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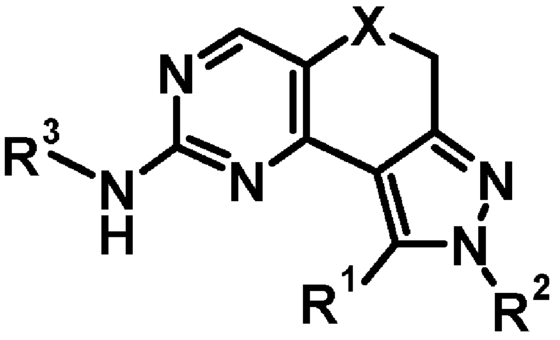
(54) Title: NEW AMINOPYRAZOLOQUINAZOLINES

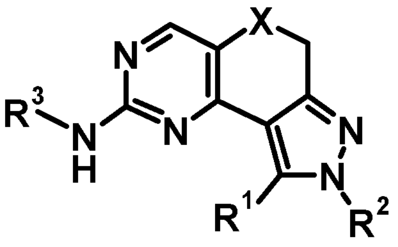


(I)

(57) Abstract: The present invention encompasses compounds of general formula (I) wherein the groups R^1 to R^3 and X are defined as in claim 1, which are suitable for the treatment of diseases characterised by excessive or abnormal cell proliferation, pharmaceutical preparations which contain such compounds and their use as medicaments.

NEW AMINOPYRAZOLOQUINAZOLINES

The present invention relates to new aminopyrazoloquinazolines of general formula **(I)**



(I) ,

wherein the groups **R**^{1} to **R**^{3} and **X** have the meanings given in the claims and specification, which are suitable for the treatment of diseases characterised by excessive or abnormal cell proliferation, pharmaceutical preparations which contain such compounds and their use as medicaments. The compounds according to the invention display an inhibitory effect on the phosphorylation activity of the IGF-1 receptor located in cell membranes.

Background to the invention

WO 2005/037843 describes partially saturated quinazolines anellated with heteroaryls as kinase inhibitors.

The aim of the present invention is to indicate new compounds which can be used for the prevention and/or treatment of diseases characterised by excessive or abnormal cell proliferation. The compounds according to the invention are characterised by a powerful inhibitory effect on the phosphorylation activity of the IGF-1 receptor located in cell membranes and a potent efficacy against tumour cells, e.g. glioblastoma cells, which is mediated through the inhibition of phosphorylation of the receptor. In addition to the inhibitory effect and cell activity the compounds have good solubility and good PK properties.

The insulin-like growth factor (IGF) and insulin signalling network is a highly conserved and essential pathway involved in biological processes including growth, metabolism and homeostasis. In addition, deregulated signalling via this network can enhance tumorigenesis and metastasis of certain cancers.

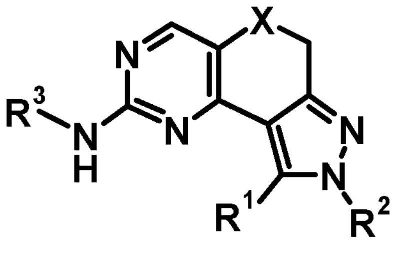
The ligands IGF-1, IGF-2 and insulin are highly homologous and activate specific hetero or homodimers of the IGF-1R and IR. Following ligand binding, the IGF-1R and IR undergo autophosphorylation mediated via the receptor tyrosine kinase domains. The phosphorylated receptors activate the canonical Ras-Raf-MEK-ERK1/2 and PI3K- PDK1-Akt intracellular signaling cascades, which leads to cell proliferation and survival. In addition, activation of the IR by insulin stimulates the uptake of glucose and storage of glycogen in metabolic tissues such as the liver, adipose and muscle.

Published research articles as well as medical and epidemiological investigations have identified a strong correlation between expression of the IGF-1R and IR and ligands for these receptors in tumor development and progression. Developing a small molecule competitive inhibitor of the ATP-binding pocket of the IGF-1R and IR as a means of blocking growth and survival signaling cascades in cancer is therefore desirable. The anticipated clinical benefit of blocking such an interaction would be to reduced tumor growth rate and potentially sensitize tumors to cytotoxic agents or targeted therapies.

Detailed description of the invention

Surprisingly it has been found that compounds of general formula **(I)**, wherein the groups **R**^{1} to **R**^{3} and **X** have the meanings stated hereinafter act as inhibitors of receptors that are involved in controlling cell proliferation. Thus, the compounds according to the invention may be used for example for the treatment of diseases associated with the activity of these receptors and characterised by excessive or abnormal cell proliferation.

The present invention therefore relates to compounds of general formula **(I)**



(I) , wherein

(A0)

R^1 denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{a} and/or **R**^{b}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

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(B0)

R^2 denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{a} and/or **R**^{b}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

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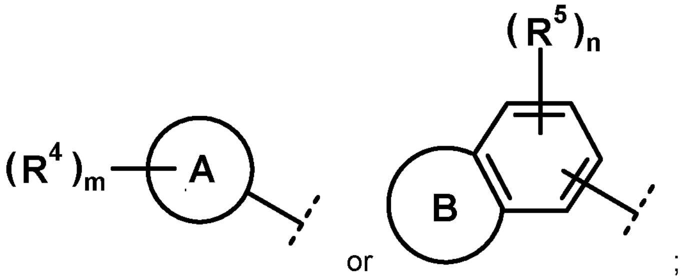
R^3 denotes a group



(C0)

A is selected from among C_{6-10}aryl and 5-12 membered heteroaryl;

B denotes a 5- to 7-membered, non-aromatic hetero ring with at least one heteroatom, selected from among nitrogen, sulphur and oxygen, which optionally carries one or more substituents selected from among C_{1-6}alkyl and =O;

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(D0)

each **R**^{4} is independently selected from among **R**^{a} and **R**^{b};

m denotes 0, 1, 2 or 3;

R^5 is selected from among **R**^{a} and **R**^{b};

n denotes 0 or 1;

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(E0)

X denotes a bond or is selected from among $-CH_2-$ and $-CH_2-CH_2-$ and in the above-mentioned $-CH_2-$ and $-CH_2-CH_2-$ one or two hydrogen atoms are optionally substituted independently of one another by C_{1-4}alkyl, C_{1-4}haloalkyl, -O-C_{1-4}alkyl or halogen;

--

each **R**^{a} independently denotes a group optionally substituted by one or more identical or different **R**^{b} and/or **R**^{c}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R**^{b} is independently selected from among -OR^c, -SR^c, -NR^{c}R^c, halogen, -CN, -NO$_2$, -C(O)R^c, -C(O)OR^c, -C(O)NR^{c}R^c, -C(NR^h)NR^{c}R^c, -OC(O)R^c, -OC(O)OR^c, -S(O)$_2$R^c, -S(O)$_2$NR^{c}R^c, -NR^{h}C(O)R^c, -NR^{h}C(O)OR^c, -NR^{h}C(O)NR^{c}R^c, -NR^{h}C(NR^h)NR^{c}R^c and -NR^{h}S(O)$_2$R^c, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R**^{c} independently denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{d} and/or **R**^{e}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R**^{d} is independently selected from among -OR^e, -SR^e, -NR^{e}R^e, halogen, -CN, -NO$_2$, -C(O)R^e, -C(O)OR^e, -C(O)NR^{e}R^e, -C(NR^h)NR^{e}R^e, -OC(O)R^e, -OC(O)OR^e, -S(O)$_2$R^e, -S(O)$_2$NR^{e}R^e, -NR^{h}C(O)R^e, -NR^{h}C(O)OR^e, -NR^{h}C(O)NR^{e}R^e, -NR^{h}C(NR^h)NR^{e}R^e and -NR^{h}S(O)$_2$R^e, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R**^{e} independently denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{f} and/or **R**^{g}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R**^{f} is independently selected from among -OR^g, -SR^g, -NR^{g}R^g, halogen, -CN, -NO$_2$, -C(O)R^g, -C(O)OR^g, -C(O)NR^{g}R^g, -C(NR^h)NR^{g}R^g, -OC(O)R^g, -OC(O)OR^g, -S(O)$_2$R^g, -S(O)$_2$NR^{g}R^g, -NR^{h}C(O)R^g, -NR^{h}C(O)OR^g, -NR^{h}C(O)NR^{g}R^g, -NR^{h}C(NR^h)NR^{g}R^g and -NR^{h}S(O)$_2$R^g, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R**^{g} is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl, and

each **R^h** is independently selected from among hydrogen and C_{1-6}alkyl,

while the compounds **(I)** may optionally also be present in the form of their tautomers, their racemates, their enantiomers, their diastereomers or their mixtures or as the respective salts of all the above-mentioned forms.

In one aspect **(A1)** the invention relates to compounds **(I)**, wherein

R^1 is a group optionally substituted by one or more identical or different **R^{a1}** and/or **R^{b1}**, selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^{a1}** independently denotes a group optionally substituted by one or more identical or different **R^{b1}** and/or C_{1-6}alkyl, selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and C_{6-10}aryl, and

each **R^{b1}** is independently selected from among -OH, -O-C_{1-6}alkyl, halogen and -CN.

In another aspect **(A2)** the invention relates to compounds **(I)**, wherein

R^1 is a group optionally substituted by one or more identical or different **R^{a1}** and/or **R^{b1}**, selected from among C_{1-4}alkyl, C_{3-6}cycloalkyl, phenyl, 5- to 6-membered heteroaryl and 3-7 membered heterocyclyl;

each **R^{a1}** independently denotes a group optionally substituted by one or more identical or different **R^{b1}** and/or C_{1-4}alkyl, selected from among C_{1-4}alkyl, C_{3-6}cycloalkyl and phenyl, and

each **R^{b1}** is independently selected from among -O-C_{1-4}alkyl, halogen and –CN.

In another aspect **(A3)** the invention relates to compounds **(I)**, wherein

R^1 denotes C_{3-6}alkyl.

In another aspect **(A4)** the invention relates to compounds **(I)**, wherein

R^1 denotes phenyl or benzyl, while the above-mentioned phenyl and benzyl optionally carry one or more substituents selected from among C_{1-6}alkyl, halogen, -O-C_{1-6}alkyl and -CN.

In another aspect **(A5)** the invention relates to compounds **(I)**, wherein

R^1 denotes phenyl or benzyl, while the above-mentioned phenyl and benzyl optionally carry one or more substituents selected from among C_{1-4}alkyl, C_{1-4}haloalkyl, halogen, -O-C_{1-4}alkyl, -O-C_{1-4}haloalkyl and -CN.

In another aspect **(A6)** the invention relates to compounds **(I)**, wherein

R^1 denotes thienyl, this thienyl optionally carrying one or more substituents selected from among C_{1-4}alkyl and halogen.

In another aspect **(B1)** the invention relates to compounds **(I)**, wherein

R^2 is hydrogen or a group optionally substituted by one or more identical or different **R^{b2}** and/or C_{6-10}aryl selected from among C_{1-6}alkyl, C_{2-6}alkenyl and 5-12 membered heteroaryl;

each **R^{b2}** is independently selected from among -OH, -O-C_{1-6}alkyl, -NH$_2$, -NH(C_{1-6}alkyl) and -N(C_{1-6}alkyl)$_2$.

In another aspect **(B2)** the invention relates to compounds **(I)**, wherein

R^2 is a group optionally substituted by one or more identical or different **R^{b2}** and/or phenyl selected from among C_{1-4}alkyl, and 5- to 6-membered heteroaryl;

each **R^{b2}** is independently selected from among -O-C_{1-4}alkyl and -N(C_{1-4}alkyl)$_2$.

In another aspect **(B3)** the invention relates to compounds **(I)**, wherein

R^2 denotes methyl or ethyl.

In another aspect **(E1)** the invention relates to compounds **(I)**, wherein

X denotes a bond or is selected from among -CH$_2$- and -CH$_2$-CH$_2$- and in the above-mentioned -CH$_2$- and -CH$_2$-CH$_2$- optionally one or two hydrogen atoms are substituted by C_{1-4}alkyl.

In another aspect **(E2)** the invention relates to compounds **(I)**, wherein

X is selected from among -CH$_2$- and -CH$_2$-CH$_2$- and in the above-mentioned -CH$_2$- and -CH$_2$-CH$_2$- optionally one or two hydrogen atoms are substituted by C_{1-4}alkyl.

In another aspect **(E3)** the invention relates to compounds **(I)**, wherein

X is selected from among $-CH_2$, $-CH(CH_3)$, $-C(CH_3)_2-$ and $-CH_2-CH_2-$.

In another aspect **(E4)** the invention relates to compounds **(I)**, wherein

X denotes $-CH_2$ or $-CH(CH_3)-$.

In another aspect **(C1)** the invention relates to compounds **(I)**, wherein

A is selected from among phenyl, naphthyl, 5- to 6-membered, monocyclic heteroaryl and 9- to 10-membered bicyclic heteroaryl.

In another aspect **(C2)** the invention relates to compounds **(I)**, wherein

A is selected from among phenyl, benzofuryl, benzothienyl, naphthyl, isoquinolinyl, pyrazolyl, indazolyl, isoxazolyl and imidazo[1,2-*a*]pyridyl.

In another aspect **(C3)** the invention relates to compounds **(I)**, wherein

A denotes phenyl.

In another aspect **(C4)** the invention relates to compounds **(I)**, wherein

A denotes pyrazolyl.

In another aspect **(D1)** the invention relates to compounds **(I)**, wherein

each $\mathbf{R^4}$ is independently selected from among $\mathbf{R^{a3}}$ and $\mathbf{R^{b3}}$;

m denotes 0, 1, 2 or 3;

each $\mathbf{R^{a3}}$ independently denotes a group optionally substituted by one or more identical or different $\mathbf{R^{b3}}$ and/or $\mathbf{R^{c3}}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{b3}}$ is independently selected from among $-OR^{c3}$, $-NR^{c3}R^{c3}$, halogen, $-C(O)R^{c3}$, $-C(O)OR^{c3}$, $-C(O)NR^{c3}R^{c3}$ and $-S(O)_2R^{c3}$;

each $\mathbf{R^{c3}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d3}}$ and/or $\mathbf{R^{e3}}$ selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{d3}}$ is independently selected from among $-OR^{e3}$, $-NR^{e3}R^{e3}$, halogen, $-C(O)R^{e3}$, $-C(O)OR^{e3}$ and $-C(O)NR^{e3}R^{e3}$;

each **R^{e3}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f3}** and/or **R^{g3}** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

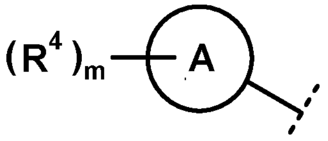
each **R^{f3}** is independently selected from among $-OR^{g3}$, $-NR^{g3}R^{g3}$, halogen, $-C(O)R^{g3}$, $-C(O)OR^{g3}$ and $-C(O)NR^{g3}R^{g3}$ and

each **R^{g3}** is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{6-10}aryl, and 5-12 membered heteroaryl.

In another aspect **(D2)** the invention relates to compounds with the structural aspect **(D1)**, wherein **m** denotes 1, 2 or 3.

In another aspect **(D3)** the invention relates to compounds with the structural aspect **(D1)**, wherein **m** denotes 2.

In another aspect **(CD1)** the invention relates to compounds **(I)**, wherein **R^3** denotes a group



;

A is selected from among C_{6-10}aryl and 5-12 membered heteroaryl;

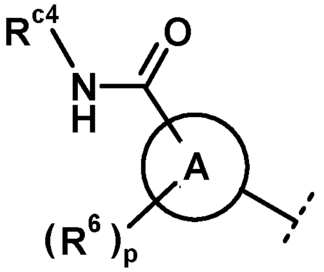
each **R^4** is independently selected from among **R^a** and **R^b**;

m denotes 0, 1, 2 or 3 and

R^a and **R^b** are as hereinbefore defined.

In another aspect **(CD2)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group



;

A is selected from among $C_{6\text{-}10}$aryl and 5-12 membered heteroaryl;

each **R^6** is independently selected from among $C_{1\text{-}4}$alkyl, -O-$C_{1\text{-}4}$alkyl and halogen;

p denotes 0, 1 or 2;

R^{c4} denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d4}** and/or **R^{e4}** selected from among $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkenyl, $C_{6\text{-}10}$aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^{d4}** is independently selected from among $-OR^{e4}$, $-SR^{e4}$, $-NR^{e4}R^{e4}$, halogen, -CN, $-NO_2$, $-C(O)R^{e4}$, $-C(O)OR^{e4}$, $-C(O)NR^{e4}R^{e4}$, $-C(NR^{h4})NR^{e4}R^{e4}$, $-OC(O)R^{e4}$, $-OC(O)OR^{e4}$, $-S(O)_2R^{e4}$, $-S(O)_2NR^{e4}R^{e4}$, $-NR^{h4}C(O)R^{e4}$, $-NR^{h4}C(O)OR^{e4}$, $-NR^{h4}C(O)NR^{e4}R^{e4}$, $-NR^{h4}C(NR^{h4})NR^{e4}R^{e4}$ and $-NR^{h4}S(O)_2R^{e4}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{e4}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f4}** and/or **R^{g4}** selected from among $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkenyl, $C_{6\text{-}10}$aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

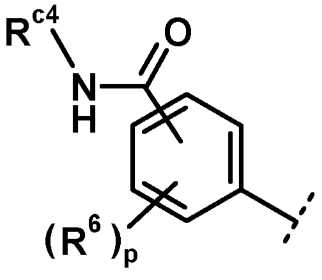
each **R^{f4}** is independently selected from among $-OR^{g4}$, $-SR^{g4}$, $-NR^{g4}R^{g4}$, halogen, -CN, $-NO_2$, $-C(O)R^{g4}$, $-C(O)OR^{g4}$, $-C(O)NR^{g4}R^{g4}$, $-C(NR^{h4})NR^{g4}R^{g4}$, $-OC(O)R^{g4}$, $-OC(O)OR^{g4}$, $-S(O)_2R^{g4}$, $-S(O)_2NR^{g4}R^{g4}$, $-NR^{h4}C(O)R^{g4}$, $-NR^{h4}C(O)OR^{g4}$, $-NR^{h4}C(O)NR^{g4}R^{g4}$, $-NR^{h4}C(NR^{g4})NR^{g4}R^{g4}$ and $-NR^{h4}S(O)_2R^{g4}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{g4}** is independently selected from among hydrogen, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{1\text{-}6}$haloalkyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkylalkyl, $C_{4\text{-}10}$cycloalkenyl, $C_{6\text{-}10}$aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl and

each **R^{h4}** is independently selected from among hydrogen and $C_{1\text{-}4}$alkyl.

