7$ Hz, 1H), 4.27 (dd, $J = 15.7, 6.0$ Hz, 1H), 4.12 (s, 2H), 4.00 – 3.91 (m, 2H), 2.68 – 2.59 (m, 1H), 2.53 (d, $J = 5.8$ Hz, 3H), 2.20 (dt, J $= 13.0, 7.8$ Hz, 1H).	2.63 [546.2]	
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5	"B144"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide	2.24 [416.1]
10	"B145"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-hydroxymethyl-2-oxopyrrolidine-3-carboxamide	8.63 – 8.54 (m, 1H), 7.26 (dt, J = 8.7, 2.2 Hz, 1H), 7.21 (s, 1H), 7.17 – 7.05 (m, 1H), 6.49 (s, 1H), 5.96 (t, J = 7.1 Hz, 1H), 4.62 (qd, J = 10.2, 7.0 Hz, 2H), 4.37 (dd, J = 15.7, 6.7 Hz, 1H), 4.23 (dd, J = 15.8, 5.9 Hz, 1H), 3.50 – 3.36 (m, 2H), 2.56 – 2.39 (m, 2H), 2.06 – 1.88 (m, 1H).
20	"B146"	 N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-hydroxymethyl-2-oxopyrrolidine-3-carboxamide	8.66 – 8.48 (m, 1H), 7.25 (dt, J = 8.7, 2.0 Hz, 1H), 7.21 (s, 1H), 7.10 (d, J = 9.2 Hz, 1H), 6.49 (s, 1H), 5.96 (t, J = 7.0 Hz, 1H), 4.62 (qd, J = 10.2, 7.1 Hz, 2H), 4.37 (dd, J = 15.7, 6.7 Hz, 1H), 4.23 (dd, J = 15.7, 6.0 Hz, 1H), 3.50 – 3.36 (m, 2H), 2.48 (ddd, J = 12.8, 5.8, 3.4 Hz, 2H), 2.06 – 1.86 (m, 1H).
30	"B147"	 N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxopyrrolidine-3-carboxamide	2.131 [437.0 + 439.0]

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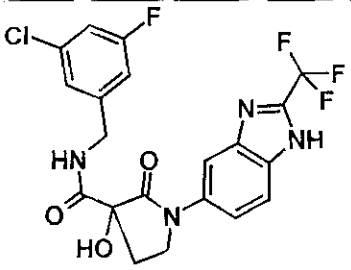
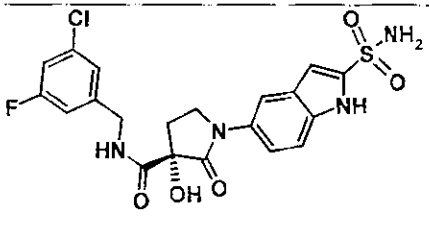
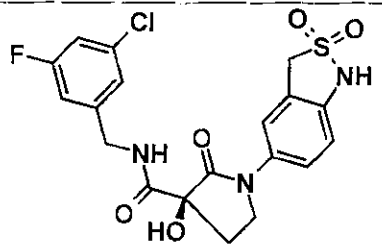
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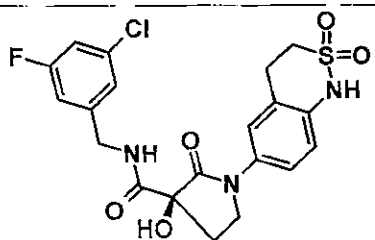
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	pyridin-5-yl)-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide		
"B148"	 N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-benzimidazol-5-yl)pyrrolidine-3-carboxamide	2.093 [471.1]	
"B149"	 N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-sulfamoyl-1H-indol-5-yl)pyrrolidine-3-carboxamide		
"B150"	 (3S)-N-[(3-Chloro-5-fluorophenyl)methyl]-1-(2,2-dioxo-1,3-dihydro-2,1-benzothiazol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide		

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"B151"

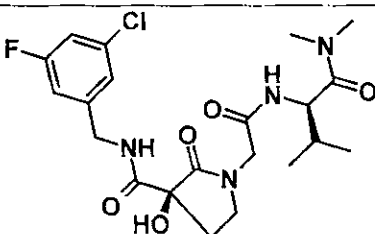


N-(3-Chloro-5-fluorobenzyl)-(S)-
1-(2,2-dioxo-1,2,3,4-tetrahydro-
2λ6-benzo[c]thiazin-6-yl)-
3-hydroxy-2-oxo-1-(2-sulfamoyl-
1H-indol-5-yl)pyrrolidine-3-
carboxamide

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"B152"



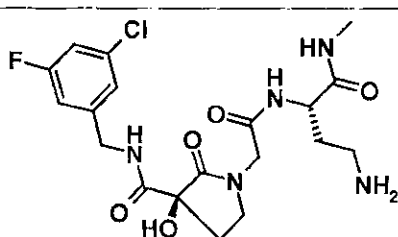
N-(3-Chloro-5-fluorobenzyl)-(S)-
1-(((R)-1-dimethylcarbamoyl-2-
methylpropylcarbamoyl)methyl)-
3-hydroxy-2-oxo-1-(2-sulfamoyl-
1H-indol-5-yl)pyrrolidine-3-
carboxamide

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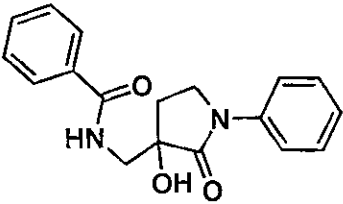
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"B153"



N-(3-Chloro-5-fluorobenzyl)-(S)-
1-(((S)-3-amino-1-
methylcarbamoyl-
propylcarbamoyl)methyl)-3-
hydroxy-2-oxo-1-(2-sulfamoyl-
1H-indol-5-yl)pyrrolidine-3-
carboxamide

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"B154"	 N-(3-Hydroxy-2-oxo-1-phenylpyrrolidin-3-yl)benzamide		
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Table 1

Inhibition of MetAP-2

IC₅₀ of compounds of the formula I according to the invention

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Compound No.	IC ₅₀ enzyme	Compound No.	IC ₅₀ enzyme
"A56"	C		
"A57"	C		
"A58"	C		
"A59"	C		
"A60"	C		

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"A61"	C	"A71"	C
"A62"	C	"A72"	A
"A63"	C	"A73"	A
"A64"	C	"A74"	C
"A65"	A	"A75"	A
"A66"	B	"A76"	A
"A67"	C	"A77"	A
"A68"	A	"A78"	A
"A69"	A	"A79"	A
"A70"	C	"A80"	A

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"A81"	A	"A91"	C
"A82"	B	"A92"	B
"A83"	C	"A93"	B
"A84"	B	"A94"	A
"A85"	C	"A95"	A
"A86"	C	"A96"	A
"A87"	A	"A97"	A
"A88"	A	"A98"	C
"A89"	C	"A99"	A
"A90"	A	"A100"	A
"A101"	C	"A111"	C
"A102"	B	"A112"	A
"A103"	B	"A113"	C
"A104"	C	"A114"	A
"A105"	C	"A115"	A
"A106"	C	"A116"	A
"A107"	B	"A117"	A
"A108"	C	"A118"	A
"A109"	C	"A119"	B
"A110"	C	"A120"	C
"A121"	B	"A131"	C
"A122"	B	"A132"	B
"A123"	B	"A133"	A
"A124"	B	"A134"	A
"A125"	B	"A135"	A
"A126"	B	"A136"	A
"A127"	B	"A137"	A