In another aspect **(CD3)** the invention relates to compounds **(I)**, wherein

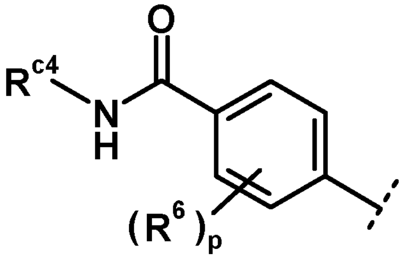
R^3 denotes a group

 and

R^{c4}, R^6 and **p** are as hereinbefore defined.

In another aspect **(CD4)** the invention relates to compounds **(I)**, wherein

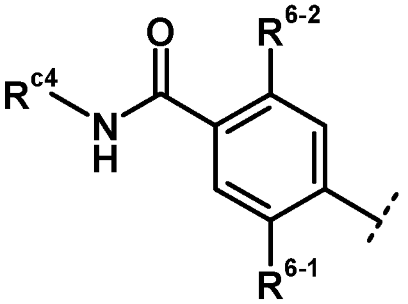
R^3 denotes a group

 and

R^{c4}, R^6 and **p** are as hereinbefore defined.

In another aspect **(CD5)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group

 ;

R^{6-1} and R^{6-2} is independently selected from among hydrogen, C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen and

R^{c4} is as hereinbefore defined.

In further aspects **(CD6)**, **(CD7)**, **(CD8)** and **(CD9)** the invention relates to compounds with the structural aspect **(CD2)**, **(CD3)**, **(CD4)** and **(CD5)**, wherein

R^{c4} denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d4}}$ and/or $\mathbf{R^{e4}}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{d4}}$ is independently selected from among $-OR^{e4}$, $-NR^{e4}R^{e4}$, halogen, $-C(O)R^{e4}$ and $-C(O)NR^{e4}R^{e4}$;

each $\mathbf{R^{e4}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{f4}}$ and/or $\mathbf{R^{g4}}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{f4}}$ is independently selected from among $-OR^{g4}$, $-NR^{g4}R^{g4}$, halogen, $-C(O)R^{g4}$, $-C(O)NR^{g4}R^{g4}$ and

each $\mathbf{R^{g4}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{6-10}aryl and 5-12 membered heteroaryl.

In further aspects **(CD10)**, **(CD11)**, **(CD12)** and **(CD13)** the invention relates to compounds with the structural aspect **(CD2)**, **(CD3)**, **(CD4)** and **(CD5)**, wherein

$\mathbf{R^{c4}}$ denotes a group optionally substituted by one or more identical or different $\mathbf{R^{d4}}$ and/or $\mathbf{R^{e4}}$ selected from among C_{1-6}alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, azetidinyl, pyrrolidinyl, tetrahydropyranyl, 1-aza-bicyclo[2.2.2]octyl, 8-methyl-8-aza-bicyclo[3.2.1]octyl, morpholinyl, piperidinyl and piperazinyl;

each $\mathbf{R^{d4}}$ is independently selected from among $-OR^{e4}$, $-NR^{e4}R^{e4}$, halogen, $-C(O)R^{e4}$ and $-C(O)NR^{e4}R^{e4}$;

each $\mathbf{R^{e4}}$ independently denotes a group optionally substituted by one or more identical or different $\mathbf{R^{f4}}$ and/or $\mathbf{R^{g4}}$ selected from among C_{1-6}alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, azetidinyl, pyrrolidinyl, tetrahydropyranyl, 1-aza-bicyclo[2.2.2]octyl, 8-methyl-8-aza-bicyclo[3.2.1]octyl, morpholinyl, piperidinyl and piperazinyl;

each $\mathbf{R^{f4}}$ is independently selected from among $-OR^{g4}$, $-NR^{g4}R^{g4}$, halogen, $-C(O)R^{g4}$, $-C(O)NR^{g4}R^{g4}$ and

each $\mathbf{R^{g4}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, phenyl and 5- to 6-membered heteroaryl.

In further aspects **(CD14)**, **(CD15)**, **(CD16)** and **(CD17)** the invention relates to compounds with the structural aspect **(CD2)**, **(CD3)**, **(CD4)** and **(CD5)**, wherein

R^{c4} is selected from among methyl, methoxyethyl, *N*,*N*-dimethyl-ethyl, *N*,*N*-dimethyl-propyl,

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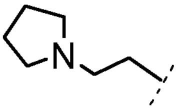

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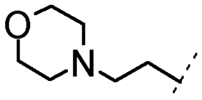

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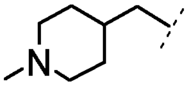

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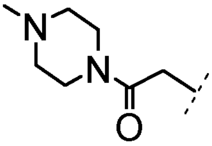

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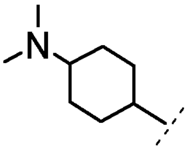

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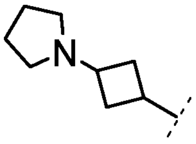

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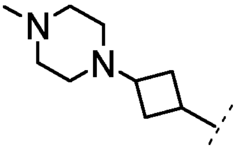

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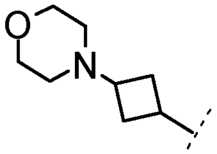

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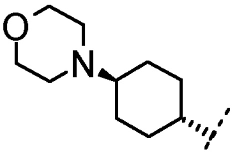

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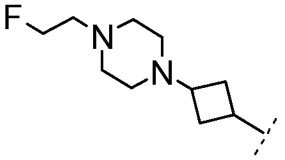

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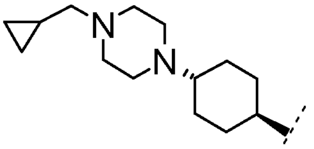

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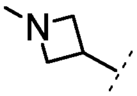

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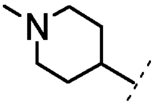

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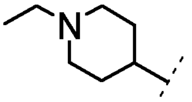

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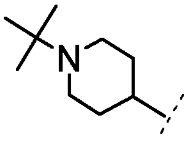

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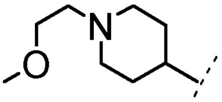

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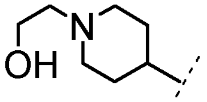

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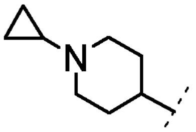

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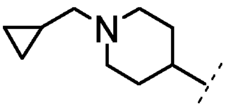

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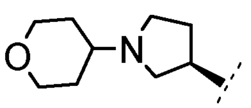

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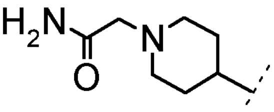

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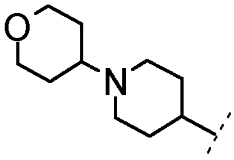

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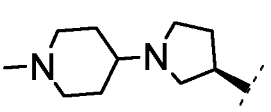

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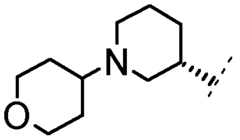
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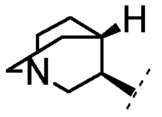
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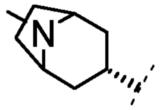
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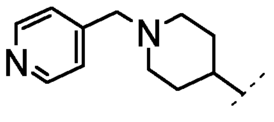
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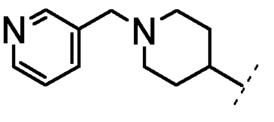
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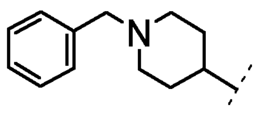
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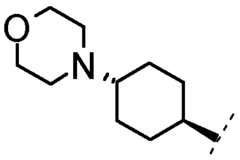
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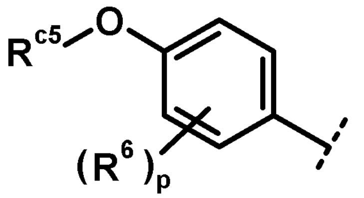
In another aspect **(CD18)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group


;

each **R^6** is independently selected from among C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen;

p denotes 0, 1 or 2;

R^{c5} denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}** selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^{d5}** is independently selected from among -OR^{e5}, -SR^{e5}, -$NR^{e5}R^{e5}$, halogen, -CN, -NO_2, -C(O)R^{e5}, -C(O)OR^{e5}, -C(O)N$R^{e5}R^{e5}$, -C(NR^{h5})N$R^{e5}R^{e5}$, -OC(O)R^{e5}, -OC(O)OR^{e5}, -S(O)$_2R^{e5}$, -S(O)$_2$N$R^{e5}R^{e5}$, -NR^{h5}C(O)R^{e5}, -NR^{h5}C(O)OR^{e5}, -NR^{h5}C(O)N$R^{e5}R^{e5}$, -NR^{h5}C(NR^{h5})N$R^{e5}R^{e5}$ and -NR^{h5}S(O)$_2R^{e5}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{e5}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f5}** and/or **R^{g5}** selected from among C_{1-6}alkyl, C_{2-6}alkenyl,

$C_{2\text{-}6}$alkynyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkenyl, $C_{6\text{-}10}$aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

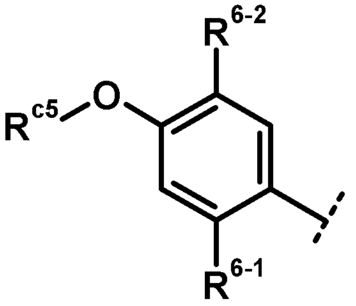
each **R^{f5}** is independently selected from among $-OR^{g5}$, $-SR^{g5}$, $-NR^{g5}R^{g5}$, halogen, -CN, $-NO_2$, $-C(O)R^{g5}$, $-C(O)OR^{g5}$, $-C(O)NR^{g5}R^{g5}$, $-C(NR^{h5})NR^{g5}R^{g5}$, $-OC(O)R^{g5}$, $-OC(O)OR^{g5}$, $-S(O)_2R^{g5}$, $-S(O)_2NR^{g5}R^{g5}$, $-NR^{h5}C(O)R^{g5}$, $-NR^{h5}C(O)OR^{g5}$, $-NR^{h5}C(O)NR^{g5}R^{g5}$, $-NR^{h5}C(NR^{h5})NR^{g5}R^{g5}$ and $-NR^{h5}S(O)_2R^{g5}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{g5}** is independently selected from among hydrogen, $C_{1\text{-}6}$alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, $C_{1\text{-}6}$haloalkyl, $C_{3\text{-}10}$cycloalkyl, $C_{4\text{-}10}$cycloalkylalkyl, $C_{4\text{-}10}$cycloalkenyl, $C_{6\text{-}10}$aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl and

each **R^{h5}** is independently selected from among hydrogen and $C_{1\text{-}4}$alkyl.

In another aspect **(CD19)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group



;

$R^{6\text{-}1}$ and **$R^{6\text{-}2}$** is independently selected from among hydrogen, $C_{1\text{-}4}$alkyl, $-O-C_{1\text{-}4}$alkyl and halogen and

R^{c5} are as hereinbefore defined.

In further aspects **(CD20)** and **(CD21)** the invention relates to compounds with the structural aspect **(CD18)** and **(CD19)**, wherein

R^{c5} denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}**, selected from among $C_{1\text{-}6}$alkyl, $C_{3\text{-}10}$cycloalkyl and 3- to 14-membered heterocyclyl;

each **R^{d5}** is independently selected from among $-OR^{e5}$, $-NR^{e5}R^{e5}$, halogen, $-C(O)R^{e5}$ and $-C(O)NR^{e5}R^{e5}$ and each **R^{e5}** is independently selected from among hydrogen, C$_{1\text{-}6}$alkyl, C$_{3\text{-}10}$cycloalkyl and 3- to 14-membered heterocyclyl.

In further aspects **(CD22)** and **(CD23)** the invention relates to compounds with the structural aspect **(CD18)** and **(CD19)**, wherein

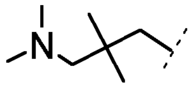
R^{c5} denotes a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}** selected from among C$_{1\text{-}6}$alkyl and 5- to 6-membered, nitrogen-containing heterocyclyl;

each **R^{d5}** is independently selected from among -OR^{e5}, -NR^{e5}R^{e5}, halogen, -C(O)R^{e5} and -C(O)NR^{e5}R^{e5} and

each **R^{e5}** is independently selected from among C$_{1\text{-}6}$alkyl and 5- to 6-membered, nitrogen-containing heterocyclyl.

In further aspects **(CD24)** and **(CD25)** the invention relates to compounds with the structural aspect **(CD18)** and **(CD19)**, wherein

R^{c5} is selected from among *N*,*N*-dimethylethyl, *N*,*N*-dimethyl-propyl,



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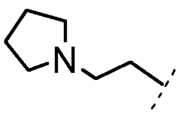

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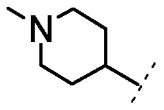

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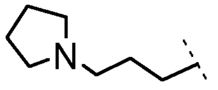
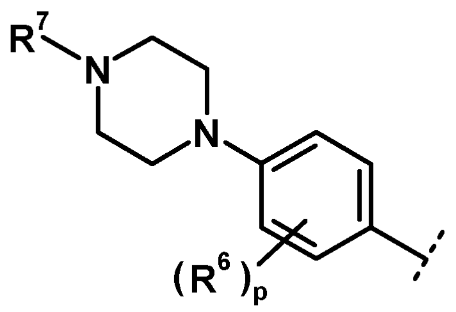


.

In another aspect **(CD26)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group



;

each **R^6** is independently selected from among C$_{1\text{-}4}$alkyl, -O-C$_{1\text{-}4}$alkyl and halogen;

R^7 is selected from among **R^{b6}** and **R^{c6}**;

p denotes 0, 1 or 2;

R^{b6} is selected from among -C(O)R^{c6}, -C(O)OR^{c6}, -C(O)N$R^{c6}R^{c6}$, -S(O)$_2R^{c6}$ and -S(O)$_2$N$R^{c6}R^{c6}$;

each **R^{c6}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d6}** and/or **R^{e6}** selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

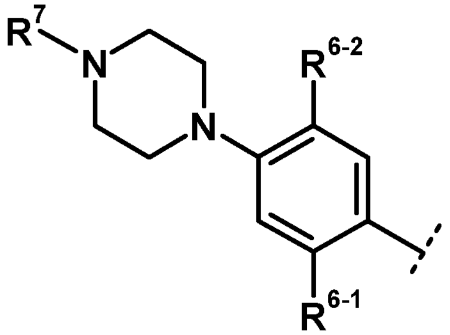
each **R^{d6}** is independently selected from among -OR^{e6}, -SR^{e6}, -N$R^{e6}R^{e6}$, halogen, -CN, -NO$_2$, -C(O)R^{e6}, -C(O)OR^{e6}, -C(O)N$R^{e6}R^{e6}$, -C(NR^{h6})N$R^{e6}R^{e6}$, -OC(O)R^{e6}, -OC(O)OR^{e6}, -S(O)$_2R^{e6}$, -S(O)$_2$N$R^{e6}R^{e6}$, -NR^{h6}C(O)R^{e6}, -NR^{h6}C(O)OR^{e6}, -NR^{h6}C(O)N$R^{e6}R^{e6}$, -NR^{h6}C(NR^{h6})N$R^{e6}R^{e6}$ and -NR^{h6}S(O)$_2R^{e6}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{e6}** is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl, and

each **R^{h6}** is independently selected from among hydrogen and C_{1-4}alkyl.

In another aspect **(CD27)** the invention relates to compounds **(I)**, wherein

R^3 denotes a group



;

R^{6-1} and **R^{6-2}** is independently selected from among hydrogen, C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen and

R^7 are as hereinbefore defined.

In further aspects **(CD28)** and **(CD29)** the invention relates to compounds with the structural aspect **(CD26)** and **(CD27)**, wherein

$\mathbf{R^7}$ is selected from among $\mathbf{R^{b6}}$ and $\mathbf{R^{c6}}$;

$\mathbf{R^{b6}}$ is selected from among -C(O)R^{c6}, -C(O)N$R^{c6}R^{c6}$ and -S(O)$_2$$R^{c6}$;

each $\mathbf{R^{c6}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d6}}$ and/or $\mathbf{R^{e6}}$ selected from among C_{1-6}alkyl, C_{3-6}cycloalkyl and 5- to 6-membered heterocyclyl;

each $\mathbf{R^{d6}}$ is independently selected from among -OR^{e6}, -N$R^{e6}R^{e6}$, halogen, -C(O)R^{e6} and -C(O)N$R^{e6}R^{e6}$ and

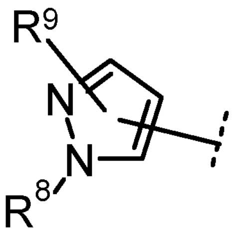
each $\mathbf{R^{e6}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl and 5- to 6-membered heterocyclyl.

In another aspect **(CD30)** the invention relates to compounds **(I)**, wherein

$\mathbf{R^3}$ denotes pyrazolyl, which is optionally mono- or disubstituted by C_{1-4}alkyl or C_{3-5}cycloalkyl.

In another aspect **(CD31)** the invention relates to compounds **(I)**, wherein

$\mathbf{R^3}$ denotes a group



;

$\mathbf{R^8}$ denotes a group optionally substituted by one or more identical or different $\mathbf{R^{b7}}$ and/or $\mathbf{R^{c7}}$ selected from among C_{1-6}alkyl, C_{3-6}cycloalkyl and 5- to 7-membered heterocyclyl;

each $\mathbf{R^{b7}}$ is independently selected from among -OR^{c7}, -N$R^{c7}R^{c7}$, halogen, -C(O)R^{c7} and -C(O)N$R^{c7}R^{c7}$;

each $\mathbf{R^{c7}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d7}}$ and/or $\mathbf{R^{e7}}$ selected from among C_{1-6}alkyl, C_{3-6}cycloalkyl, 5- to 6-membered heteroaryl and 5- to 7-membered heterocyclyl;

each $\mathbf{R^{d7}}$ is independently selected from among -OR^{e7}, -N$R^{e7}R^{e7}$, halogen, -C(O)R^{e7} and -C(O)N$R^{e7}R^{e7}$;

each **R**^{e7} independently denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{f7} and/or **R**^{g7} selected from among C_{1-6}alkyl, C_{3-6}cycloalkyl, 5- to 6-membered heteroaryl and 5- to 7-membered heterocyclyl;

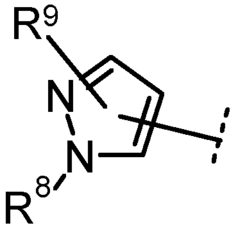
each **R**^{f7} is independently selected from among -OR^{g7}, -NR^{g7}R^{g7}, halogen, -C(O)R^{g7} and -C(O)NR^{g7}R^{g7};

each **R**^{g7} independently denotes hydrogen or C_{1-6}alkyl;

R^{9} is selected from among hydrogen, C_{1-4}alkyl and C_{3-5}cycloalkyl.

In another aspect **(CD32)** the invention relates to compounds **(I)**, wherein

R^{3} denotes a group



;

R^{8} is selected from among C_{1-4}alkyl, C_{3-5}cycloalkyl, C_{1-4}alkoxy-C_{1-4}alkyl, (C_{1-4}alkyl)NH-C_{1-4}alkyl and (C_{1-4}alkyl)$_2$N-C_{1-4}alkyl;

R^{9} is selected from among hydrogen, C_{1-4}alkyl and C_{3-5}cycloalkyl.

All the structural aspects **A1** to **A6**, **B1** to **B3**, **C1** to **C4**, **D1** to **D3**, **E1** to **E4** and **CD1** to **CD32** mentioned hereinbefore are preferred embodiments of the respective aspects **A0**, **B0**, **C0**, **D0**, **E0** and **CD0**, while **CD0** is a combination of **C0** and **D0**. The structural aspects **A0** to **A6**, **B0** to **B3**, **C0** to **C4**, **D0** to **D3**, **E0** to **E4** and **CD0** to **CD32** with respect to different molecular parts of the compounds **(I)** according to the invention may be permutated with one another as desired to form **ABCDE** combinations, thus obtaining preferred compounds **(I)**. Each **ABCDE** combination represents and defines individual embodiments or generic partial amounts of compounds **A0B0C0D0E0** according to the invention. Every individual embodiment or partial quantity defined by this combination is expressly included in and a subject of the invention.

Preferred compounds **(I)** are:

I-168 (5S)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-

	dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-194	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-201	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-204	N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-222	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-271	(5S)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-225	N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-9-[(3-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine
I-205	1-[4-[4-[[9-[4-(difluoromethoxy)phenyl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]pyrazol-1-yl]piperidin-1-yl]ethanone;
I-198	N-[1-[2-[2-methoxyethyl(methyl)amino]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-197	8-methyl-9-phenyl-N-[1-(2-pyrrolidin-1-ylethyl)pyrazol-3-yl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-195	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-(naphthalen-1-ylmethyl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-193	9-[(2-chlorophenyl)methyl]-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-189	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-(3-methylthiophen-2-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-187	N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-9-[(2-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-186	1-[4-[4-[(5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl)amino]pyrazol-1-yl]piperidin-1-yl]ethanone;
I-185	8-methyl-N-[1-[2-(4-methylpiperazin-1-yl)ethyl]pyrazol-3-yl]-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-171	9-(4-chlorophenyl)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;

I-166	2-[4-[2-[3-[(8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl)amino]pyrazol-1-yl]ethyl]piperazin-1-yl]ethanol;
I-167	N-[1-[2-[4-(2-methoxyethyl)piperazin-1-yl]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-217	9-[(3-methoxyphenyl)methyl]-8-methyl-N-(1-methylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-210	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-208	9-benzyl-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-192	9-[(2-chlorophenyl)methyl]-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-182	8-methyl-9-phenyl-N-[1-(2-piperazin-1-ylethyl)pyrazol-3-yl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-180	9-(3-chlorothiophen-2-yl)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-176	1-[4-[4-[[9-(4-methoxyphenyl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]pyrazol-1-yl]piperidin-1-yl]ethanone;
I-175	N-[1-[2-[4-(dimethylamino)piperidin-1-yl]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-181	9-(3-chlorothiophen-2-yl)-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-202	9-[(2-chlorophenyl)methyl]-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-224	N-(1-ethylpyrazol-3-yl)-8-methyl-9-[(3-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-237	9-[4-(difluoromethoxy)phenyl]-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-236	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-dimethylaminoethyl)pyrazol-4-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-30	9-(2-chlorophenyl)-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-112	4-[[9-(2-chlorophenyl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-

	yl]amino]-3-methoxy-N-(1-methylpiperidin-4-yl)benzamide;
I-40	9-(2-chlorophenyl)-5,8-dimethyl-N-(1-propane-2-ylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-42	9-(2-chlorophenyl)-5,8-dimethyl-N-(1-methylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-97	9-(2-chlorophenyl)-N-[2-methoxy-4-(4-methylpiperazin-1-yl)phenyl]-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-157	4-[[9-(2-chlorophenyl)-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]-3-methoxy-N-(1-methylpiperidin-4-yl)benzamide;
II-8	4-[[9-(2-chlorophenyl)-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]-3-methoxybenzoic acid;

The present invention further relates to hydrates, solvates, polymorphs, metabolites, derivatives and prodrugs of compounds of general formula **(I)**.

In another aspect the invention relates to compounds of general formula **(I)** – or the pharmaceutically acceptable salts thereof – as medicaments.

In another aspect the invention relates to compounds of general formula **(I)** – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer, infections, inflammations and autoimmune diseases.

In another aspect the invention relates to compounds of general formula **(I)** – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer.

In another aspect the invention relates to compounds of general formula **(I)** – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of non-small-cell lung cancers (NSCLC) and hepatocellular carcinomas (HCC).

In another aspect the invention relates to a method for the treatment and/or prevention of cancer comprising administering a therapeutically effective amount of a compound of general formula **(I)** – or one of the pharmaceutically acceptable salts thereof – to a human.

In another aspect the invention relates to a pharmaceutical preparation containing as active substance one or more compounds of general formula **(I)** – or the pharmaceutically acceptable salts thereof – optionally in combination with conventional excipients and/or carriers.

In another aspect the invention relates to a pharmaceutical preparation comprising a compound of general formula **(I)** – or one of the pharmaceutically acceptable salts thereof – and at least one further cytostatic or cytotoxic active substance, different from formula **(I)**.

Definitions

Terms that are not specifically defined here have the meanings that are apparent to the skilled man in the light of the overall disclosure and the context as a whole.

As used herein, the following definitions apply, unless stated otherwise:

The use of the prefix $\mathbf{C}_{\mathbf{x}\text{-}\mathbf{y}}$, wherein **x** and **y** each represent a natural number (**x** < **y**), indicates that the chains or ring structure or combination of chains and ring structure as a whole, specified and mentioned in direct association, may consist of a maximum of **y** and a minimum of **x** carbon atoms.

The indication of the number of members in groups that contain one or more heteroatom(s) (heteroalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocyclylalkyl) relates to the total atomic number of all the ring members or chain members or the total of all the ring and chain members.

Alkyl denotes monovalent, saturated hydrocarbon chains, which may be present in both straight-chain (unbranched) and branched form. If an **alkyl** is substituted, the substitution may take place independently of one another, by mono- or polysubstitution in each case, on all the hydrogen-carrying carbon atoms.

The term "**$\mathbf{C}_{1\text{-}5}$-alkyl**" includes for example H_3C-, H_3C-CH_2-, H_3C-CH_2-CH_2-, H_3C-$CH(CH_3)$-, H_3C-CH_2-CH_2-CH_2-, H_3C-CH_2-$CH(CH_3)$-, H_3C-$CH(CH_3)$-CH_2-, H_3C-$C(CH_3)_2$-, H_3C-CH_2-CH_2-CH_2-CH_2-, H_3C-CH_2-CH_2-$CH(CH_3)$-, H_3C-CH_2-$CH(CH_3)$-CH_2-, H_3C-$CH(CH_3)$-CH_2-CH_2-, H_3C-CH_2-$C(CH_3)_2$-, H_3C-$C(CH_3)_2$-CH_2-, H_3C-$CH(CH_3)$-$CH(CH_3)$- and H_3C-CH_2-$CH(CH_2CH_3)$-.

Further examples of **alkyl** are methyl (Me; -CH_3), ethyl (Et; -CH_2CH_3), 1-propyl (*n*-propyl; *n*-Pr; -$CH_2CH_2CH_3$), 2-propyl (*i*-Pr; *iso*-propyl; -$CH(CH_3)_2$), 1-butyl (*n*-butyl; *n*-Bu;

$-CH_2CH_2CH_2CH_3$), 2-methyl-1-propyl (*iso*-butyl; *i*-Bu; $-CH_2CH(CH_3)_2$), 2-butyl (*sec*-butyl; *sec*-Bu; $-CH(CH_3)CH_2CH_3$), 2-methyl-2-propyl (*tert*-butyl; *t*-Bu; $-C(CH_3)_3$), 1-pentyl (*n*-pentyl; $-CH_2CH_2CH_2CH_2CH_3$), 2-pentyl ($-CH(CH_3)CH_2CH_2CH_3$), 3-pentyl ($-CH(CH_2CH_3)_2$), 3-methyl-1-butyl (*iso*-pentyl; $-CH_2CH_2CH(CH_3)_2$), 2-methyl-2-butyl ($-C(CH_3)_2CH_2CH_3$), 3-methyl-2-butyl ($-CH(CH_3)CH(CH_3)_2$), 2,2-dimethyl-1-propyl (*neo*-pentyl; $-CH_2C(CH_3)_3$), 2-methyl-1-butyl ($-CH_2CH(CH_3)CH_2CH_3$), 1-hexyl (*n*-hexyl; $-CH_2CH_2CH_2CH_2CH_2CH_3$), 2-hexyl ($-CH(CH_3)CH_2CH_2CH_2CH_3$), 3-hexyl ($-CH(CH_2CH_3)(CH_2CH_2CH_3)$), 2-methyl-2-pentyl ($-C(CH_3)_2CH_2CH_2CH_3$), 3-methyl-2-pentyl ($-CH(CH_3)CH(CH_3)CH_2CH_3$), 4-methyl-2-pentyl ($-CH(CH_3)CH_2CH(CH_3)_2$), 3-methyl-3-pentyl ($-C(CH_3)(CH_2CH_3)_2$), 2-methyl-3-pentyl ($-CH(CH_2CH_3)CH(CH_3)_2$), 2,3-dimethyl-2-butyl ($-C(CH_3)_2CH(CH_3)_2$), 3,3-dimethyl-2-butyl ($-CH(CH_3)C(CH_3)_3$), 2,3-dimethyl-1-butyl ($-CH_2CH(CH_3)CH(CH_3)CH_3$), 2,2-dimethyl-1-butyl ($-CH_2C(CH_3)_2CH_2CH_3$), 3,3-dimethyl-1-butyl ($-CH_2CH_2C(CH_3)_3$), 2-methyl-1-pentyl ($-CH_2CH(CH_3)CH_2CH_2CH_3$), 3-methyl-1-pentyl ($-CH_2CH_2CH(CH_3)CH_2CH_3$), 1-heptyl (*n*-heptyl), 2-methyl-1-hexyl, 3-methyl-1-hexyl, 2,2-dimethyl-1-pentyl, 2,3-dimethyl-1-pentyl, 2,4-dimethyl-1-pentyl, 3,3-dimethyl-1-pentyl, 2,2,3-trimethyl-1-butyl, 3-ethyl-1-pentyl, 1-octyl (*n*-octyl), 1-nonyl (*n*-nonyl); 1-decyl (*n*-decyl) etc.

By the terms propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl etc. without any further definition are meant saturated hydrocarbon groups with the corresponding number of carbon atoms, wherein all isomeric forms are included.

The above definition for **alkyl** also applies if **alkyl** is a part of another group such as for example C_{x-y}-**alkyl**amino or C_{x-y}-**alkyl**oxy.

The term **alkylene** can also be derived from **alkyl**. **Alkylene** is bivalent, unlike **alkyl,** and requires two binding partners. Formally, the second valency is produced by removing a hydrogen atom in an **alkyl**. Corresponding groups are for example $-CH_3$ and $-CH_2$, $-CH_2CH_3$ and $-CH_2CH_2$ or $>CHCH_3$ etc.

The term "**C_{1-4}-alkylene**" includes for example $-(CH_2)-$, $-(CH_2-CH_2)-$, $-(CH(CH_3))-$, $-(CH_2-CH_2-CH_2)-$, $-(C(CH_3)_2)-$, $-(CH(CH_2CH_3))-$, $-(CH(CH_3)-CH_2)-$, $-(CH_2-CH(CH_3))-$, $-(CH_2-CH_2-CH_2-CH_2)-$, $-(CH_2-CH_2-CH(CH_3))-$, $-(CH(CH_3)-CH_2-CH_2)-$, $-(CH_2-CH(CH_3)-CH_2)-$, $-(CH_2-C(CH_3)_2)-$, $-(C (CH_3)_2-CH_2)-$, $-(CH(CH_3)-CH(CH_3))-$, $-(CH_2-CH(CH_2CH_3))-$, $-(CH(CH_2CH_3)-CH_2)-$, $-(CH(CH_2CH_2CH_3))-$, $-(CHCH(CH_3)_2)-$ and $-C(CH_3)(CH_2CH_3)-$.

Other examples of **alkylene** are methylene, ethylene, propylene, 1-methylethylene, butylene, 1-methylpropylene, 1,1-dimethylethylene, 1,2-dimethylethylene, pentylene, 1,1-dimethylpropylene, 2,2-dimethylpropylene, 1,2-dimethylpropylene, 1,3-dimethylpropylene, hexylene etc.

By the generic terms propylene, butylene, pentylene, hexylene etc. without any further definition are meant all the conceivable isomeric forms with the corresponding number of carbon atoms, i.e. propylene includes 1-methylethylene and butylene includes 1-methylpropylene, 2-methylpropylene, 1,1-dimethylethylene and 1,2-dimethylethylene.

The above definition for **alkylene** also applies if **alkylene** is part of another group such as for example in HO-C_{x-y}-**alkylen**amino or H_2N-C_{x-y}-**alkylen**oxy.

Unlike **alkyl, <u>alkenyl</u>** consists of at least two carbon atoms, wherein at least two adjacent carbon atoms are joined together by a C-C double bond. If in an **alkyl** as hereinbefore defined having at least two carbon atoms, two hydrogen atoms on adjacent carbon atoms are formally removed and the free valencies are saturated to form a second bond, the corresponding **alkenyl** is formed.

Examples of **alkenyl** are vinyl (ethenyl), prop-1-enyl, allyl (prop-2-enyl), isopropenyl, but-1-enyl, but-2-enyl, but-3-enyl, 2-methyl-prop-2-enyl, 2-methyl-prop-1-enyl, 1-methyl-prop-2-enyl, 1-methyl-prop-1-enyl, 1-methylidenepropyl, pent-1-enyl, pent-2-enyl, pent-3-enyl, pent-4-enyl, 3-methyl-but-3-enyl, 3-methyl-but-2-enyl, 3-methyl-but-1-enyl, hex-1-enyl, hex-2-enyl, hex-3-enyl, hex-4-enyl, hex-5-enyl, 2,3-dimethyl-but-3-enyl, 2,3-dimethyl-but-2-enyl, 2-methylidene-3-methylbutyl, 2,3-dimethyl-but-1-enyl, hexa-1,3-dienyl, hexa-1,4-dienyl, penta-1,4-dienyl, penta-1,3-dienyl, buta-1,3-dienyl, 2,3-dimethylbuta-1,3-diene etc.

By the generic terms propenyl, butenyl, pentenyl, hexenyl, butadienyl, pentadienyl, hexadienyl, heptadienyl, octadienyl, nonadienyl, decadienyl etc. without any further definition are meant all the conceivable isomeric forms with the corresponding number of carbon atoms, i.e. propenyl includes prop-1-enyl and prop-2-enyl, butenyl includes but-1-enyl, but-2-enyl, but-3-enyl, 1-methyl-prop-1-enyl, 1-methyl-prop-2-enyl etc.

Alkenyl may optionally be present in the *cis* or *trans* or *E* or *Z* orientation with regard to the double bond(s).

The above definition for **alkenyl** also applies when **alkenyl** is part of another group such as for example in C_{x-y}-**alkenyl**amino or C_{x-y}-**alkenyl**oxy.

Unlike **alkylene,** **alkenylene** consists of at least two carbon atoms, wherein at least two adjacent carbon atoms are joined together by a C-C double bond. If in an **alkylene** as hereinbefore defined having at least two carbon atoms, two hydrogen atoms at adjacent carbon atoms are formally removed and the free valencies are saturated to form a second bond, the corresponding **alkenylene** is formed.