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"A128"	B	"A138"	A
"A129"	B	"A139"	A
"A130"	B	"A140"	A
"A141"	C	"A151"	A
"A142"	A	"A152"	B
"A143"	A	"A153"	A
"A144"	A	"A154"	C
"A145"	B	"A155"	A
"A146"	A	"A156"	C
"A147"	A	"A157"	B
"A148"	B	"A158"	C
"A149"	A	"A159"	B
"A150"	C	"A160"	C
"A161"	A	"A171"	A
"A162"	C	"A172"	B
"A163"	A	"A173"	A
"A164"	C	"A174"	A
"A165"	A	"A175"	A
"A166"	B	"A176"	A
"A167"	A	"A177"	A
"A168"	A	"A178"	A
"A169"	A	"A179"	A
"A170"	A	"A180"	A
"A181"	A	"A191"	A
"A182"	C	"A192"	B
"A183"	A	"A193"	A
"A184"	A	"A194"	A

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"A185"	A	"A195"	C
"A186"	A	"A196"	A
"A187"	B	"A197"	A
"A188"	A	"A198"	C
"A189"	A	"A199"	A
"A190"	B	"A200"	A
"A201"	A	"A211"	A
"A202"	B	"A212"	A
"A203"	C	"A213"	B
"A204"	B	"A214"	A
"A205"	A	"A215"	A
"A206"	A	"A216"	A
"A207"	A	"A217"	A
"A208"	B	"A218"	C
"A209"	A	"A219"	A
"A210"	A	"A220"	B
"A221"	A	"A231"	B
"A222"	A	"A232"	B
"A223"	C	"A233"	C
"A224"	B	"A234"	A
"A225"	B	"A235"	A
"A226"	B	"A236"	A
"A227"	B	"A237"	B
"A228"	B	"A238"	A
"A229"	C	"A239"	A
"A230"	B	"A240"	B
"A241"	A	"A251"	A

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"A242"	A	"A252"	B
"A243"		"A253"	B
"A244"	A	"A254"	A
"A245"	A	"A255"	B
"A246"	A	"A256"	A
"A247"	A	"A257"	B
"A248"	B	"A258"	C
"A249"	A	"A259"	C
"A250"	A	"A260"	C
"A261"	C	"A271"	C
"A262"	C	"A272"	B
"A263"	C	"A273"	B
"A264"	A	"A274"	B
"A265"	B	"A275"	C
"A266"	A	"A276"	B
"A267"	B	"A277"	A
"A268"	C	"A278"	A
"A269"	B	"A279"	B
"A270"	A	"A280"	B
"A281"	B	"A291"	B
"A282"	B	"A292"	B
"A283"	A	"A293"	A
"A284"	A	"A294"	
"A285"	A	"A295"	
"A286"	A	"A296"	
"A287"		"A297"	
"A288"	C	"A298"	
"A289"	A	"A299"	

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"A290"	B	"A300"	B
"B1"	A	"B11"	A
"B2"	A	"B12"	B
"B3"	A	"B13"	B
"B4"	A	"B14"	A
"B5"	A	"B15"	A
"B6"	A	"B16"	B
"B7"	A	"B17"	A
"B8"	A	"B18"	A
"B9"	A	"B19"	C
"B10"	A	"B20"	C
"B21"	C	"B31"	A
"B22"	A	"B32"	A
"B23"	B	"B33"	A
"B24"	A	"B34"	A
"B25"	A	"B35"	A
"B26"	A	"B36"	B
"B27"	A	"B37"	A
"B28"	A	"B38"	B
"B29"	A	"B39"	A
"B30"	C	"B40"	A
"B41"	B	"B51"	C
"B42"	B	"B52"	A
"B43"	A	"B53"	C
"B44"	C	"B54"	A
"B45"	B	"B55"	B
"B46"	A	"B56"	A
"B47"	B	"B57"	C
"B48"	B	"B58"	B
"B49"	A	"B59"	A

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"B50"	C	"B60"	A
"B61"	B	"B71"	A
"B62"	A	"B72"	A
"B63"	A	"B73"	C
"B64"	C	"B74"	A
"B65"	A	"B75"	A
"B66"	A	"B76"	A
"B67"	B	"B77"	A
"B68"	B	"B78"	A
"B69"	A	"B79"	B
"B70"	A	"B80"	A
"B81"	C	"B91"	B
"B82"	A	"B92"	A
"B83"	A	"B93"	B
"B84"	A	"B94"	A
"B85"	C	"B95"	A
"B86"	A	"B96"	A
"B87"	A	"B97"	A
"B88"	C	"B98"	A
"B89"	C	"B99"	A
"B90"	C	"B100"	C
"B101"	A	"B111"	B
"B102"	C	"B112"	A
"B103"	C	"B113"	A
"B104"	A	"B114"	A
"B105"	A	"B115"	A
"B106"	B	"B116"	A
"B107"	A	"B117"	C
"B108"	A	"B118"	A
"B109"	A	"B119"	A

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"B110"	A	"B120"	A
"B121"	A	"B131"	C
"B122"	A	"B132"	A
"B123"	A	"B133"	A
"B124"	A	"B134"	A
"B125"	A	"B135"	A
"B126"	A	"B136"	A
"B127"		"B137"	
"B128"		"B138"	C
"B129"	A	"B139"	A
"B130"	A	"B140"	C
"B141"	A		

IC₅₀: 10 nM - 1 μ M = A

1 μ M - 10 μ M = B

> 10 μ M = C

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The following examples relate to medicaments:

Example A: Injection vials

A solution of 100 g of an active compound 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 compound.

Example B: Suppositories

A mixture of 20 g of an active compound 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 compound.

Example C: Solution

A solution is prepared from 1 g of an active compound of the formula I, 9.38 g of $\text{NaH}_2\text{PO}_4 \cdot 2 \text{H}_2\text{O}$, 28.48 g of $\text{Na}_2\text{HPO}_4 \cdot 12 \text{H}_2\text{O}$ 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 compound 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 compound 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 compound.

Example F: Dragees

5 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

10 2 kg of active compound 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 compound.

Example H: Ampoules

15 A solution of 1 kg of active compound 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
20 compound.

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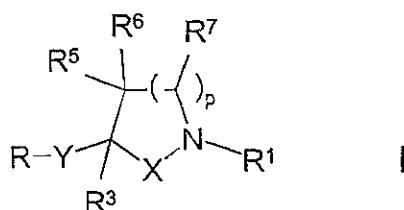
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Patent Claims

1. Compounds of the formula I

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in which

R denotes NR^2R^4 , Alk, $\text{C}(=\text{CH}_2)[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, Het^2 , $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$ or OA ,

X denotes CO or CH_2 ,

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Y denotes CO or CH_2 ,

R^1 denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $(\text{CH}_2)_n\text{Het}$, $(\text{CH}_2)_n\text{Cyc}$, $[\text{C}(\text{R}^4)_2]_n\text{COOH}$, $[\text{C}(\text{R}^4)_2]_n\text{CONHAr}^1$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}_2$, $[\text{C}(\text{R}^4)_2]_n\text{NHA}$, $[\text{C}(\text{R}^4)_2]_n\text{NA}_2$, $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{OR}^7$, $[\text{C}(\text{R}^4)_2]_n\text{COO}(\text{CH}_2)_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{COOA}$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}[\text{C}(\text{R}^4)_2]_p\text{CON}(\text{R}^4)_2$ or $[\text{C}(\text{R}^4)_2]_n\text{CONHCR}^4$ -
 $[(\text{CH}_2)_n\text{N}(\text{R}^4)_2]\text{CON}(\text{R}^4)_2$,

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R^2 denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, $(\text{CH}_2)_n\text{COHet}^1$, $(\text{CH}_2)_n\text{COAr}^2$, $(\text{CH}_2)_m\text{NA}_2$ or $(\text{CH}_2)_n\text{Het}$,