Examples of **alkenylene** are ethenylene, propenylene, 1-methylethenylene, butenylene, 1-methylpropenylene, 1,1-dimethylethenylene, 1,2-dimethylethenylene, pentenylene, 1,1-dimethylpropenylene, 2,2-dimethylpropenylene, 1,2-dimethylpropenylene, 1,3-dimethylpropenylene, hexenylene etc.

By the generic terms propenylene, butenylene, pentenylene, hexenylene etc. without any further definition are meant all the conceivable isomeric forms with the corresponding number of carbon atoms, i.e. propenylene includes 1-methylethenylene and butenylene includes 1-methylpropenylene, 2-methylpropenylene, 1,1-dimethylethenylene and 1,2-dimethylethenylene.

Alkenylene may optionally be present in the *cis* or *trans* or *E* or *Z* orientation with regard to the double bond(s).

The above definition for **alkenylene** also applies when **alkenylene** is a part of another group as in for example HO-C_{x-y}-**alkenylen**amino or H_2N-C_{x-y}-**alkenylen**oxy.

Unlike **alkyl,** **alkynyl** consists of at least two carbon atoms, wherein at least two adjacent carbon atoms are joined together by a C-C triple bond. If in an **alkyl** as hereinbefore defined having at least two carbon atoms, two hydrogen atoms in each case at adjacent carbon atoms are formally removed and the free valencies are saturated to form two further bonds, the corresponding **alkynyl** is formed.

Examples of **alkynyl** are ethynyl, prop-1-ynyl, prop-2-ynyl, but-1-ynyl, but-2-ynyl, but-3-ynyl, 1-methyl-prop-2-ynyl, pent-1-ynyl, pent-2-ynyl, pent-3-ynyl, pent-4-ynyl, 3-methyl-but-1-ynyl, hex-1-ynyl, hex-2-ynyl, hex-3-ynyl, hex-4-ynyl, hex-5-ynyl etc.

By the generic terms propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl etc. without any further definition are meant all the conceivable isomeric forms with the corresponding number of carbon atoms, i.e. propynyl includes prop-1-ynyl and prop-2-ynyl, butynyl includes but-1-ynyl, but-2-ynyl, but-3-ynyl, 1-methyl-prop-1-ynyl, 1-methyl-prop-2-ynyl, etc.

If a hydrocarbon chain carries both at least one double bond and also at least one triple bond, by definition it belongs to the **alkynyl** subgroup.

The above definition for **alkynyl** also applies if **alkynyl** is part of another group, as in C_{x-y}-**alkynyl**amino or C_{x-y}-**alkynyl**oxy, for example.

Unlike **alkylene, <u>alkynylene</u>** consists of at least two carbon atoms, wherein at least two adjacent carbon atoms are joined together by a C-C triple bond. If in an **alkylene** as hereinbefore defined having at least two carbon atoms, two hydrogen atoms in each case at adjacent carbon atoms are formally removed and the free valencies are saturated to form two further bonds, the corresponding **alkynylene** is formed.

Examples of **alkynylene** are ethynylene, propynylene, 1-methylethynylene, butynylene, 1-methylpropynylene, 1,1-dimethylethynylene, 1,2-dimethylethynylene, pentynylene, 1,1-dimethylpropynylene, 2,2-dimethylpropynylene, 1,2-dimethylpropynylene, 1,3-dimethylpropynylene, hexynylene etc.

By the generic terms propynylene, butynylene, pentynylene, hexynylene etc. without any further definition are meant all the conceivable isomeric forms with the corresponding number of carbon atoms, *i.e.* propynylene includes 1-methylethynylene and butynylene includes 1-methylpropynylene, 2-methylpropynylene, 1,1-dimethylethynylene and 1,2-dimethylethynylene.

The above definition for **alkynylene** also applies if **alkynylene** is part of another group, as in HO-C_{x-y}-**alkynylene**amino or H_2N-C_{x-y}-**alkynylene**oxy, for example.

By **<u>heteroatoms</u>** are meant oxygen, nitrogen and sulphur atoms.

<u>Haloalkyl (haloalkenyl, haloalkynyl)</u> is derived from the previously defined **alkyl (alkenyl, alkynyl)** by replacing one or more hydrogen atoms of the hydrocarbon chain independently of one another by halogen atoms, which may be identical or different. If a **haloalkyl (haloalkenyl, haloalkynyl)** is to be further substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon atoms.

Examples of **haloalkyl (haloalkenyl, haloalkynyl)** are $-CF_3$, $-CHF_2$, $-CH_2F$, $-CF_2CF_3$, $-CHFCF_3$, $-CH_2CF_3$, $-CF_2CH_3$, $-CHFCH_3$, $-CF_2CF_2CF_3$, $-CF_2CH_2CH_3$, $-CF{=}CF_2$, $-CCl{=}CH_2$, $-CBr{=}CH_2$, $-CI{=}CH_2$, $-C{\equiv}C{-}CF_3$, $-CHFCH_2CH_3$, $-CHFCH_2CF_3$ etc.

From the previously defined **haloalkyl (haloalkenyl, haloalkynyl)** are also derived the terms **<u>haloalkylene (haloalkenylene, haloalkynylene)</u>**. **Haloalkylene (haloalkenyl,**

haloalkynyl), unlike **haloalkyl**, is bivalent and requires two binding partners. Formally, the second valency is formed by removing a hydrogen atom from a **haloalkyl**.

Corresponding groups are for example $-CH_2F$ and -CHF-, $-CHFCH_2F$ and -CHFCHF- or $>CFCH_2F$ etc.

The above definitions also apply if the corresponding halogen groups are part of another group.

__Halogen__ relates to fluorine, chlorine, bromine and/or iodine atoms.

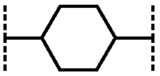
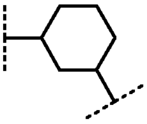
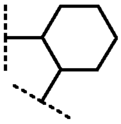
__Cycloalkyl__ is made up of the subgroups **monocyclic hydrocarbon rings**, **bicyclic hydrocarbon rings** and **spiro-hydrocarbon rings**. The systems are saturated. In bicyclic hydrocarbon rings two rings are joined together so that they have at least two carbon atoms together. In spiro-hydrocarbon rings a carbon atom (spiroatom) belongs to two rings together. If a **cycloalkyl** is to be substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon atoms. **Cycloalkyl** itself may be linked as a substituent to the molecule via every suitable position of the ring system.

Examples of **cycloalkyl** are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, bicyclo[2.2.0]hexyl, bicyclo[3.2.0]heptyl, bicyclo[3.2.1]octyl, bicyclo[2.2.2]octyl, bicyclo[4.3.0]nonyl (octahydroindenyl), bicyclo[4.4.0]decyl (decahydronaphthalene), bicyclo[2.2.1]heptyl (norbornyl), bicyclo[4.1.0]heptyl (norcaranyl), bicyclo-[3.1.1]heptyl (pinanyl), spiro[2.5]octyl, spiro[3.3]heptyl etc.

The above definition for **cycloalkyl** also applies if **cycloalkyl** is part of another group as in C_{x-y}-**cycloalkyl**amino or C_{x-y}-**cycloalkyl**oxy, for example.

If the free valency of a **cycloalkyl** is saturated, then an __alicyclic group__ is obtained.

The term __cycloalkylene__ can thus be derived from the previously defined **cycloalkyl**. **Cycloalkylene**, unlike **cycloalkyl**, is bivalent and requires two binding partners. Formally, the second valency is obtained by removing a hydrogen atom from a **cycloalkyl**. Corresponding groups are for example

cyclohexyl and  or  or  (cyclohexylene).

The above definition for **cycloalkylene** also applies if **cycloalkylene** is part of another group as in HO-C_{x-y}-**cycloalkylene**amino or H_2N-C_{x-y}-**cycloalkylene**oxy, for example.

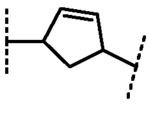
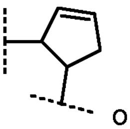
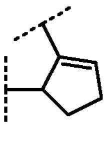
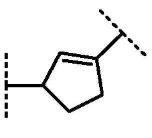
Cycloalkenyl is also made up of the subgroups **monocyclic hydrocarbon rings**, **bicyclic hydrocarbon rings** and **spiro-hydrocarbon rings**. However, the systems are unsaturated, i.e. there is at least one C-C double bond but no aromatic system. If in a **cycloalkyl** as hereinbefore defined two hydrogen atoms at adjacent cyclic carbon atoms are formally removed and the free valencies are saturated to form a second bond, the corresponding **cycloalkenyl** is obtained. If a **cycloalkenyl** is to be substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon atoms. **Cycloalkenyl** itself may be linked as a substituent to the molecule via every suitable position of the ring system.

Examples of **cycloalkenyl** are cycloprop-1-enyl, cycloprop-2-enyl, cyclobut-1-enyl, cyclobut-2-enyl, cyclopent-1-enyl, cyclopent-2-enyl, cyclopent-3-enyl, cyclohex-1-enyl, cyclohex-2-enyl, cyclohex-3-enyl, cyclohept-1-enyl, cyclohept-2-enyl, cyclohept-3-enyl, cyclohept-4-enyl, cyclobuta-1,3-dienyl, cyclopenta-1,4-dienyl, cyclopenta-1,3-dienyl, cyclopenta-2,4-dienyl, cyclohexa-1,3-dienyl, cyclohexa-1,5-dienyl, cyclohexa-2,4-dienyl, cyclohexa-1,4-dienyl, cyclohexa-2,5-dienyl, bicyclo[2.2.1]hepta-2,5-dienyl (norborna-2,5-dienyl), bicyclo[2.2.1]hept-2-enyl (norbornenyl), spiro[4.5]dec-2-ene etc.

The above definition for **cycloalkenyl** also applies when **cycloalkenyl** is part of another group as in C_{x-y}-**cycloalkenyl**amino or C_{x-y}-**cycloalkenyl**oxy, for example.

If the free valency of a **cycloalkenyl** is saturated, then an **unsaturated alicyclic group** is obtained.

The term **cycloalkenylene** can thus be derived from the previously defined **cycloalkenyl**. **Cycloalkenylene**, unlike **cycloalkenyl**, is bivalent and requires two binding partners. Formally the second valency is obtained by removing a hydrogen atom from a **cycloalkenyl**. Corresponding groups are for example

cyclopentenyl and  or  or  or  (cyclopentenylene)

etc.

The above definition for **cycloalkenylene** also applies when **cycloalkenylene** is part of another group as in HO-C_{x-y}-**cycloalkenylene**amino or H_2N-C_{x-y}-**cycloalkenylene**oxy, for example.

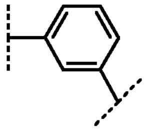
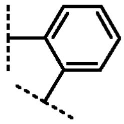
Aryl denotes a mono-, bi- or tricyclic group with at least one aromatic carbocycle. Preferably it denotes a monocyclic group with six carbon atoms (phenyl) or a bicyclic group with nine or ten carbon atoms (two six-membered rings or one six-membered ring with a five-membered ring), wherein the second ring may also be aromatic or, however, may also be saturated or partially saturated. If an **aryl** is to be substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon atoms. **Aryl** itself may be linked as a substituent to the molecule via every suitable position of the ring system.

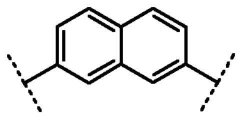
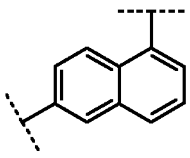
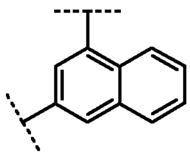
Examples of **aryl** are phenyl, naphthyl, indanyl (2,3-dihydroindenyl), indenyl, anthracenyl, phenanthrenyl, tetrahydronaphthyl (1,2,3,4-tetrahydronaphthyl, tetralinyl), dihydronaphthyl (1,2- dihydronaphthyl), fluorenyl etc.

The above definition of **aryl** also applies when **aryl** is part of another group as in **aryl**amino or **aryl**oxy, for example.

If the free valency of an **aryl** is saturated, then an **aromatic group** is obtained.

The term **arylene** can also be derived from the previously defined **aryl**. **Arylene**, unlike **aryl**, is bivalent and requires two binding partners. Formally, the second valency is formed by removing a hydrogen atom from an **aryl**. Corresponding groups are e.g.

phenyl and  or  or  (*o*, *m*, *p*-phenylene),

naphthyl and  or  or  etc.

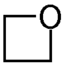
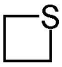
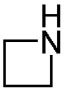
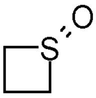
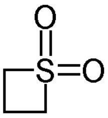
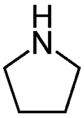
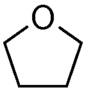
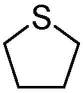
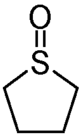
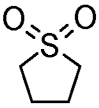
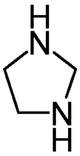
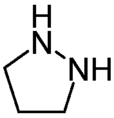
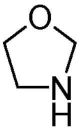
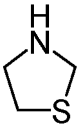
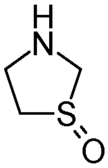
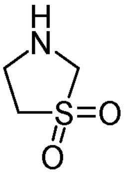
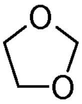
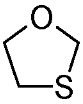
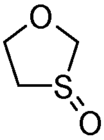
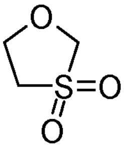
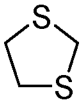
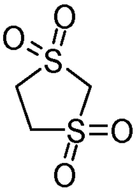
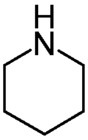
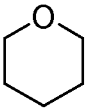
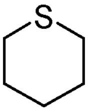
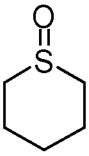
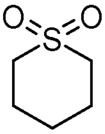
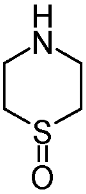
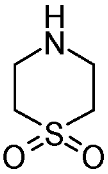
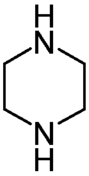
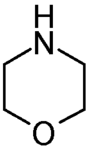
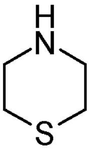
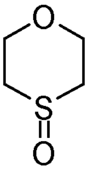
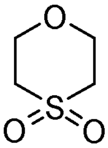
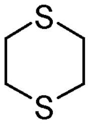
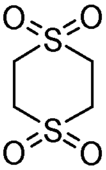
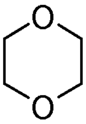
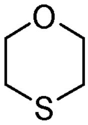
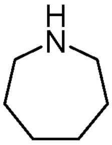
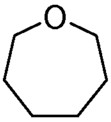
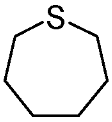
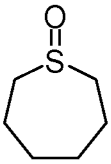
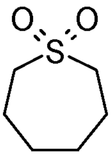
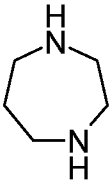
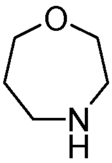
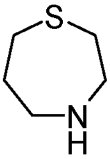
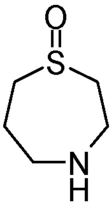
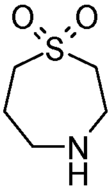
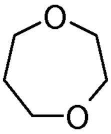
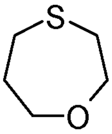
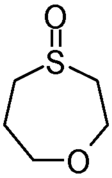
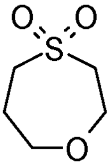
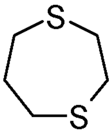
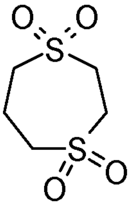
The above definition for **arylene** also applies when **arylene** is part of another group as in HO-**arylene**amino or H_2N-**arylene**oxy for example.

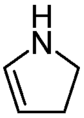
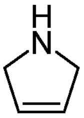
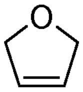
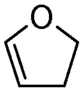
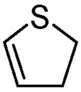
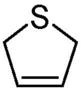
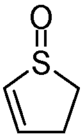
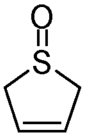
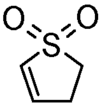
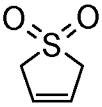
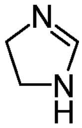
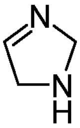
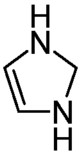
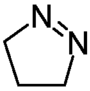
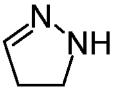
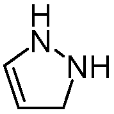
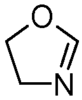
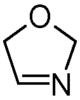
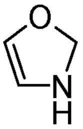
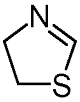
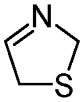
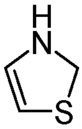
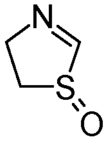
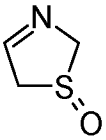
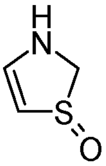
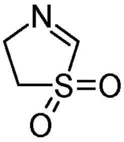
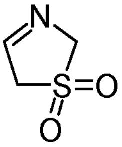
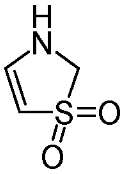
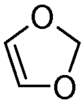
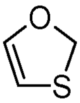
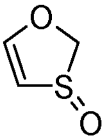
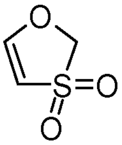
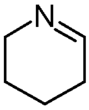
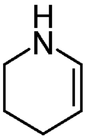
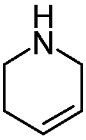
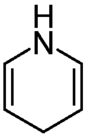
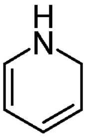
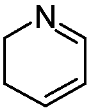
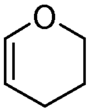
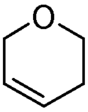
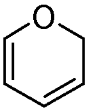
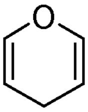
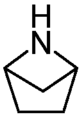
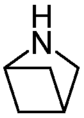
Heterocyclyl denotes ring systems, which are derived from the previously defined **cycloalkyl**, **cycloalkenyl** and **aryl** by replacing one or more of the groups $-CH_2-$ independently of one another in the hydrocarbon rings by the groups -O-, -S- or -NH- or by replacing one or more of the groups =CH- by the group =N-, wherein a total of not more than five heteroatoms may be present, at least one carbon atom may be present between two oxygen atoms and between two sulphur atoms or between one oxygen and one sulphur atom and the ring as a whole must have chemical stability. Heteroatoms may optionally be present in all the possible oxidation stages (sulphur → sulphoxide -SO-, sulphone $-SO_2-$; nitrogen → N-oxide). In a **heterocyclyl** there is no heteroaromatic ring, i.e. no heteratom is part of an aromatic system.