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R^3 denotes OH or OCoA ,

R^4 denotes H or alkyl having 1, 2, 3 or 4 C atoms,

R^2 and R^4 together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by $\text{N}(\text{CH}_2)_m\text{OH}$ or SO_2 ,

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R^5 , R^6 each, independently of one another, denote H, F or A,

R^5 and R^6 together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by NCoA or O ,

R^7 denotes H or A,

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Ar^1 denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, OH, OA, CONH_2 ,

		CONHA, CONA ₂ , NHSO ₂ A, CONHCyc, NHSO ₂ Cyc, CONHA ² , COHet ¹ and/or NASO ₂ A,
5	Ar ²	denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, CONH ₂ , and/or OAr ³ ,
	Ar ³	denotes phenyl which is unsubstituted or monosubstituted by NH ₂ ,
10	Het	denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, and/or O and/or S atoms which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OA, CN, NH ₂ , NHA, NA ₂ , NO ₂ , CN, COOH, COOA, (CH ₂) _n CONH ₂ , (CH ₂) _n CONHA, (CH ₂) _n CONA ₂ , NHCOA, COA, CHO, Het ¹ , SO ₂ A, SO ₂ NH ₂ , SO ₂ NHA, SO ₂ NA ₂ , CONHNH ₂ , CONHAr ³ , =O and/or Ar ³ ,
15	Het ¹	denotes a monocyclic saturated heterocycle having 1 to 4 N, and/or O and/or S atoms which is unsubstituted or mono-, di- or trisubstituted by =O and/or COOA,
20	Het ²	denotes isoindolyl,
	A	denotes unbranched or branched alkyl having 1-10 C atoms, in which 1-7 H atoms may be replaced by F, Cl, Br, OH, CHO, COA, COOA, CN, CONA ₂ , CONHA and/or CONH ₂ ,
25		and/or in which one or two non-adjacent CH and/or CH ₂ groups may be replaced by O, or Cyc,
	Alk	denotes alkenyl having 2, 3, 4, 5 or 6 C atoms
30	Cyc	denotes cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by NHCOA, NHSO ₂ , OH, OA, A, NH ₂ , NHA, NA ₂ , COOA, COOH and/or CONHA,
	Hal	denotes F, Cl, Br or I,
35	m	denotes 1, 2, 3 or 4,
	n	denotes 0, 1, 2, 3 or 4,
	p	denotes 1, 2 or 3,

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

with the proviso that the following compounds are excluded:

methyl-3-hydroxypiperidin-3-carboxylate,

1-tert.-butyl-3-methyl-3-hydroxypiperidin-1,3-dicarboxylate,

tert.-butyl-3-allyl-3-hydroxypyrrolidin-1-carboxylate,

tert.-butyl-3-allyl-3-hydroxypiperidin-1-carboxylate.

2. Compounds according to Claim 1 in which

Het denotes pyrazinyl, pyrazolyl, benzimidazolyl, pyridyl, indolyl,
dihydroindolyl, benzofuranyl, tetrahydropyranyl, dihydro-
quinolinyl, dihydroisoquinolinyl, tetrahydroquinolinyl, tetra-
hydroisoquinolinyl, indazolyl, imidazolyl, pyrrolyl, oxazolyl,
oxadiazolyl, isoxazolyl, benzothiazolyl, piperidin-1-yl,
pyrrolidin-1-yl, 3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl,
3,4-dihydro-2H-benzo-1,4-oxazinyl, benzofuranyl, azetid-
inyl, 3-azabicyclo[3.2.0]hexyl, pyrrolo[2,3-b]pyridinyl, tetra-
hydrofuranyl, tetrahydro-1,8-naphthyridinyl, 2,3-dihydro-
benzoisothiazolyl, 1,2,3,4-tetrahydrobenzothiazinyl or
hexahydrobenzo-1,3-dioxolyl, each of which is unsubsti-
tuted or mono-, di- or trisubstituted by Hal, A, OA, CN, NH₂,
NHA, NA₂, NO₂, CN, COOH, COOA, (CH₂)_nCONH₂, (CH₂)_n-
CONHA, (CH₂)_nCONA₂, NHCOA, COA, CHO, Het¹, SO₂A,
SO₂NH₂, SO₂NHA, SO₂NA₂, CONHNH₂, CONHAr³, =O
and/or Ar³,

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

3. Compounds according to Claim 1 or 2 in which

Het¹ denotes pyridazinyl, pyrazolyl, pyridyl, piperazinyl, morpho-
linyl, pyrimidinyl, furyl, thienyl, imidazolyl, pyrrolyl, oxazolyl,
oxadiazolyl, isoxazolyl, thiazolyl, triazolyl, tetrazolyl, thia-

diazole, piperidin-1-yl, pyrrolidin-1-yl, tetrahydropyranyl, 1,2-oxazinan-2-yl, 1,2,5-oxadiazinan-2-yl, 1,3-oxazinan-3-yl or hexahydropyrimidinyl, each of which is unsubstituted or mono-, di- or trisubstituted by A and/or OA,
 5 and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to Claim 1 in which
- 10 R denotes NR^2R^4 , Alk, $\text{C}(\text{=CH}_2)[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, Het^2 , $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$ or OA,
- X denotes CO or CH_2 ,
- Y denotes CO or CH_2 ,
- 15 R^1 denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $(\text{CH}_2)_n\text{Het}$, $(\text{CH}_2)_n\text{Cyc}$, $[\text{C}(\text{R}^4)_2]_n\text{COOH}$, $[\text{C}(\text{R}^4)_2]_n\text{CONHAr}^1$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}_2$, $[\text{C}(\text{R}^4)_2]_n\text{NHA}$, $[\text{C}(\text{R}^4)_2]_n\text{NA}_2$, $\text{O}[\text{C}(\text{R}^4)_2]_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{OR}^7$, $[\text{C}(\text{R}^4)_2]_n\text{COO}(\text{CH}_2)_n\text{Ar}^1$, $[\text{C}(\text{R}^4)_2]_n\text{COOA}$, $[\text{C}(\text{R}^4)_2]_n\text{CONH}[\text{C}(\text{R}^4)_2]_p\text{CON}(\text{R}^4)_2$ or $[\text{C}(\text{R}^4)_2]_n\text{CONHCR}^4[(\text{CH}_2)_n\text{N}(\text{R}^4)_2]\text{CON}(\text{R}^4)_2$,
- 20 R^2 denotes H, $[\text{C}(\text{R}^4)_2]_n\text{Ar}^2$, $(\text{CH}_2)_n\text{COHet}^1$, $(\text{CH}_2)_n\text{COAr}^2$, $(\text{CH}_2)_m\text{NA}_2$ or $(\text{CH}_2)_n\text{Het}$,
- R^3 denotes OH or OCOA,
- R^4 denotes H or alkyl having 1, 2, 3 or 4 C atoms,
- 25 R^2 and R^4 together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by $\text{N}(\text{CH}_2)_m\text{OH}$ or SO_2 ,
- R^5 , R^6 each, independently of one another, denote H, F or A,
- 30 R^5 and R^6 together also denote alkylene having 2, 3, 4 or 5 C atoms, where a CH_2 group may also be replaced by NCOA or O,
- R^7 denotes H or A,
- Ar^1 denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, OH, OA, CONH_2 , CONHA , CONA_2 , NHSO_2A , CONHCyc , NHSO_2Cyc , CONHAr^2 , COHet^1 and/or NASO_2A ,
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	Ar ²	denotes phenyl which is unsubstituted or mono-, di-, tri-, tetra- or pentasubstituted by Hal, A, CONH ₂ , and/or OAr ³ ,
	Ar ³	denotes phenyl which is unsubstituted or monosubstituted by NH ₂ ,
5	Het	denotes pyrazinyl, pyrazolyl, benzimidazolyl, pyridyl, indolyl, dihydroindolyl, benzofuranyl, tetrahydropyranyl, dihydro-
		quinoliny, dihydroisoquinoliny, tetrahydroquinoliny, tetra-
10		hydroisoquinoliny, indazolyl, imidazolyl, pyrrolyl, oxazolyl, oxadiazolyl, isoxazolyl, benzothiazolyl, piperidin-1-yl,
		pyrrolidin-1-yl, 3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl, 3,4-dihydro-2H-benzo-1,4-oxazinyl, benzofuranyl, azetid-
15		inyl, 3-azabicyclo[3.2.0]hexyl, pyrrolo[2,3-b]pyridinyl, tetra-
		hydrofuranyl, tetrahydro-1,8-naphthyridinyl 2,3-dihydro-
		benzothiazolyl, 1,2,3,4-tetrahydrobenzothiazinyl or hexa-
20		hydrobenzo-1,3-dioxolyl, each of which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OA, CN, NH ₂ , NHA, NA ₂ , NO ₂ , CN, COOH, COOA, (CH ₂) _n CONH ₂ , (CH ₂) _n -CONHA, (CH ₂) _n CONA ₂ , NHCOA, COA, CHO, Het ¹ , SO ₂ A, SO ₂ NH ₂ , SO ₂ NHA, SO ₂ NA ₂ , CONHNH ₂ , CONHAr ³ , =O and/or Ar ³ ,
	Het ¹	denotes pyridazinyl, pyrazolyl, pyridyl, piperazinyl, morpho-
25		linyl, pyrimidinyl, furyl, thienyl, imidazolyl, pyrrolyl, oxazolyl, oxadiazolyl, isoxazolyl, thiazolyl, triazolyl, tetrazolyl, thia-
		diazole, piperidin-1-yl, pyrrolidin-1-yl, tetrahydropyranyl, 1,2-
30		oxazinan-2-yl, 1,2,5-oxadiazinan-2-yl, 1,3-oxazinan-3-yl or hexahydropyrimidinyl, each of which is unsubstituted or mono-, di- or trisubstituted by A and/or OA,
	Het ²	denotes isoindolyl,
	A	denotes unbranched or branched alkyl having 1-10 C atoms, in which 1-7 H atoms may be replaced by F, Cl, Br, OH, CHO, COA, COOA, CN, CONA ₂ , CONHA and/or CONH ₂ ,
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and/or in which one or two non-adjacent CH and/or CH₂ groups may be replaced by O, or Cyc,