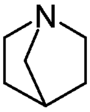
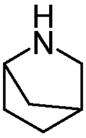
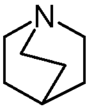
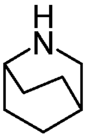
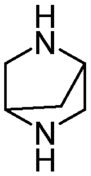
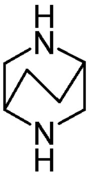
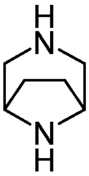
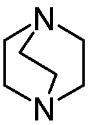
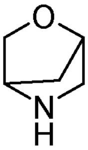
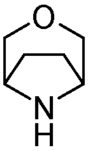
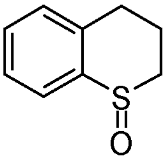
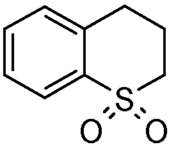
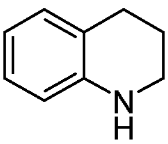
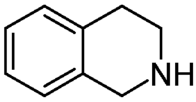
A direct result of the derivation from **cycloalkyl**, **cycloalkenyl** and **aryl** is that **heterocyclyl** is made up of the subgroups **monocyclic heterorings**, **bicyclic heterorings**, **tricyclic heterorings** and **spiro-heterorings**, which may be present in saturated or unsaturated form. By unsaturated is meant that there is at least one double bond in the ring system in question, but no heteroaromatic system is formed. In bicyclic heterorings two rings are linked together so that they have at least two (hetero)atoms in common. In spiro-heterorings a carbon atom (spiroatom) belongs to two rings together. If a **heterocyclyl** is substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon and/or nitrogen atoms. **Heterocyclyl** itself may be linked as a substituent to the molecule via every suitable position of the ring system.

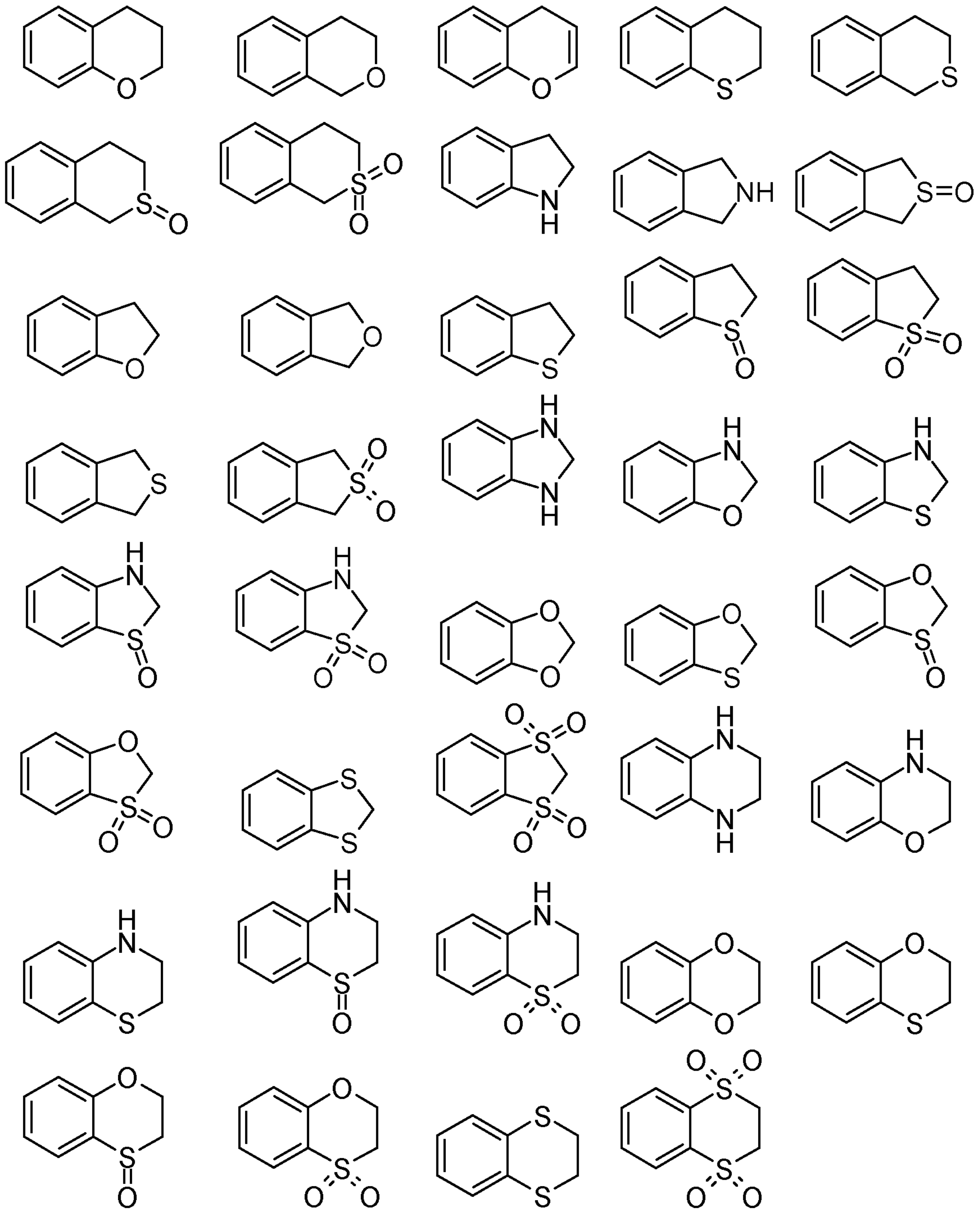
Examples of **heterocyclyl** are tetrahydrofuryl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, thiazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidinyl, piperazinyl, oxiranyl, aziridinyl, azetidinyl, 1,4-dioxanyl, azepanyl, diazepanyl, morpholinyl, thiomorpholinyl, homomorpholinyl, homopiperidinyl, homopiperazinyl, homothiomorpholinyl, thiomorpholinyl-*S*-oxide, thiomorpholinyl-*S,S*-dioxide, 1,3-dioxolanyl, tetrahydropyranyl, tetrahydrothiopyranyl, [1,4]-oxazepanyl, tetrahydrothienyl, homothiomorpholinyl-*S,S*-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridyl, dihydro-pyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl-*S*-oxide, tetrahydrothienyl-*S,S*-dioxide, homothiomorpholinyl-*S*-oxide, 2,3-dihydroazet, 2*H*-pyrrolyl, 4*H*-pyranyl, 1,4-dihydropyridinyl, 8-azabicyclo[3.2.1]octyl, 8-azabicyclo[5.1.0]octyl, 2-oxa-5-azabicyclo[2.2.1]heptyl, 8-oxa-3-aza-bicyclo[3.2.1]octyl, 3,8-diaza-bicyclo[3.2.1]octyl, 2,5-diaza-bicyclo-[2.2.1]heptyl, 1-aza-bicyclo[2.2.2]octyl, 3,8-diaza-bicyclo[3.2.1]octyl, 3,9-diaza-bicyclo[4.2.1]nonyl, 2,6-diaza-bicyclo[3.2.2]nonyl, 1,4-dioxa-spiro[4.5]decyl, 1-oxa-3,8-diaza-spiro[4.5]decyl, 2,6-diaza-spiro[3.3]heptyl, 2,7-diaza-spiro[4.4]nonyl, 2,6-diaza-spiro[3.4]octyl, 3,9-diaza-spiro[5.5]undecyl, 2,8-diaza-spiro[4.5]decyl etc.

Further examples are the structures illustrated below, which may be attached via each hydrogen-carrying atom (exchanged for hydrogen):

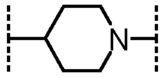
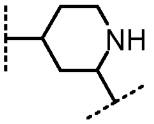
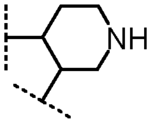


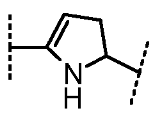
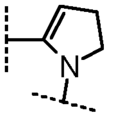
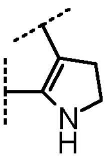
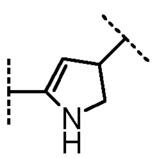
The above definition of **heterocyclyl** also applies if **heterocyclyl** is part of another group as in **heterocyclyl**amino or **heterocyclyl**oxy for example.

If the free valency of a **heterocyclyl** is saturated, then a **heterocyclic group** is obtained.

The term **heterocyclylene** is also derived from the previously defined **heterocyclyl**. **Heterocyclylene**, unlike **heterocyclyl**, is bivalent and requires two binding partners.

Formally, the second valency is obtained by removing a hydrogen atom from a **heterocyclyl**. Corresponding groups are for example

piperidinyl and  or  or  ,

2,3-dihydro-1*H*-pyrrolyl and  or  or  or  etc.

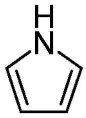
The above definition of **heterocyclylene** also applies if **heterocyclylene** is part of another group as in HO-**heterocyclylene**amino or H_2N-**heterocyclylene**oxy for example.

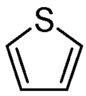
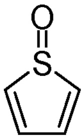
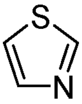
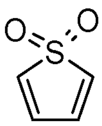
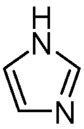
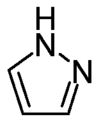
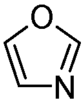
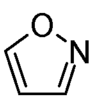
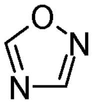
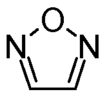
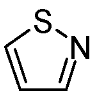
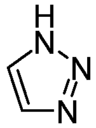
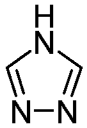
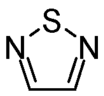
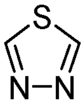
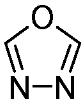
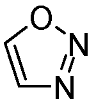
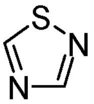
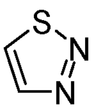
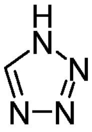
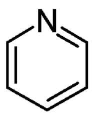
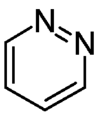
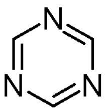
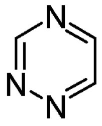
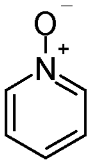
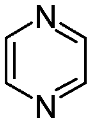
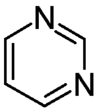
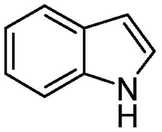
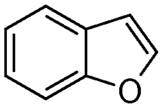
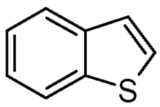
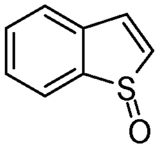
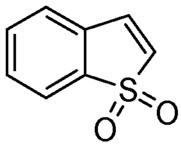
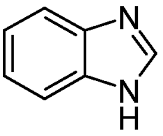
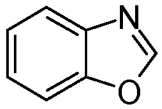
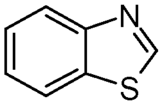
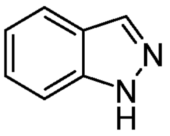
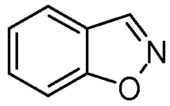
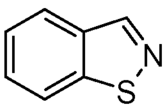
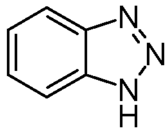
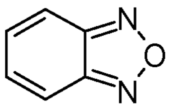
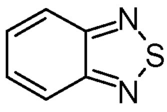
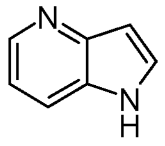
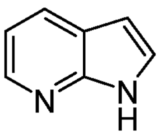
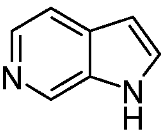
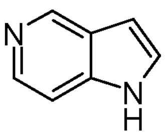
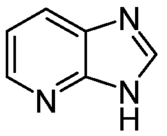
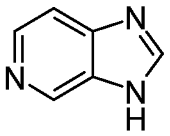
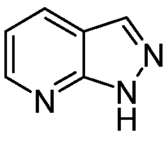
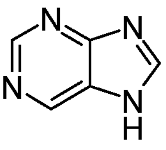
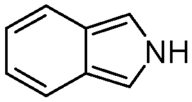
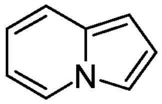
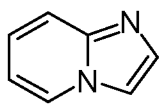
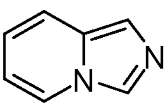
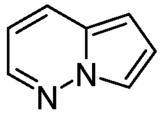
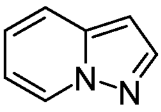
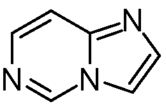
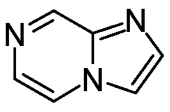
Heteroaryl denotes monocyclic heteroaromatic rings or polycyclic rings with at least one heteroaromatic ring, which compared with the corresponding **aryl** or **cycloalkyl (cycloalkenyl)** contain, instead of one or more carbon atoms, one or more identical or different heteroatoms, selected independently of one another from among nitrogen, sulphur and oxygen, wherein the resulting group must be chemically stable. The prerequisite for the presence of **heteroaryl** is a heteroatom and a heteroaromatic system. If a **heteroaryl** is to be substituted, the substitutions may take place independently of one another, in the form of mono- or polysubstitutions in each case, on all the hydrogen-carrying carbon and/or nitrogen atoms. **Heteroaryl** itself may be linked as a substituent to the molecule via every suitable position of the ring system, both carbon and nitrogen.

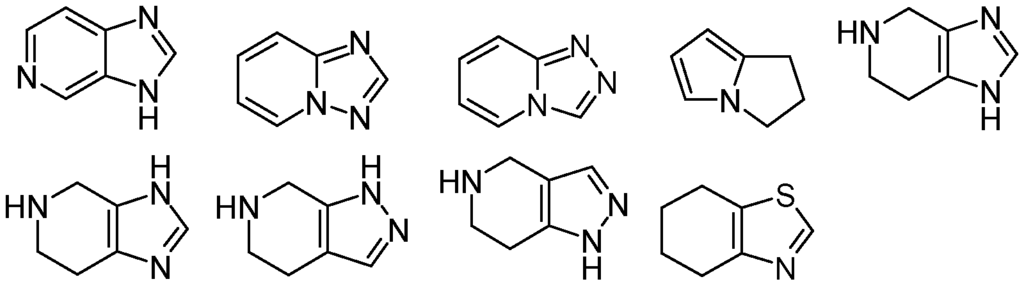
Examples of **heteroaryl** are furyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrimidyl, pyridazinyl, pyrazinyl, triazinyl, pyridyl-*N*-oxide, pyrrolyl-*N*-oxide, pyrimidinyl-*N*-oxide, pyridazinyl-*N*-oxide, pyrazinyl-*N*-oxide, imidazolyl-*N*-oxide, isoxazolyl-*N*-oxide, oxazolyl-*N*-oxide, thiazolyl-*N*-oxide, oxadiazolyl-*N*-oxide, thiadiazolyl-*N*-oxide, triazolyl-*N*-oxide, tetrazolyl-*N*-oxide, indolyl, isoindolyl, benzofuryl, benzothienyl, benzoxazolyl, benzothiazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolyl, indazolyl, isoquinolinyl, quinolinyl, quinoxalinyl, cinnolinyl, phthalazinyl, quinazolinyl, benzotriazinyl, indolizinyl, oxazolopyridyl, imidazopyridyl, naphthyridinyl, benzoxazolyl, pyridopyridyl, purinyl, pteridinyl, benzothiazolyl, imidazopyridyl, imidazothiazolyl, quinolinyl-*N*-oxide, indolyl-*N*-oxide, isoquinolyl-*N*-oxide, quinazolinyl-*N*-oxide, quinoxalinyl-*N*-oxide, phthalazinyl-*N*-oxide, indolizinyl-*N*-oxide, indazolyl-*N*-oxide, benzothiazolyl-*N*-oxide, benzimidazolyl-*N*-

oxide etc.

Further examples are the structures illustrated below, which may be attached via each hydrogen-carrying atom (exchanged for hydrogen):



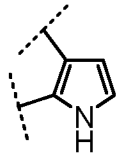
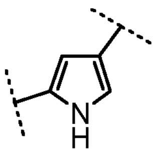
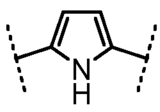
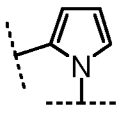




























































The above definition of **heteroaryl** also applies when **heteroaryl** is part of another group as in **heteroaryl**amino or **heteroaryl**oxy, for example.

If the free valency of a **heteroaryl** is saturated, a **heteroaromatic group** is obtained.

The term **heteroarylene** can therefore be derived from the previously defined **heteroaryl**. **Heteroarylene**, unlike **heteroaryl**, is bivalent and requires two binding partners. Formally, the second valency is obtained by removing a hydrogen atom from a **heteroaryl**. Corresponding groups are for example

pyrrolyl and  or  or  or  etc.

The above definition of **heteroarylene** also applies when **heteroarylene** is part of another group as in HO-**heteroarylene**amino or H_2N-**heteroarylene**oxy, for example.