- 5 Alk denotes alkenyl having 2, 3, 4, 5 or 6 C atoms
Cyc denotes cyclic alkyl having 3-7 C atoms which is unsubstituted or mono-, di- or trisubstituted by NHCOA, NHSO₂, OH, OA, A, NH₂, NHA, NA₂, COOA, COOH and/or CONHA,
10 Hal denotes F, Cl, Br or I,
m denotes 1, 2, 3 or 4,
n denotes 0, 1, 2, 3 or 4,
p denotes 1, 2 or 3,
and pharmaceutically usable salts, tautomers and stereoisomers thereof,
15 including mixtures thereof in all ratios.

5. Compounds according to Claim 1, selected from the group

20	Compound No.	Name
	"A56"	(S)-3-(1,1-Dioxo-16-thiomorpholine-4-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one
25	"A57"	(S)-3-Hydroxy-3-[4-(2-hydroxyethyl)piperazine-1-carbonyl]-1-phenylpyrrolidin-2-one
	"A58"	N-(3-Imidazol-1-ylpropyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
	"A59"	N-(2-Dimethylaminoethyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
30	"A60"	N-[2-(4-Phenoxyphenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
35	"A61"	N-(2-Dimethylaminoethyl)methyl-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide

5	"A62"	N-(2-Morpholin-4-yl-2-oxoethyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
	"A63"	N-[2-(1-Methylpyrrolidin-2-yl)ethyl]-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
	"A64"	N-(3-Dimethylaminopropyl)-(S)-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
10	"A65"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-phenylpiperidine-3-carboxamide
	"A66"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide
	"A67"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-phenylazepane-3-carboxamide
15	"A68"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1H-indol-6-yl)-2-oxopyrrolidine-3-carboxamide
20	"A69"	N-(3-Chloro-5-fluorobenzyl)-1-[3-(3-carbamoylphenylcarbamoyl)phenyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A70"	(S)-3-((E)-But-2-enoyl)-3-hydroxy-1-phenylpyrrolidin-2-one
	"A71"	N-(3-Chloro-5-fluorobenzyl)-(S)-8-acetyl-4-hydroxy-3-oxo-2-phenyl-2,8-diazaspiro[4.5]decane-4-carboxamide
25	"A72"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(morpholine-4-carbonyl)phenyl]-2-oxopyrrolidine-3-carboxamide
	"A73"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[3-(methanesulfonylmethylamino)phenyl]-2-oxopyrrolidine-3-carboxamide
30	"A74"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(morpholine-4-carbonyl)phenyl]-2-oxopyrrolidine-3-carboxamide
35	"A75"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyclopropylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

	"A76"	N-(3-Chloro-5-fluorobenzyl)-1-(3-cyclobutylcarbamoyl-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
5	"A77"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-[3-(pyrrolidine-1-carbonyl)phenyl]pyrrolidine-3-carboxamide
	"A78"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(6-propionylaminopyridin-3-yl)pyrrolidine-3-carboxamide
	"A79"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-ethanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
10	"A80"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyclopropane-sulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A81"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyl-3-hydroxy-2-oxo-piperidine-3-carboxamide
15	"A82"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclopropylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A83"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-[3-(pyrrolidine-1-carbonyl)phenyl]pyrrolidine-3-carboxamide
20	"A84"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-ethanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A85"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclopropanesulfonylamino-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
25	"A86"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyl-3-hydroxy-2-oxo-piperidine-3-carboxamide
	"A87"	N-(3-Chloro-5-fluorobenzyl)-1-(3-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A88"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(2-hydroxy-ethylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide
30	"A89"	3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-on
	"A90"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-phenethyl-pyrrolidine-3-carboxamide
35	"A91"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(2-hydroxy-ethylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide

	"A92"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-phenethylpyrrolidine-3-carboxamide
5	"A93"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-{3-[(2-hydroxyethyl)methylcarbamoyl]phenyl}-2-oxopyrrolidine-3-carboxamide
	"A94"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(3-hydroxypropylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide
	"A95"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-[3-(piperidin-1-carbonyl)phenyl]pyrrolidine-3-carboxamide
10	"A96"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-6-yl)pyrrolidine-3-carboxamide
	"A97"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(6-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
15	"A98"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(5-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A99"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(6-trifluoromethylpyridin-3-yl)pyrrolidine-3-carboxamide
	"A100"	Methyl 5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-2-methylnicotinate
20	"A101"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxamide
	"A102"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-{3-[(2-hydroxyethyl)methylcarbamoyl]phenyl}-2-oxopyrrolidine-3-carboxamide
25	"A103"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(3-hydroxypropylcarbamoyl)phenyl]-2-oxopyrrolidine-3-carboxamide
	"A104"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-[3-(piperidin-1-carbonyl)phenyl]pyrrolidine-3-carboxamide
30	"A105"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-6-yl)pyrrolidine-3-carboxamide
	"A106"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(6-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A107"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(5-cyanopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
35	"A108"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(6-trifluoromethylpyridin-3-yl)pyrrolidine-3-carboxamide