The above-mentioned bivalent groups (alkylene, alkenylene, alkynylene etc.) may also be a part of composite groups (e.g. H_2N-C_{1-4}alkylene or HO-C_{1-4}alkylene-). In this case one of the valencies is saturated by the attached group (in this case: $-NH_2$, -OH), so that a composite group of this kind in this nomenclature amounts in total to only a monovalent substituent.

By **substituted** is meant that a hydrogen atom which is bound directly to the atom under consideration, is replaced by another atom or another group of atoms (**substituent**). Depending on the starting conditions (number of hydrogen atoms) mono- or polysubstitution may take place on one atom. Substitution with a particular substituent is only possible if the permitted valencies of the substituent and of the atom that is to be substituted correspond to one another and the substitution leads to a stable compound (i.e. to a compound which is not converted spontaneously, e.g. by rearrangement, cyclisation or elimination).

Bivalent substituents such as =S, =NR, =NOR, =NNRR, =NN(R)C(O)NRR, $=N_2$ or the like, may only be substituents at carbon atoms, wherein the bivalent substituent =O may also be a substituent at sulphur. Generally, substitution may be carried out by a bivalent substituent only at ring systems and requires replacement by two geminal hydrogen atoms, i.e. hydrogen atoms that are bound to the same carbon atom that is saturated prior to the substitution. Substitution by a bivalent substituent is therefore only possible at the group $-CH_2-$ or sulphur atoms of a ring system.

Stereochemistry/Solvates/Hydrates: Unless stated otherwise a structural formula given in the description or in the claims or a chemical name refers to the corresponding compound itself, but also encompasses the tautomers, stereoisomers, optical and geometric isomers (e.g. enantiomers, diastereomers, *E*/*Z* isomers, etc.), racemates, mixtures of separate enantiomers in any desired combinations, mixtures of diastereomers, mixtures of the forms mentioned hereinbefore (if such forms exist) as well as salts, particularly pharmaceutically acceptable salts thereof. The compounds and salts according to the invention may be present in solvated form (e.g. with pharmaceutically acceptable solvents such as e.g. water, ethanol etc.) or in unsolvated form. Generally, for the purposes of the present invention the solvated forms, e.g. hydrates, are to be regarded as of equal value to the unsolvated forms.

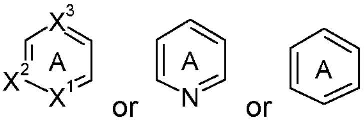
Salts: The term "**pharmaceutically acceptable**" is used herein to denote compounds, materials, compositions and/or formulations which are suitable, according to generally recognised medical opinion, for use in conjunction with human and/or animal tissue and do not have or give rise to any excessive toxicity, irritation or immune response or lead to other problems or complications, i.e. correspond overall to an acceptable risk/benefit ratio.

The term "**pharmaceutically acceptable salts**" relates to derivatives of the chemical compounds disclosed in which the parent compound is modified by the addition of acid or base. Examples of pharmaceutically acceptable salts include (without being restricted thereto) salts of mineral or organic acids in relation to basic functional groups such as for example amines, alkali metal or organic salts of acid functional groups such as for example carboxylic acids, etc. These salts include in particular acetate, ascorbate, benzenesulphonate, benzoate, besylate, bicarbonate, bitartrate, bromide/hydrobromide, Ca-edetate/edetate, camsylate, carbonate, chloride/hydrochloride, citrate, edisylate, ethane disulphonate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycolate, glycollylarsnilate, hexylresorcinate, hydrabamine, hydroxymaleate, hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, malate, maleate, mandelate, methanesulphonate, mesylate, methylbromide, methylnitrate, methylsulphate, mucate, napsylate, nitrate, oxalate, pamoate, pantothenate, phenyl acetate, phosphate/diphosphate, polygalacturonate, propionate, salicylate, stearate, subacetate, succinate, sulphamide, sulphate, tannate, tartrate, teoclate, toluenesulphonate, triethiodide, ammonium, benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumin and procaine. Other pharmaceutically acceptable salts may be formed with cations of metals such as aluminium, calcium, lithium, magnesium, potassium, sodium, zinc, etc. (cf. also Pharmaceutical salts, Birge, S.M. et al., J. Pharm. Sci., (1977), 66, 1-19).

The pharmaceutically acceptable salts of the present invention may be prepared starting from the parent compound which carries a basic or acidic functionality, by conventional chemical methods. Generally, such salts may be synthesised by reacting the free acid or base form of these compounds with a sufficient amount of the corresponding base or acid in water or an organic solvent such as for example ether, ethyl acetate, ethanol, isopropanol, acetonitrile (or mixtures thereof).

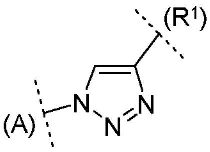
Salts of acids other than those mentioned above, which are useful for example for purifying or isolating the compounds from the reaction mixtures (e.g. trifluoroacetates), are also to be regarded as part of the invention.

In a representation such as for example



the letter A has the function of a ring designation in order to make it easier, for example, to indicate the attachment of the ring in question to other rings.

For bivalent groups in which it is crucial to determine which adjacent groups they bind and with which valency, the corresponding binding partners are indicated in brackets, where necessary for clarification purposes, as in the following representations:

 or (R^2)-C(O)NH- or (R^2)-NHC(O)-;

Groups or substituents are frequently selected from among a number of alternative groups/ substituents with a corresponding group designation (e.g. $\mathbf{R^a}$, $\mathbf{R^b}$ etc). If such a group is used repeatedly to define a compound according to the invention in different molecular parts, it must always be borne in mind that the various uses are to be regarded as totally independent of one another.

By a **therapeutically effective amount** for the purposes of this invention is meant a quantity of substance that is capable of obviating symptoms of illness or of preventing or alleviating these symptoms, or which prolong the survival of a treated patient.

List of abbreviations

aa	amino acid
Ac	acetyl
equiv.	equivalent(s)
Ar	aryl
ATP	adenosine triphosphate
Boc	*tert*-butyloxycarbonyl
BSA	bovine serum albumin
Bu	butyl
d	day(s)
TLC	thin layer chromatography
DCC	dicyclohexylcarbodiimide
DCM	dichloromethane
DEA	diethylamine
DIC	diisopropylcarbodiimide
DIPEA	*N*-ethyl-*N*,*N*-diisopropylamine (HÜNIG-base)
DMA	*N*,*N*-dimethylacetamide
DMAP	4-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide

DMF-DMA	*N,N*-dimethylformamide-dimethylacetal
DMSO	dimethylsulphoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
EDC	*N*-(3-dimethylaminopropyl)-*N4*-ethylcarbodiimide hydrochloride
ESI	electron spray ionization
Et	ethyl
EtOH	ethanol
h	hour(s)
HATU	*O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyl-uronium hexafluorophosphate
HCl	hydrochloric acid
het	hetero
HPLC	high performance liquid chromatography
HÜNIG base	*N*-ethyl-*N*,*N*-diisopropylamine
i	iso
*i*Pr$_2$NEt	diisopropylethylamine (HÜNIG base)
*i*PrOH	isopropanol
cat.	catalyst, catalytic
conc.	concentrated
LC	liquid chromatography
sln.	solution
M	molar
Me	methyl
MeOH	methanol
min	minute(s)
mL	millilitres
MPLC	medium pressure liquid chromatography
MS	mass spectrometry
MW	microwave
N	normal
NMP	*N*-methylpyrrolidinone
PBS	phosphate-buffered saline

Pd-dppf	1,1´-bis(diphenylphosphino)ferrocene palladium(II)-dichloride dichloromethane
Ph	phenyl
PK	pharmacokinetics
Pr	propyl
R_f (Rf)	retention factor
RP	reversed phase
RT	ambient temperature
s	second(s)
TBTU	*O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyl-uronium tetrafluoroborate
TEA	triethylamine
tert	tertiary
Tf	triflate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	trimethylsilyl
Tos	tosyl
$t_{Ret.}$	retention time (HPLC)
TRIS	tris(hydroxymethyl)-aminomethane
UV	ultraviolet

Features and advantages of the present invention will become apparent from the following detailed Examples, which illustrate the fundamentals of the invention by way of example, without restricting its scope:

Preparation of the compounds according to the invention

General

Unless stated otherwise, all the reactions are carried out in commercially obtainable apparatus using methods that are commonly used in chemical laboratories. Starting materials that are sensitive to air and/or moisture are stored under protective gas and corresponding reactions and manipulations therewith are carried out under protective gas (nitrogen or argon).

The compounds are named according to the Beilstein rules using the Autonom software (Beilstein). If a compound is to be represented both by a structural formula and by its nomenclature, in the event of a conflict the structural formula is decisive.

Microwave reactions are carried out in an initiator/reactor made by Biotage or Synthos 3000 and Monowave 300 made by the company Anton Paar in sealed containers (preferably 2, 5 or 20 mL), preferably with stirring.

Chromatography

Thin layer chromatography is carried out on ready-made TLC plates of silica gel 60 on glass (with fluorescence indicator F-254) made by Merck.

The **preparative high pressure chromatography (HPLC)** of the example compounds according to the invention is carried out with columns made by Waters (names: Sunfire C18, 5 µm, 30 x 100 mm Part. No. 186002572; X-Bridge C18, 5 µm, 30 x 100 mm Part. No. 186002982).

The compounds are eluted using either different gradients of H_2O/acetonitrile or H_2O/MeOH, wherein preferably 0.1 % HCOOH is added to the water (acid conditions). For chromatography under basic conditions H_2O/acetonitrile gradients are also used, and the water is made basic according to the following recipe: 5 mL of an ammonium hydrogen carbonate solution (158 g to 1 L H_2O) and 2 mL ammonia (7M in MeOH) are made up to 1 L with H_2O.

The **normal-phase preparative high pressure chromatography (HPLC)** of the example compounds according to the invention is carried out with columns made by Macherey & Nagel (name: Nucleosil, 50-7, 40 x 250 mm) and VDSoptilab (name: Kromasil 100 NH_2, 10 µM, 50 x 250 mm). The compounds are eluted using different gradients of DCM/ MeOH, with 0.1 % NH_3 added to the MeOH.

The **analytical HPLC (reaction monitoring)** of intermediate compounds is carried out with columns made by Agilent, Waters and Phenomenex. The analytical equipment is also provided with a mass detector in each case.

HPLC mass spectroscopy/UV spectrometry

The retention times/MS-ESI$^+$ for characterising the example compounds according to the invention are produced using an HPLC-MS apparatus (high performance liquid chromatography with mass detector) made by Agilent. Compounds that elute at the injection peak are given the retention time $t_{Ret.} = 0.00$.

HPLC-methods

Preparative

prep. HPLC1

HPLC:	333 and 334 Pumps	
Column:	Waters X-Bridge C18, 5 µm, 30 x 100 mm, Part. No. 186002982	
Eluant:	A: 10 mM NH_4HCO_3 in H_2O; B: acetonitrile (HPLC grade)	
Detection:	UV/Vis-155	
Flow:	50 mL/min	
Gradient:	0.00 min:	5 % B
	3.00 – 15.00 min:	variable (see individual methods)
	15.00 – 17.00 min:	100 % B

prep. HPLC2

HPLC:	333 and 334 Pumps	
Column:	Waters Sunfire C18, 5 µm, 30 x 100 mm, Part. No. 186002572	
Eluant:	A: H_2O + 0.2 % HCOOH; B: acetonitrile (HPLC grade) + 0.2 % HCOOH	
Detection:	UV/Vis-155	
Flow:	50 mL/min	
Gradient:	0.00 min:	5 % B
	3.00 – 15.00 min:	variable (see individual methods)
	15.00 – 17.00 min:	100 % B

analytical

Method A

HPLC	Agilent 1100 Series
MS	1100 Series LC/MSD SL (MM-ES + APCI, + 3000 V, Quadrupol, G1956B)
MSD signal settings	Scan pos 120 – 750
column	Waters, XBridge, C18, 3.5 µm, 135 Å, 30 x 2.1 mm column, Part. No: 186003020
eluant	**A**: 5 mM NH_4HCO_3/20 mM NH_3 (pH = 9.5)

	B: acetonitrile (HPLC grade)	
detection signal	UV 254/214 nm (bandwidth 8, reference off)	
spectrum	range: 190 – 400 nm; step: 2.0 nm	
peak width	> 00025 min (0.05 s)	
injection	2 µL standard injection	
flow	1.0 mL/min	
column temperature	35°C	
gradient	0.0 – 1.0 min	15 % → 95 % B
	1.0 – 1.6 min	95 % B
	1.6 – 1.7 min	95 % → 15 % B
	1.7 – 2.3 min	15 % B

Method B

HPLC	Agilent 1100 Series	
MS	1100 Series LC/MSD SL (MM-ES + APCI, + 3000 V, Quadrupol, G1956B)	
MSD signal settings	Scan pos 120 – 750	
column	Waters, XBridge, C18, 3.5 µm, 135 Å, 30 x 2.1 mm column, Part. No.: 186003020	
eluant	**A**: 5 mM NH_4HCO_3/ 20 mM NH_3 (pH = 9.5) **B**:MeOH (HPLC grade)	
detection signal	UV 254/214 nm (bandwidth 8, reference off)	
spectrum	range: 190 – 400 nm; step: 2.0 nm	
peak width	> 00025 min (0.05 s)	
injection	2 µL standard injection	
flow	1.0 mL/min	
column temperature	40°C	
gradient	0.0 – 1.0 min	20 % → 95 % B
	1.0 – 2.0 min	95 % B
	2.0 – 2.1 min	95 % → 20 % B
	2.1 – 2.3 min	20 % B

Method C

HPLC	Agilent 1100 Series	
MS	1200 Series LC/MSD (API-ES + 3000 V, Quadrupol, G6140A)	
MSD signal settings	Scan pos 150 – 750	
column	Agilent. Zorbax SB, C8, 3.5 µm, 80 Å, 50 x 2.1 mm column, Part. No.: 871700-906	
eluant	**A**: water + 0.11 % formic acid	
	B: acetonitrile (HPLC grade) + 0.1 % formic acid	
detection signal	UV 254/214/230 nm (bandwidth 8, reference off)	
spectrum	range: 190 – 450 nm; step: 4.0 nm	
peak width	> 0.01 min (0.2 s)	
injection	1.5 µL standard injection	
flow	1.1 mL/min	
column temperature	45°C	
gradient	0.0 – 1.75 min	15 % → 95 % B
	1.75 – 1.9 min	95 % B
	1.9 – 1.92 min	95 % → 15 % B
	1.92 – 2.1 min	15 % B

Method D

HPLC	Agilent 1100 Series
MS	1100 Series LC/MSD SL (MM-ES + APCI, + 2500 V, Quadrupol, G1956B)
MSD signal settings	Scan pos 70 – 500
column	Agilent Zorbax SB, C8, 3.5 µm, 80 Å, 50 x 2.1 mm column, Part. No.: 871700-906
eluant	**A**: water + 0.11 % formic acid
	B: MeOH (HPLC grade)
detection signal	UV 254/214/230 nm (bandwidth 8, reference off)
spectrum	range: 190 – 450 nm; step: 4.0 nm
peak width	> 0.01 min (0.2 s)
injection	1.5 µL standard injection

flow	1.0 mL/min	
column temperature	45°C	
gradient	0.0 – 1.5 min	20 % → 95 % B
	1.5 – 2.1 min	95 % B
	2.1 – 2.2 min	95 % → 20 % B
	2.2 – 2.4 min	20 % B

Method E

HPLC	Agilent 1100 Series	
MS	1100 Series LC/MSD SL (MM-ES + APCI, + 3000 V, Quadrupol, G1956B)	
MSD signal settings	Scan pos 100 – 750	
column	Waters, XBridge, C18, 3.5 µm, 135 Å, 30 x 2.1 mm column, Part. No.: 186003020	
eluant	**A**: 5 mM NH_4HCO_3/20 mM NH_3 (pH = 9.5) **B**: acetonitrile (HPLC grade)	
detection signal	UV 254/214 nm (bandwidth 8, reference off)	
spectrum	range: 190 – 400 nm; step: 2.0 nm	
peak width	> 0005 min (0.1 s)	
injection	2 µL standard injection	
flow	1.0 mL/min	
column temperature	35°C	
gradient	0.0 – 1.0 min	15 % → 95 % B
	1.0 – 1.6 min	95 % B
	1.6 – 1.7 min	95 % → 15 % B
	1.7 – 2.3 min	15 % B

Method F

HPLC	Agilent 1100 Series
MS	1200 Series LC/MSD (API-ES + 2500 V, Quadrupol, G6140A)
MSD signal settings	Scan pos 75 – 500
column	Agilent Zorbax SB, C8, 3.5 µm, 80 Å, 50 x 2.1 mm column,