5	"A109"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxamide
	"A110"	(S)-3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one
	"A111"	(R)-3-(2-Benzylacryloyl)-3-hydroxy-1-phenylpyrrolidin-2-one
	"A112"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-hydroxymethyl-3-trifluoromethyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"A113"	N-(3-Chloro-5-fluorobenzyl)-8-hydroxy-7-oxo-6-phenyl-2-oxa-6-azaspiro[3.4]octane-8-carboxamide
10	"A114"	N-(3-Chloro-5-fluorobenzyl)-1-(8-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A115"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-oxo-1,2,3,4-tetrahydroisoquinolin-7-yl)pyrrolidine-3-carboxamide
	"A116"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-methylaminopyridin-3-yl)-2-oxopyrrolidine-3-carboxamide
15	"A117"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(5-methylpyridin-3-yl)-2-oxopyrrolidine-3-carboxamide
	"A118"	N-(3-Chloro-5-fluorobenzyl)-1-(3,4-Dihydro-2H-pyrido[3,2-b]-1,4-oxazin-7-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A119"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-5-methyl-2-oxo-1-phenylpyrrolidine-3-carboxamide
20	"A120"	3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-phenylpyrrolidin-3-ol
	"A121"	N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypyrrolidine-3-carboxamide
	"A122"	N-(3-Chloro-5-fluorobenzyl)-1-(4-acetylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
25	"A123"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methanesulfonylamino-cyclohexyl)-2-oxopyrrolidine-3-carboxamide
	"A124"	N-(3-Chloro-5-fluorobenzyl)-1-(4-ethanesulfonylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A125"	N-(3-Chloro-5-fluorobenzyl)-1-((1S,2R,3S)-2,3-dihydroxycyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
30	"A126"	N-(3-Chloro-5-fluorobenzyl)-1-(3-acetylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
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5	"A127"	N-(3-Chloro-5-fluorobenzyl)-1-(4-ethylaminocyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A128"	N-(3-Chloro-5-fluorobenzyl)-1-(3-ethanesulfonylamino-cyclohexyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A129"	N-(3-Chloro-5-fluorobenzyl)-1-((3aR,4S,7aS)-2,2-dimethyl-hexahydrobenzo-1,3-dioxol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
10	"A130"	5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-isophthalamide
	"A131"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-[1,3']bipyrrolidinyl-3-carboxamide
	"A132"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
15	"A133"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(3-methylcarbamoyl-phenyl)-2-oxopyrrolidine-3-carboxamide
	"A134"	N-(3-Chloro-5-fluorobenzyl)-1-(3-Dimethylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A135"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methoxybenzyl)-2-oxopyrrolidine-3-carboxamide
20	"A136"	N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide
	"A137"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A138"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-methoxypyridin-3-yl)-2-oxopyrrolidine-3-carboxamide
25	"A139"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-1-(6-acetylamino-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A140"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyl-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide
	"A141"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyl-3-hydroxy-2-oxo-pyrrolidine-3-carboxamide
30	"A142"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[5-methyl-6-(3-oxo-morpholin-4-yl)-pyridin-3-yl]-2-oxopyrrolidine-3-carboxamide
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"A143"	N-[2-(2-Trifluoromethylphenyl)ethyl]-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A144"	N-[2-(2-Trifluoromethylphenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A145"	N-[1-(3-Fluorophenyl)ethyl]-3-hydroxy-2-oxo-1-phenylpyrrolidine-3-carboxamide
"A146"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methylcarbamoyl-benzofuran-5-yl)-2-oxopyrrolidine-3-carboxamide
"A147"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A148"	Ethyl 4-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-cyclohexanecarboxylate
"A149"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A150"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A151"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide
"A152"	4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-cyclohexanecarboxylic acid
"A153"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(1H-indol-6-yl)-2-oxopyrrolidine-3-carboxamide
"A154"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(1H-indol-6-yl)-2-oxopyrrolidine-3-carboxamide
"A155"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(S)-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A156"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(R)-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A157"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcarbamoyl-cyclohexyl)-2-oxopyrrolidine-3-carboxamide
"A158"	N-(2-Oxo-1,2,3,4-tetrahydroquinolin-6-yl)-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A159"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-(R)-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

5	"A160"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(3-methanesulfonylaminophenyl)-2-oxopyrrolidine-3-carboxamide
	"A161"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(3-methylcarbamoylphenyl)-2-oxopyrrolidine-3-carboxamide
	"A162"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(3-methylcarbamoylphenyl)-2-oxopyrrolidine-3-carboxamide
	"A163"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyclobutylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
10	"A164"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyclobutylcarbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A165"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[3-(methanesulfonylmethylamino)phenyl]-2-oxopyrrolidine-3-carboxamide
15	"A166"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[3-(methanesulfonylmethylamino)phenyl]-2-oxopyrrolidine-3-carboxamide
	"A167"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-[6-(3-oxomorpholin-4-yl)-pyridin-3-yl]pyrrolidine-3-carboxamide
	"A168"	N-[2-(3-Chloro-5-fluorophenyl)ethyl]-3-hydroxy-1-(1H-indazol-5-yl)-2-oxopyrrolidine-3-carboxamide
20	"A169"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-phenyl-1H-pyrazol-4-yl)pyrrolidine-3-carboxamide
	"A170"	tert-Butyl 4-{4-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-pyrazol-1-yl}-piperidine-1-carboxylate
25	"A171"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(6-propionylaminopyridin-3-yl)pyrrolidine-3-carboxamide
	"A172"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(6-propionylaminopyridin-3-yl)pyrrolidine-3-carboxamide
	"A173"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(6-morpholin-4-ylpyridin-3-yl)-2-oxopyrrolidine-3-carboxamide
30	"A174"	N-[2-(3-Fluorophenyl)ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A175"	N-[2-(2-Fluorophenyl)ethyl]-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
35	"A176"	N-(3,5-Difluorobenzyl)-1-(6-acetylaminopyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

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	"A194"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-ethylcarbamoylbenzofuran-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A195"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(2-ethylcarbamoylbenzofuran-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
5	"A196"	N-(2-Chloro-3-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A197"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide
10	"A198"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(3-oxo-3,4-dihydro-2H-benzo-1,4-oxazin-7-yl)pyrrolidine-3-carboxamide
	"A199"	N-[2-(3,5-Difluorophenyl)ethyl]-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
15	"A200"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"A201"	N-[2-(3,5-Difluorophenyl)ethyl]-1-(3-carbamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A202"	Ethyl 3-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-cyclohexanecarboxylate
20	"A203"	[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-acetic acid
	"A204"	N-(3-Chloro-5-fluorobenzyl)-1-(3-carbamoyl-5-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
25	"A205"	Ethyl 5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indol-2-carboxylate
	"A206"	N-(2-Chloro-3-fluorobenzyl)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"A207"	N-[2-(3,5-Difluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
30	"A208"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-methylcarbamoylmethyl-2-oxopyrrolidine-3-carboxamide
	"A209"	N-(3,5-Difluorobenzyl)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
35	"A210"	N-[2-(2-Fluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide

	"A211"	5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-1H-indole-2-carboxamide
	"A212"	N-[2-(3-Fluorophenyl)ethyl]-3-hydroxy-1-(1H-indol-5-yl)-2-oxo-pyrrolidine-3-carboxamide
5	"A213"	tert-Butyl 3-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-ylmethyl]-azetidine-1-carboxylate
	"A214"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(7-oxo-5,6,7,8-tetrahydro-1,8-naphthyridin-3-yl)pyrrolidine-3-carboxamide
10	"A215"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
	"A216"	5-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-nicotinamide
15	"A217"	N-(3-Chloro-5-fluorobenzyl)-1-(2-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A218"	N-(3-Chloro-5-fluorobenzyl)-1-azetidin-3-ylmethyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A219"	N-(3-Chloro-5-fluorobenzyl)-1-[2-(5-fluoro-1H-indol-3-yl)ethyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
20	"A220"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(tetrahydropyran-4-ylmethyl)pyrrolidine-3-carboxamide
	"A221"	N-[2-(3,5-Difluorophenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
25	"A222"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A223"	N-[2-(3,5-Difluorophenyl)ethyl]-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
30	"A224"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A225"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-[(R)-1-(tetrahydrofuran-2-yl)methyl]pyrrolidine-3-carboxamide
	"A226"	4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid
35	"A227"	4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxo-pyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid

	"A228"	tert-Butyl (1S,5R,6S)-6-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-3-azabicyclo[3.1.0]hexane-3-carboxylate
5	"A229"	N-(3-Chloro-5-fluorobenzyl)-1-(1S,5R,6S)-3-azabicyclo[3.1.0]hex-6-yl-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A230"	N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-ethanesulfonyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
10	"A231"	N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-acetyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A232"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-methyl-1H-benzimidazol-2-ylmethyl)-2-oxopyrrolidine-3-carboxamide
15	"A233"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-[1,3']bipyrrolidinyl-3-carboxamide
	"A234"	N-(2-Chloro-4,5-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
20	"A235"	N-(5-Chloro-2,4-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A236"	N-(2,4,6-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
25	"A237"	N-(3-Chloro-5-fluorobenzyl)-1-[2-(2,4-Difluorophenyl)ethyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A238"	5-[(S)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-3-carboxamide
30	"A239"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"A240"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(2-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"A241"	N-(4-Chloro-2-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
35	"A242"	N-(2-Chloro-4-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide

	"A243"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-[(S)-1-(tetrahydrofuran-2-yl)methyl]pyrrolidine-3-carboxamide
5	"A244"	N-(2-Chloro-3,6-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A245"	N-(2,4,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A246"	N-(2,3,6-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
10	"A247"	N-(3-Chloro-4-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A248"	N-(3-Chloro-5-fluorobenzyl)-1-carbamoylmethyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide
15	"A249"	N-(4-Chloro-2,6-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A250"	N-(3-Chloro-2,6-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A251"	N-(3-Chloro-2,4-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
20	"A252"	N-(3,5-Difluorobenzyl)-1-cyclobutylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A253"	N-(3-Fluorobenzyl)-1-(3,4-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
25	"A254"	N-(3-Fluorobenzyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A255"	N-(4-Fluorobenzyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
30	"A256"	N-(3-Fluorobenzyl)-(S)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A257"	N-(4-Fluorobenzyl)-1-(3,4-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A258"	N-(5-Methylisoxazol-3-ylmethyl)-1-(3,4-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
35	"A259"	N-(Pyridin-2-ylmethyl)-(S)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide

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"A260"	N-(Pyridin-2-ylmethyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
"A261"	N-(3-Fluorobenzyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
"A262"	N-(4-Fluorobenzyl)-(R)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
"A263"	N-(3-Fluorobenzyl)-(R)-1-cyclohexylmethyl-3-hydroxy-2-oxopiperidine-3-carboxamide
"A264"	N-(3,4,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A265"	N-(4-Chloro-3-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A266"	N-(2,3,5-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A267"	3-(1,3-Dihydroisindole-2-carbonyl)-3-hydroxy-1-phenylpyrrolidin-2-one
"A268"	1-Benzyl-3-(1,3-dihydroisindole-2-carbonyl)-3-hydroxy-pyrrolidin-2-one
"A269"	N-(3-Chloro-5-fluorobenzyl)-1-(1H-benzimidazol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A270"	N-(3-Chloro-5-fluorobenzyl)-1-benzothiazol-2-ylmethyl-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A271"	3-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-propionic acid
"A272"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(3-methyl-3H-imidazol-4-ylmethyl)-2-oxopyrrolidine-3-carboxamide
"A273"	4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid
"A274"	4-[3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-ylmethyl]cyclohexanecarboxylic acid
"A275"	N-(3-Chloro-5-fluorobenzyl)-1-((1S,5R,6S)-3-ethyl-3-azabicyclo[3.1.0]hex-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

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"A276"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-2H-pyrazol-3-ylmethyl)-2-oxopyrrolidine-3-carboxamide
"A277"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1H-pyrazol-3-ylmethyl)pyrrolidine-3-carboxamide
"A278"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcarbamoylcyclohexylmethyl)-2-oxopyrrolidine-3-carboxamide
"A279"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1H-imidazol-4-ylmethyl)-2-oxopyrrolidine-3-carboxamide
"A280"	N-(3-Chloro-5-fluorobenzyl)-1-(1,5-Dimethyl-1H-pyrrol-2-ylmethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A281"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1'-methanesulfonyl-2-oxo[1,3']bipyrrolidinyl-3-carboxamide
"A282"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[(2-hydroxyethylcarbamoyl)methyl]-2-oxopyrrolidine-3-carboxamide
"A283"	N-(2-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A284"	N-(2,3,4-Trifluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A285"	N-(2,3-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A286"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3,3-difluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A287"	N-(3-Fluorobenzyl)-1-(4-fluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
"A288"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(3,3-difluoro-2-oxo-2,3-dihydro-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"A289"	N-(2,6-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"A290"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(5-methyl-1,3,4-oxadiazol-2-ylmethyl)-2-oxopyrrolidine-3-carboxamide
"A291"	N-(3-chloro-5-fluorobenzyl)-(R)-1'-acetyl-3-hydroxy-2-oxo-[1,3']bipyrrolidinyl-3-carboxamide

5	"A292"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1'-methanesulfonyl-2-oxo[1,3']bipyrrolidiny-3-carboxamide
	"A293"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(4-methylcyclohexyl)-2-oxopyrrolidine-3-carboxamide
	"A294"	N-(5-Methylisoxazol-3-ylmethyl)-1-(2,3-Difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A295"	N-(4-Methylbenzyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A296"	N-(2-Fluorobenzyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
10	"A297"	N-(5-Methylpyrazin-2-ylmethyl)-1-(2,3-difluorobenzyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"A298"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-pyridin-2-ylpyrrolidine-3-carboxamide
	"A299"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-pyridin-2-ylpyrrolidine-3-carboxamide
15	"A300"	N-(3-Chloro-5-fluorobenzyl)-1-(2-carbamoylethyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"A301"	N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypiperidine-3-carboxamide
	"A302"	3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpiperidin-2-one
20	"A303"	N-(3-Chloro-5-fluorobenzyl)-3,4-dihydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"A304"	N-(3-Chloro-5-fluorobenzyl)-5-fluoro-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
25	"B1"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-cyano-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B2"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(8-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
30	"B3"	N-(2-Chloro-6-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
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"B4"	N-(5-Chloro-2-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B5"	N-[2-(2-Fluorophenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B6"	N-[2-(3-Fluorophenyl)ethyl]-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B7"	N-(3,5-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B8"	N-(3,5-Difluorobenzyl)-(S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxo-pyrrolidine-3-carboxamide
"B9"	N-(2-Chloro-3-fluorobenzyl)-(S)-1-(6-acetylamino-3-pyridin-3-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B10"	N-[2-(3-Fluorophenyl)ethyl]-(S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
"B11"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
"B12"	N-(3-Chloro-5-fluorobenzyl)-1-(4-chloro-2-methoxy-5-methylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B13"	1-(5-Chloro-2-methoxyphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxylic acid 3-chloro-5-fluorobenzylamide
"B14"	(S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxylic acid [2-(2-fluorophenyl)ethyl]-amide
"B15"	N-(2-Chloro-3-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B16"	N-(3-Chloro-5-fluorobenzyl)-1-benzyl-3-hydroxypiperidine-3-carboxamide
"B17"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(4-bromo-3-hydroxymethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B18"	3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxypiperidin-2-one
"B19"	1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-piperidin-3-ol
"B20"	1-Benzyl-3-[(3-fluorobenzylamino)methyl]-piperidin-3-ol
"B21"	(S)-1-Benzyl-3-[(4-fluorobenzylamino)methyl]-piperidin-3-ol

"B22"	(S)-1-(2,3-Difluorobenzyl)-3-[(3-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one
"B23"	(R)-1-(2,3-Difluorobenzyl)-3-[(3-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one
"B24"	N-(2,5-Difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B25"	N-(3-Chloro-2-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B26"	N-(3-Chloro-5-fluorobenzyl)-1-(2-Fluoro-5-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B27"	N-(3-Chloro-5-fluorobenzyl)-1-(4-Chloro-3-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B28"	N-(3-Chloro-5-fluorobenzyl)-1-(3-carbamoyl-4-fluorophenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B29"	3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
"B30"	1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]pyrrolidin-3-ol
"B31"	1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one
"B32"	3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpiperidin-2-one
"B33"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(2-methyl-3H-imidazo[4,5-b]pyridin-6-yl)-2-oxopyrrolidine-3-carboxamide
"B34"	N-(3-Chloro-2,5-difluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B35"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(3H-imidazo[4,5-b]pyridin-6-yl)-2-oxopyrrolidine-3-carboxamide
"B36"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-3H-imidazo[4,5-b]pyridin-6-yl)pyrrolidine-3-carboxamide
"B37"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(1H-indol-3-yl)ethyl]-2-oxopyrrolidine-3-carboxamide

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"B38"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[2-(1H-indol-3-yl)-ethyl]-2-oxopyrrolidine-3-carboxamide
"B39"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-Fluoro-5-trifluoromethyl-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B40"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B41"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2-dihydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B42"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(2-Fluoro-5-trifluoromethyl-phenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B43"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
"B44"	1-Benzyl-3-[(3,5-difluorobenzylamino)methyl]-piperidin-3-ol
"B45"	3-[(4-Fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
"B46"	3-[(3,5-Difluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
"B47"	3-{[2-(4-Fluorophenyl)ethylamino]methyl}-3-hydroxy-1-phenylpyrrolidin-2-one
"B48"	3-[(3-Fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
"B49"	3-Hydroxy-3-[(4-methylbenzylamino)methyl]-1-phenylpyrrolidin-2-one
"B50"	N-(2-Oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
"B51"	3-Benzyl 1-tert-butyl 3-hydroxy-2-oxopyrrolidine-1,3-dicarboxylate
"B52"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(4-trifluoromethylpyridin-2-yl)pyrrolidine-3-carboxamide
"B53"	1-Benzyl 3-isopropyl 3-hydroxy-2-oxopyrrolidine-1,3-dicarboxylate

5	"B54"	(S)-1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one
	"B55"	(R)-1-Benzyl-3-[(3-chloro-5-fluorobenzylamino)methyl]-3-hydroxypiperidin-2-one
10	"B56"	N-(3-Fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"B57"	N-(3-Fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
15	"B58"	(R)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
	"B59"	(S)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-1-phenylpyrrolidin-2-one
20	"B60"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(1H-indazol-3-ylmethyl)-2-oxopyrrolidine-3-carboxamide
	"B61"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxopyrrolidine-3-carboxamide
25	"B62"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(2-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-2-oxopyrrolidine-3-carboxamide
	"B63"	(S)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxypiperidin-2-one
30	"B64"	(R)-3-[(3-Chloro-5-fluorobenzylamino)methyl]-1-cyclohexylmethyl-3-hydroxypiperidin-2-one
	"B65"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-fluoro-4-trifluoromethylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
35	"B66"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-fluoro-4-methylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B67"	N-(3-Chloro-5-fluorobenzyl)-1-(2-fluoro-5-trifluoromethylphenyl)-3-hydroxy-2-oxopiperidine-3-carboxamide
	"B68"	6-{3-[(3-Chloro-5-fluorobenzylamino)methyl]-3-hydroxy-2-oxopiperidin-1-yl}-3,4-dihydro-1H-quinolin-2-one
	"B69"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-ylmethyl)pyrrolidine-3-carboxamide
	"B70"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(5-carbamoyl-2-fluorophenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

5	"B71"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)pyrrolidine-3-carboxamide
	"B72"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
	"B73"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
	"B74"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
10	"B75"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(1H-pyrazolo[3,4-b]pyridin-5-yl)pyrrolidine-3-carboxamide
15	"B76"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
	"B77"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydrobenzothiazol-6-yl)pyrrolidine-3-carboxamide
	"B78"	5-[(S)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B79"	5-[(R)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
20	"B80"	Ethyl 5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylate
25	"B81"	Ethyl 5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylate
	"B82"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxopyrrolidine-3-carboxamide
	"B83"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
	"B84"	5-[(S)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylic acid
30	"B85"	5-[(R)-3-(3-Chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxylic acid
35	"B86"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-indol-5-yl)pyrrolidine-3-carboxamide

	"B87"	N-(3-Chloro-5-fluorobenzyl)-1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
5	"B88"	N-Ethyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B89"	N-Isopropyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B90"	N,N-Dimethyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
10	"B91"	3-(3-Chloro-5-fluorobenzylcarbamoyl)-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidin-3-yl acetate
	"B92"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(3H-imidazo[4,5-b]pyridin-6-yl)-2-oxopyrrolidine-3-carboxamide
15	"B93"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-(3H-imidazo[4,5-b]pyridin-6-yl)-2-oxopyrrolidine-3-carboxamide
	"B94"	N-Ethyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B95"	N,N-Dimethyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
20	"B96"	N-Methyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B97"	N-Isopropyl-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
25	"B98"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"B99"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxopyrrolidine-3-carboxamide
30	"B100"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-[1-(2-methoxyethyl)-1H-pyrazol-4-yl]-2-oxopyrrolidine-3-carboxamide
	"B101"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(4-sulfamoylphenyl)pyrrolidine-3-carboxamide
	"B102"	N-Methyl-5-[(R)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
35	"B103"	(S)-3-Hydroxy-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-pyrrolidine-3-carboxamide

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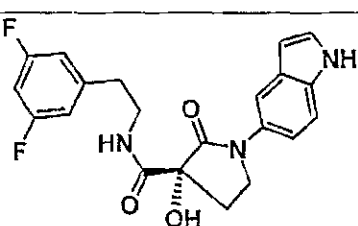
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"B104"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
"B105"	Methyl 3-{2-tert-butoxycarbonylamino-5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-phenyl}propionate
"B106"	3-{2-tert-Butoxycarbonylamino-5-[3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]phenyl}propionic acid
"B107"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(3-sulfamoylphenyl)pyrrolidine-3-carboxamide
"B108"	N-({2-[2-(2-Aminoethoxy)-ethoxy]ethyl})-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
"B109"	N-(3-Chloro-5-fluorobenzyl)-1-(7-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B110"	N-[2-(3,5-Difluorophenyl)ethyl]-(S)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
"B111"	 N-[2-(3,5-Difluorophenyl)ethyl]-(R)-3-hydroxy-1-(1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
"B112"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(morpholine-4-carbonyl)-1H-indol-5-yl]-2-oxopyrrolidine-3-carboxamide
"B113"	N-[2-(2-Aminoethoxy)ethyl]-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
"B114"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-[2-(azetidine-1-carbonyl)-1H-indol-5-yl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B115"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(4-sulfamoylphenyl)pyrrolidine-3-carboxamide
"B116"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide