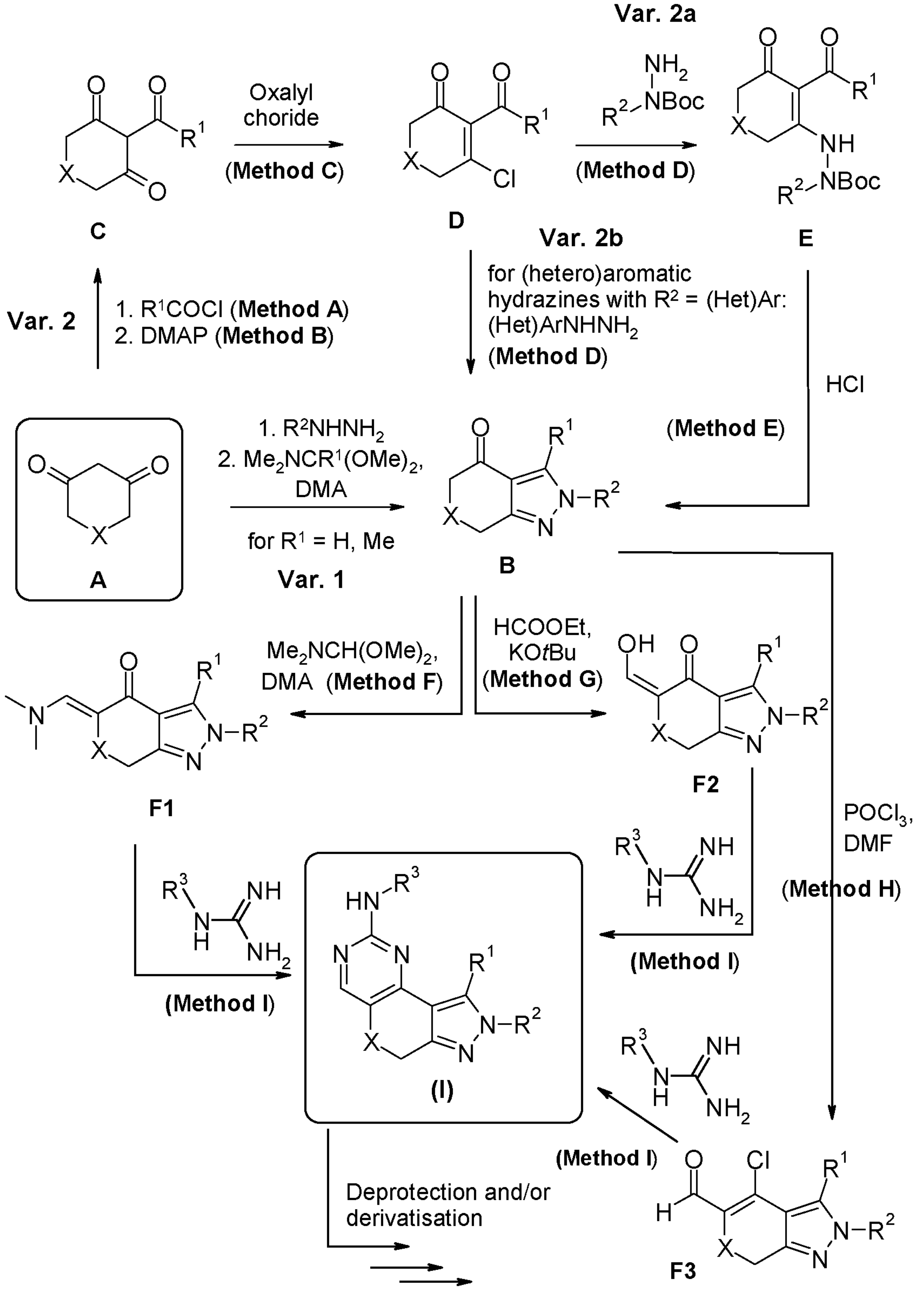
	Part. No.: 871700-906	
eluant	**A**: water + 0.11 % formic acid	
	B: acetonitrile (HPLC grade) + 0.1 % formic acid	
detection signal	UV 254/214/230 nm (bandwidth 8, reference off)	
spectrum	range: 190 – 450 nm; step: 4.0 nm	
peak width	> 0.01 min (0.2 s)	
injection	1.5 µL standard injection	
flow	1.1 mL/min	
column temperature	45°C	
gradient	0.0 – 1.75 min	15 % → 95 % B
	1.75 – 1.9 min	95 % B
	1.9 – 1.92 min	95 % → 15 % B
	1.92 – 2.1 min	15 % B

Method G

HPLC	Agilent 1100 Series	
MS	1100 Series LC/MSD (API-ES +/- 3000 V, Quadrupol, G1946D)	
MSD signal settings	Scan pos 120 – 900, Scan neg 120 – 900	
column	phenomenex; Part. No. 00M-4439-BO-CE; Gemini 3 µm, C18, 110 Å; 20 x 2.0 mm column	
eluant	**A**: 5 mM NH_4HCO_3/20 mM NH_3 (pH = 9.5)	
	B: acetonitrile (HPLC grade)	
detection signal	UV 254 nm (bandwidth 1, reference off)	
spectrum	range: 250 – 400 nm; step: 1 nm	
peak width	< 0.01 min (0.1 s)	
injection	10 µL standard injection	
flow	1.0 mL/min	
column temperature	40°C	
gradient	0.0 – 2.5 min	5 % → 95 % B
	2.5 – 2.8 min	95 % B
	2.8 – 3.1 min	95 % → 5 % B

The compounds according to the invention are prepared by the methods of synthesis described hereinafter, in which the substituents of the general formulae have the meanings given hereinbefore. These methods are intended as an illustration of the invention, without restricting its subject matter and the scope of the compounds claimed to these examples. Where the preparation of starting compounds is not described, they are commercially obtainable or may be prepared analogously to known compounds or methods described herein. Substances described in the literature are prepared according to the published methods of synthesis.

General formula scheme and summary of the synthesis route



Novel compounds of general structure **(I)** may be prepared starting from cyclic 1,3-diketones **A** by two different synthesis routes leading to the central component **B**:

The first variant (**Var. 1**) makes the intermediates **B** available by the reaction of suitable diketones **A** with substituted hydrazines $\mathbf{R^1}NHNH_2$ and dimethylformamide-dimethylacetal or analogous reagents.

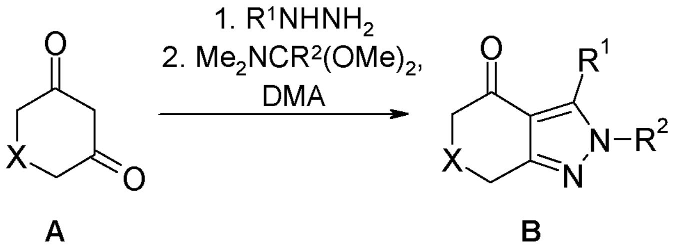
The second variant (**Var. 2**) converts the starting compounds **A** by reaction with acid chlorides $\mathbf{R^1}COCl$ and subsequent rearrangement of the intermediate enol esters into the triketones **C**, which can be converted with oxalyl chloride into the vinyl chlorides **D**. Substitution with protected hydrazines $\mathbf{R^2}NHNH_2$ (**Var. 2a**) leads to the intermediates **E**, which cyclise in the hydrochloric acid medium after the cleaving of the protective group to form the central component **B**. When arylhydrazines are used there is no need for the protective group (**Var. 2b**). Here, the reaction of the chlorine compound **D** yields the intermediate **B** directly.

By reacting **B** with dimethylformamide-dimethylacetal or formic acid esters in the presence of bases the intermediate compounds **F1** or **F2** are obtained, which may in turn be reacted to form the end compounds **(I)** by reaction with guanidines available from amines using known methods. Alternatively **B** may be reacted with phosphorus oxychloride in the presence of DMF to form the intermediate **F3** which may be cyclised with corresponding guanidines to form **(I)**.

The compounds **(I)** may be on the one hand end compounds according to the invention or on the other hand may also be prepared using correspondingly protected components, deprotected by conventional methods and then converted into other compounds (I) according to the invention by derivatisation steps such as e.g. amide formation, alkylation or amination reactions. Instead of protected reagents it is also possible to use synthesis compounds which can be directly functionalised or derivatised without recourse to protective groups.

1. Preparation of the pyrazole fragments B

1.1. Preparation of the pyrazole fragments B starting from diketones A according to Variant 1



The pyrazole fragments **B** are prepared analogously to the method of Kennedy L. J., Lawrence J. *Synlett* **2008** (4), 600 - 604.

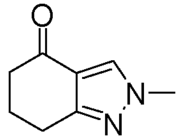
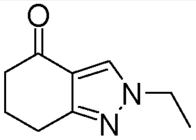
Preparation of B-01

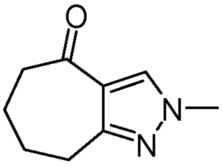
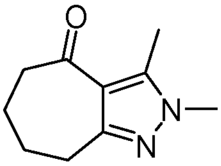
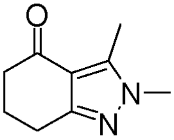
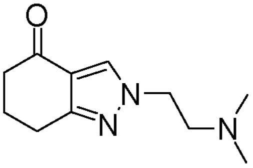
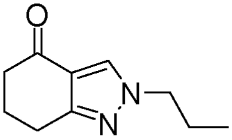
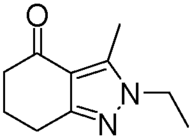
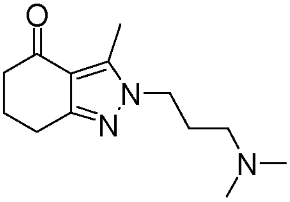
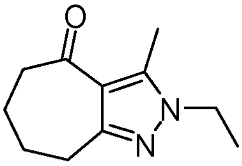
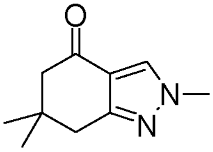
Cyclohexane-1,3-dione (6.00 g, 53.5 mmol) in MeOH (15 mL) is combined at 0°C with methylhydrazine (2.82 mL, 53.0 mmol) in THF (15 mL) and the mixture is stirred for 1.5 h. It is heated to RT, dimethylformamide-dimethylacetal (15 mL, 113.3 mmol) is added and the reaction mixture is heated in a microwave reactor (120°C, 10 min). The solvent is spun off in vacuo and the residue is purified by chromatography.

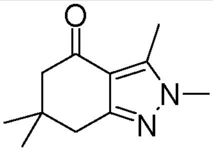
The liberation of hydrazinium salts is carried out either analogously to the Kennedy method with triethylamine or by the addition of potassium-*tert*-butoxide.
Reactions with dimethylacetamide-dimethylketal are carried out analogously to dimethylformamide-dimethylacetal. Optionally potassium-*tert*-butoxide may also be added to the cyclisation reaction here.

Analogously to **B-01** further pyrazole fragments **B** are synthesised using the corresponding educts (Table 1).

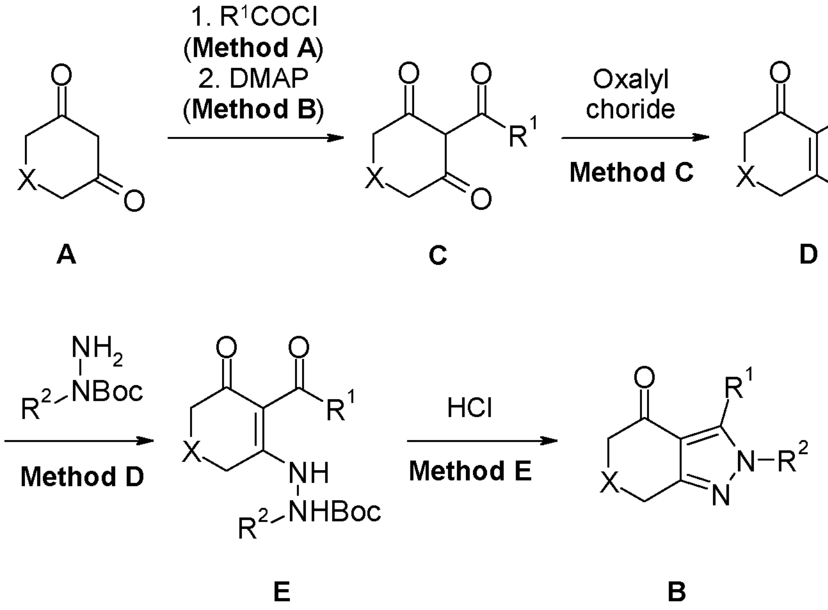
Table 1

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-01		0.35	151.2	C
B-02		0.29	165.0	A

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-03		0.49	165.2	F
B-04		0.59	179.1	C
B-05		0.46	165.2	F
B-06		0.24	208.0	E
B-07		0.59	179.3	F
B-08		0.57	179.3	F
B-09		0.35	236.2	E
B-10		0.69	193.1	F
B-11		0.58	179.3	F

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-12		0.67	193.1	F

1.2. Preparation of the pyrazole fragments B via triketones C (Variant 2/2a)



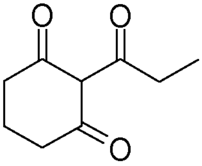
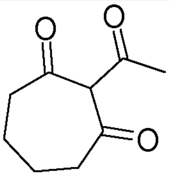
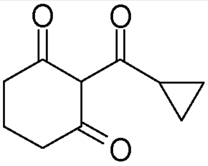
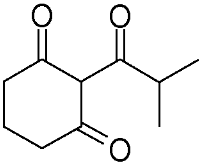
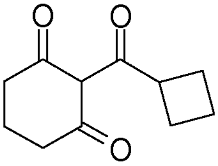
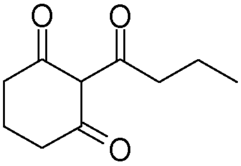
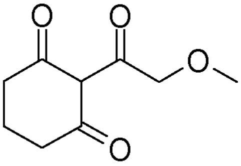
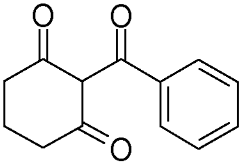
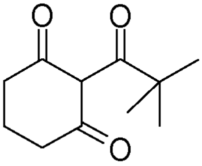
Preparation of C-01 (method A, method B)

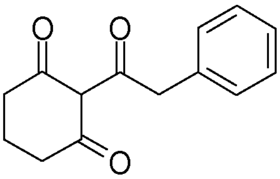
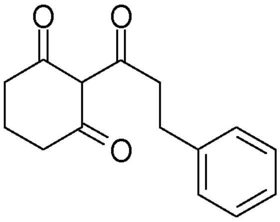
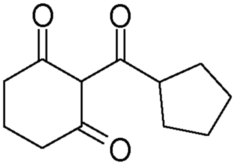
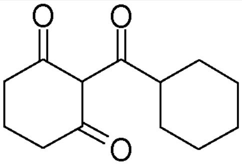
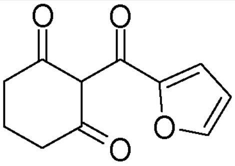
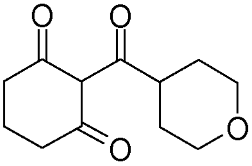
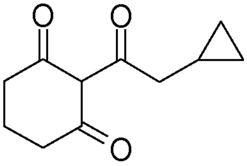
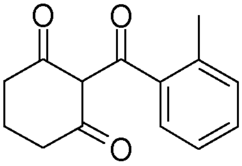
Cyclohexane-1,3-dione (2.00 g, 17.3 mmol), propionic acid chloride (2.07 mL, 23.2 mmol) and DMAP (360 mg, 3.21 mmol) are stirred in anhydrous toluene (60 mL) for 30 min at RT and refluxed for 1 h. The cooled reaction mixture is washed 3 x with water and once with saturated saline, dried on sodium sulphate, filtered and evaporated down. The residue is taken up in anhydrous toluene (100 mL), combined with DMAP (290 mg, 2.23 mmol) and refluxed for 3 h with stirring. The cooled reaction mixture is washed 3 x with water and once with saturated saline, dried on sodium sulphate, filtered and evaporated down.

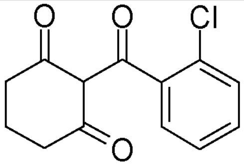
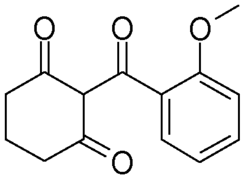
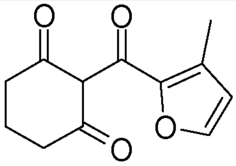
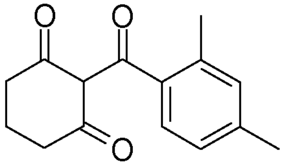
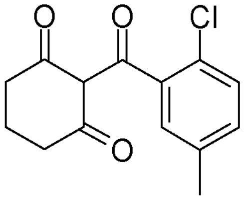
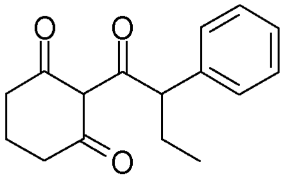
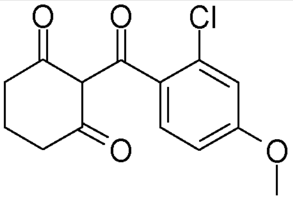
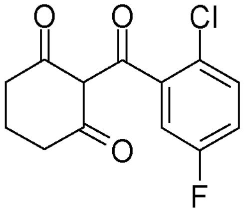
Alternatively the second partial step may be carried out in the presence of triethylamine with catalytic amounts of potassium cyanide or 1,2,4-triazole in acetonitrile.

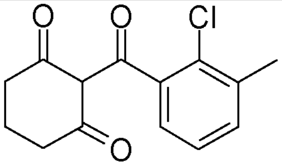
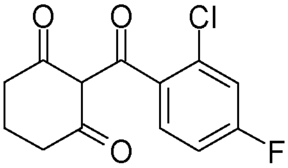
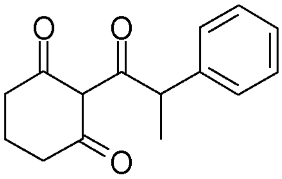
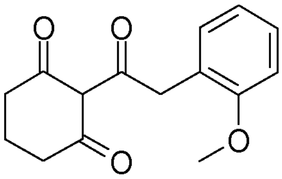
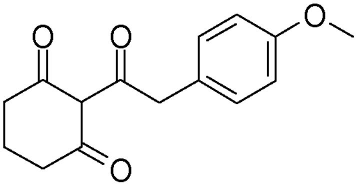
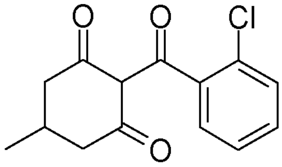
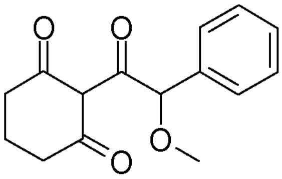
Analogously to **C-01** further triketones **C** are synthesised using the corresponding educts (Table 2).

Table 2

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
C-01		0.77	169.1	F
C-02		0.68	169.2	C
C-03		0.84	181.2	C
C-04		0.97	183.2	F
C-05		0.99	195.0	C
C-06		0.94	183.3	C
C-07		0.46	185.0	F
C-08		0.74	217.2	C
C-09		0.87	197.3	D

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
C-10		1.09	231.2	F
C-11		1.16	245.0	F
C-12		1.12	209.1	C
C-13		1.19	223.2	C
C-14		0.43	207.0	C
C-15		0.74	225.0	C
C-16		0.97	195.2	F
C-17		0.97	231.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
C-18		1.00	251.0	C
C-19		0.85	247.2	C
C-20		0.89	221.0	C
C-21		1.09	245.2	C
C-22		1.11	265.2	C
C-23		1.24	259.2	C
C-24		1.04	281.0	C
C-25		1.05	269.0	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
C-26		1.10	265.0	C
C-27		1.05	269.0	C
C-28		1.14	245.2	C
C-29		1.08	261.2	C
C-30		1.06	261.2	C
C-31		1.12	265.2	C
C-32		0.90	261.2	C

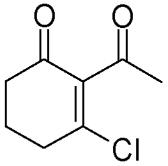
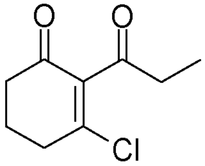
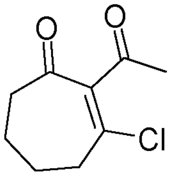
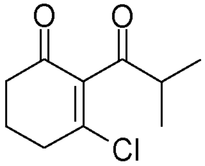
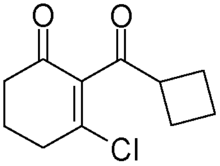
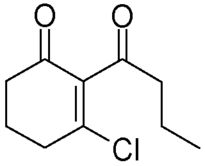
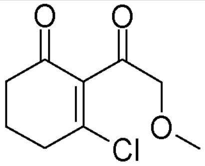
Preparation of D-01 by chlorination (method C)

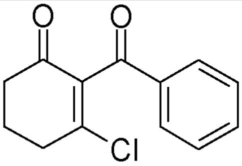
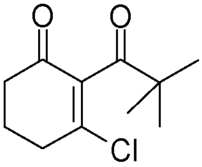
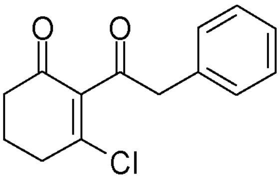
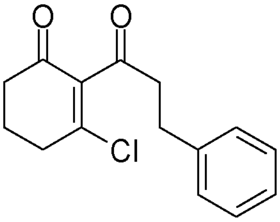
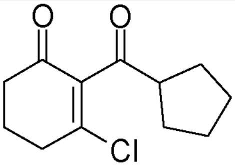
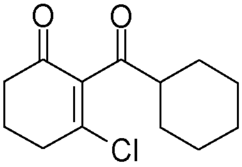
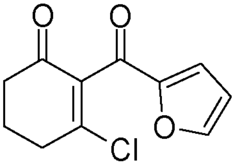
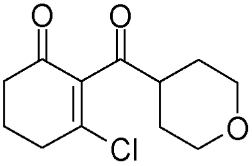
C-01 (525 mg, 3.22 mmol) and oxalyl chloride (515 µL, 5.84 mmol) are stirred in anhydrous DCM for 12 h at RT. The reaction mixture is evaporated to dryness and further reacted immediately.

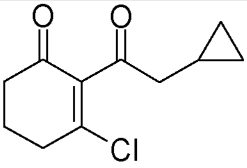
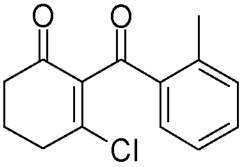
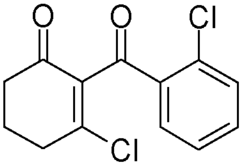
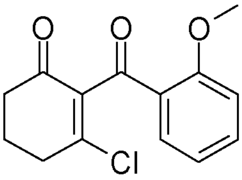
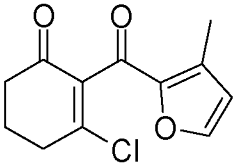
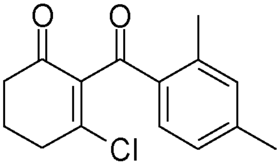
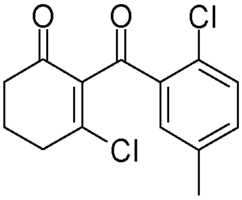
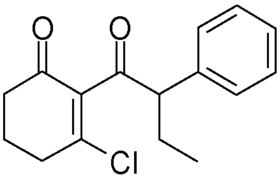
For the HPLC analysis the reaction mixture is mixed with morpholine and the product is detected as alkylated morpholine derivative. The $[M+H]^+$ value found relates to this compound.

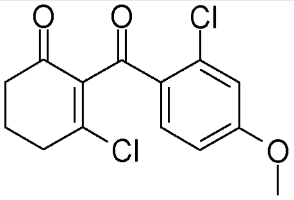
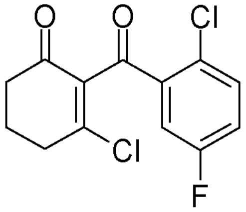
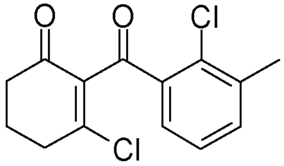
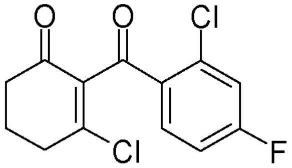
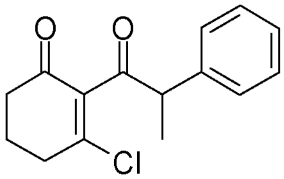
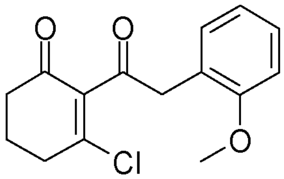
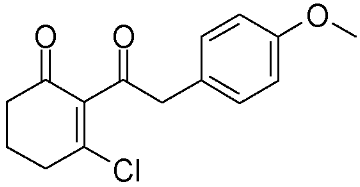
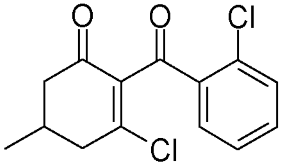
Analogously to **D-01** further chlorinated diketones **D** are synthesised using the corresponding intermediate **C** (Table 3).

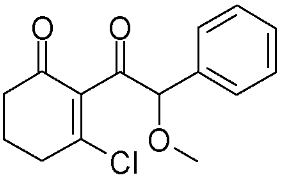
Table 3

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
D-01		0.23	224.3	F
D-02		0.33	238.1	F
D-03		0.20	238.2	C
D-04		0.45	252.3	C
D-05		0.51	264.3	C
D-06		0.30	252.2	E
D-07		0.10	254.0	A

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
D-08		0.54	286.2	C
D-09		0.42	266.2	A
D-10		0.66	300.2	F
D-11		0.75	314.1	C
D-12		0.64	278.2	B
D-13		0.74	292.2	B
D-14		0.32	276.3	C
D-15		0.35	294.3	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
D-16		0.50	264.3	C
D-17		0.59	300.2	C
D-18		0.76		C
D-19		0.48	316.2	C
D-20		0.43	290.2	C
D-21		0.73	314.2	C
D-22		0.67	334.2	C
D-23		1.26	277.2 (product mass)	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
D-24		0.64	350.2	C
D-25		0.61	338.2	C
D-26		0.65	334.2	C
D-27		0.62	338.2	C
D-28		0.76	314.2	C
D-29		0.68	330.2	C
D-30		0.66	330.2	C
D-31		0.67	334.2	C

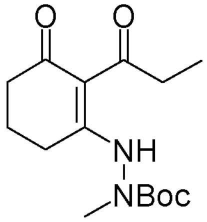
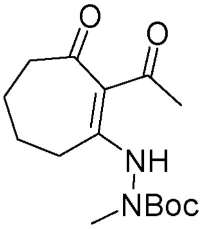
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
D-32		0.57	330.2	C

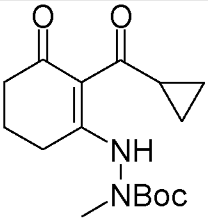
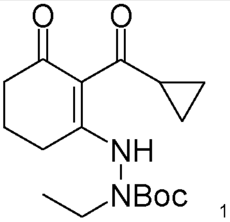
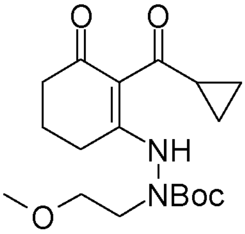
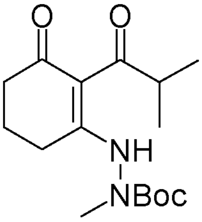
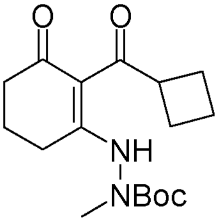
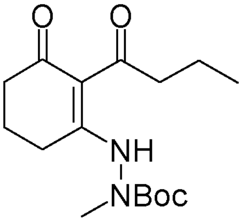
Preparation of E-01 by substitution with Boc-protected hydrazines (method D, Variant 2a)

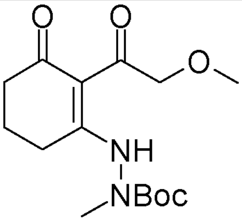
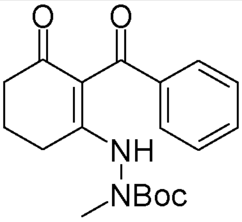
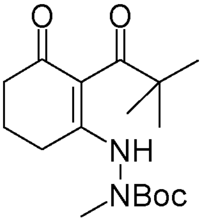
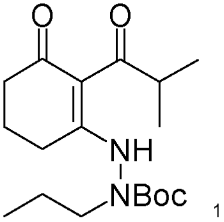
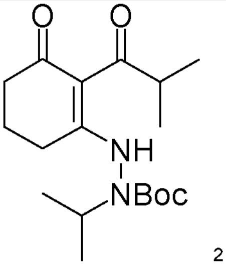
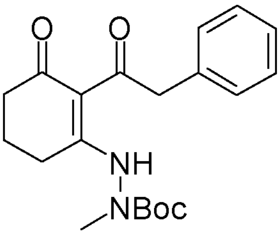
Chlorine compound **D-01** (1.20 g, 6.43 mmol) in anhydrous THF (10 mL) is combined at -35°C with *N*-ethyldiisopropylamine (1.10 mL, 6.43 mmol) and 1-Boc-1-methylhydrazine (0.969 mL, 6.43 mmol), heated to RT and stirred for 12 h at RT. The reaction mixture is evaporated down, the residue is taken up in EtOAc, washed with saturated ammonium chloride solution, water and saturated sodium chloride solution, dried (Na_2SO_4), filtered and evaporated down. Optionally the crude product may be purified by chromatography.

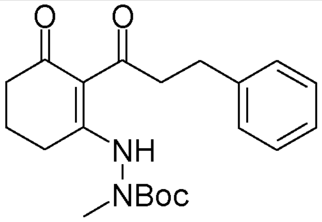
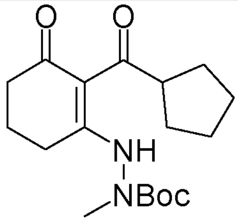
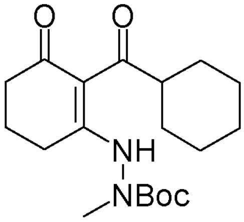
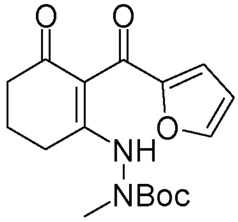
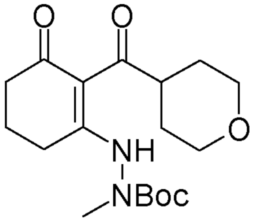
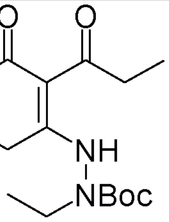
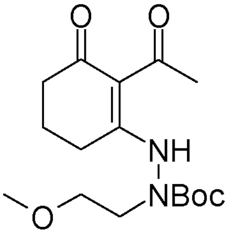
Analogously to **E-01** further intermediate compounds **E** are synthesised using the corresponding intermediate **D** and a hydrazine component (Table 4).

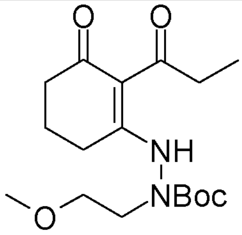
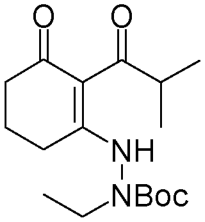
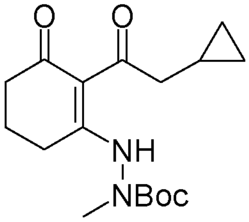
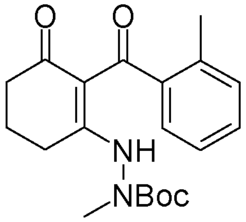
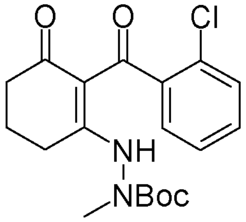
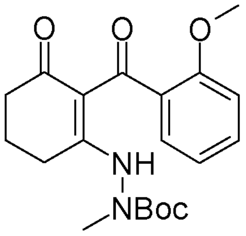
Table 4

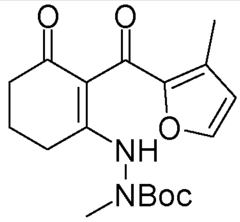
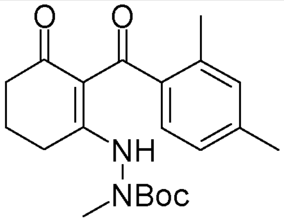
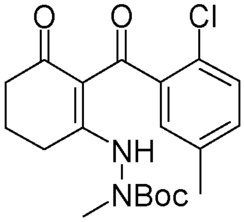
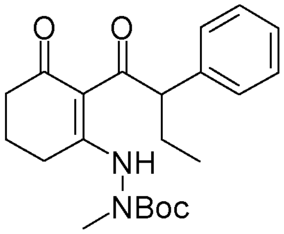
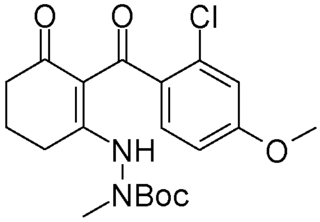
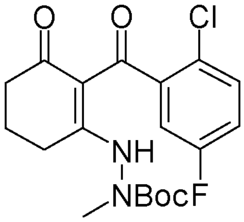
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-01		1.03	297.3	C
E-02		0.96	297.3	C

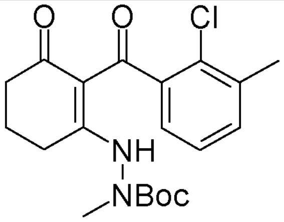
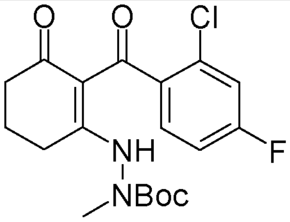
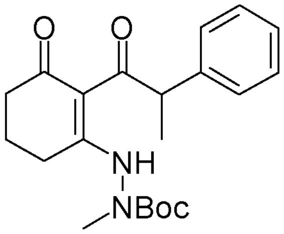
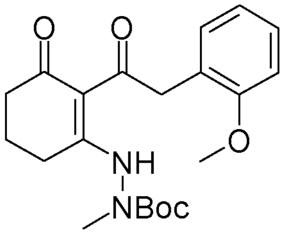
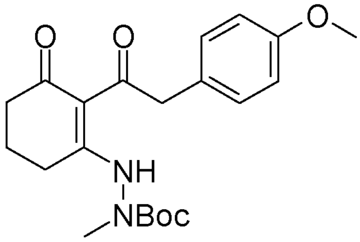
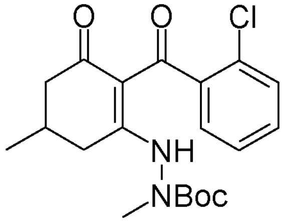
No.	Structure	t_{ret} [min]	[M+H]$^+$	Method of analysis
E-03		1.02	309.3	C
E-04		1.13	323.4	C
E-05		1.07	353.4	C
E-06		1.11	311.1	C
E-07		1.15	323.1	C
E-08		1.11	311.4	C

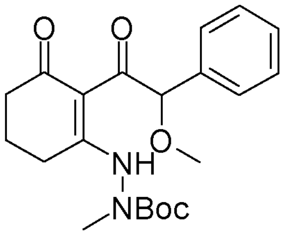
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-09		0.84	313.1	F
E-10		0.67	345.2	A
E-11		1.07	325.1	F
E-12	 1	1.36	339.2	F
E-13	 2	1.31	339.3	C
E-14		1.26	359.3	F

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-15		1.31	373.1	F
E-16		1.24	337.2	C
E-17		1.28	351.3	C
E-18		0.76	335.1	C
E-19		0.92	353.4	C
E-20		1.16	311.2	F
E-21		0.95	327.3	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-22		1.10	341.3	F
E-23		1.22	325.2	C
E-24		1.12	323.3	F
E-25		1.10	359.2	C
E-26		1.14	379.2	C
E-27		1.02	375.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-28		0.84	349.2	C
E-29		1.19	373.2	C
E-30		1.21	393.2	C
E-31		1.37	387.2	C
E-32		1.15	409.2	C
E-33		1.19	397.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-34		1.21	393.2	C
E-35		1.19	397.2	C
E-36		1.26	373.2	C
E-37		1.21	389.2	C
E-38		1.20	389.2	C