	"B117"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-(1-cyanomethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B118"	N-(3-Chloro-5-fluorobenzyl)-1-(4-acetylsulfamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
5	"B119"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(1-carbamoylmethyl-1H-pyrazol-4-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B120"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(1-phenylethyl)-pyrrolidine-3-carboxamide
10	"B121"	N-(2-hydroxyethyl)-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B122"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(4-methylpiperazin-1-carbonyl)-1H-indol-5-yl]-2-oxopyrrolidine-3-carboxamide
15	"B123"	tert-Butyl 4-{5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indol-2-carbonyl}-piperazine-1-carboxylate
	"B124"	N-(3-Chloro-5-fluorobenzyl)-1-(5-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
20	"B125"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-indol-5-yl)pyrrolidine-3-carboxamide
	"B126"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-[2-(piperazin-1-carbonyl)-1H-indol-5-yl]pyrrolidine-3-carboxamide
25	"B127"	N-(3-Chloro-5-fluorobenzyl)-3-chloro-2-oxo-1-(2-oxo-1,2,3,4-tetrahydroquinolin-6-yl)pyrrolidine-3-carboxamide
	"B128"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-dimethylsulfamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
30	"B129"	N-(2-Aminophenyl)-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide
	"B130"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-indol-5-yl)pyrrolidine-3-carboxamide
	"B131"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(2-oxo-2,3-dihydro-1H-indol-5-yl)pyrrolidine-3-carboxamide
35	"B132"	N-(2-Aminoethyl)-5-[(S)-3-(3-chloro-5-fluorobenzylcarbamoyl)-3-hydroxy-2-oxopyrrolidin-1-yl]-1H-indole-2-carboxamide

	"B133"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-[2-(1H-benzoimidazol-2-yl)-1H-indol-5-yl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B134"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2-hydrazinocarbonyl-1H-indol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
5	"B135"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-[2-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-indol-5-yl]-2-oxopyrrolidine-3-carboxamide
	"B136"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-benzyloxy-3-hydroxy-2-oxopyrrolidine-3-carboxamide
10	"B137"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B138"	N-(3-Chloro-5-fluorobenzyl)-(R)-1-benzyloxy-3-hydroxy-2-oxopyrrolidine-3-carboxamide
15	"B139"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
	"B140"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-2-oxo-1-(3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)pyrrolidine-3-carboxamide
20	"B141"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-(4-methylsulfamoylphenyl)-2-oxopyrrolidine-3-carboxamide
	"B142"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(4-benzylsulfamoylphenyl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
25	"B143"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-[4-(benzylmethylsulfamoyl)phenyl]-3-hydroxy-2-oxopyrrolidine-3-carboxamide
	"B144"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-1-(1-methyl-1H-indol-5-yl)-2-oxopyrrolidine-3-carboxamide
	"B145"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-1-hydroxymethyl-2-oxopyrrolidine-3-carboxamide
30	"B146"	N-(3-Chloro-5-fluorobenzyl)-(R)-3-hydroxy-1-hydroxymethyl-2-oxopyrrolidine-3-carboxamide
	"B147"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(3-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
35	"B148"	N-(3-Chloro-5-fluorobenzyl)-3-hydroxy-2-oxo-1-(2-trifluoromethyl-1H-benzimidazol-5-yl)pyrrolidine-3-carboxamide

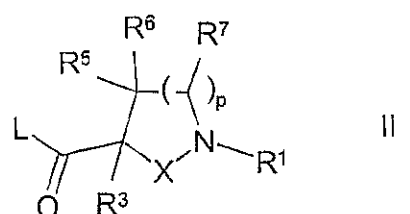
"B149"	N-(3-Chloro-5-fluorobenzyl)-(S)-3-hydroxy-2-oxo-1-(2-sulfamoyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
"B150"	(3S)-N-[(3-Chloro-5-fluorophenyl)methyl]-1-(2,2-dioxo-1,3-dihydro-2,1-benzothiazol-5-yl)-3-hydroxy-2-oxopyrrolidine-3-carboxamide
"B151"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-(2,2-dioxo-1,2,3,4-tetrahydro-2 λ 6*-benzo[c]thiazin-6-yl)-3-hydroxy-2-oxo-1-(2-sulfamoyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
"B152"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-[[[(R)-1-dimethylcarbamoyl-2-methylpropylcarbamoyl)methyl]-3-hydroxy-2-oxo-1-(2-sulfamoyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
"B153"	N-(3-Chloro-5-fluorobenzyl)-(S)-1-[[[(S)-3-amino-1-methylcarbamoylpropylcarbamoyl)methyl]-3-hydroxy-2-oxo-1-(2-sulfamoyl-1H-indol-5-yl)pyrrolidine-3-carboxamide
"B154"	N-(3-Hydroxy-2-oxo-1-phenylpyrrolidin-3-yl)benzamide

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

6. Process for the preparation of compounds of the formula I according to Claims 1-5 and pharmaceutically usable salts, tautomers and stereoisomers thereof, characterised in that

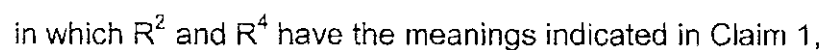
a) for the preparation of compounds of the formula I in which Y denotes CO and R denotes NR^2R^4 ,

a compound of the formula II



and L denotes Cl, Br, I or a free or reactively functionally modified OH group,

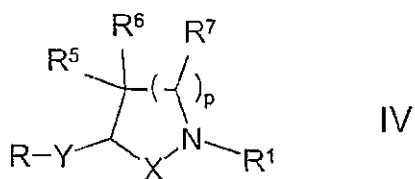
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or

b) a compound of the formula IV



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in which R^1 , R^5 , R^6 , R^7 , R , X , Y and p have the meanings indicated in Claim 1,

is oxidised,

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or

c) for the preparation of compounds of the formula I in which X and Y denote CH₂,

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a compound of the formula I in which X and Y denote CO,

is reduced,

and/or

a base or acid of the formula I is converted into one of its salts.

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7. Medicaments comprising at least one compound of the formula I according to Claim 1-5 and/or pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

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8. Compounds of the formula I according to Claim 1-5, and pharmaceutically usable salts, tautomers and stereoisomers thereof, including mixtures thereof in all ratios, for use for the treatment of tumours, tumour metastases, proliferative diseases of the mesangial cells, haemangioma, proliferative retinopathy, rheumatoid arthritis, atherosclerotic neovascularisation, psoriasis, ocular neovascularisation, osteoporosis, diabetes and obesity, lymphoid leukaemia, lymphoma, malaria and prostate hypertrophy.

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9. Compounds according to Claim 8, where the tumour disease is selected from the group of the squamous epithelium, of the bladder, of the stomach, of the kidneys, of head and neck, of the oesophagus, of the cervix, of the thyroid, of the intestine, of the liver, of the brain, of the prostate, of the urogenital tract, of the lymphatic system, of the stomach, of the larynx, of the lung, of the skin, monocytic leukaemia, lung adenocarcinoma, small-cell lung carcinoma, pancreatic cancer, glioblastoma, breast carcinoma, acute myeloid leukaemia, chronic myeloid leukaemia, acute lymphatic leukaemia, chronic lymphatic leukaemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma.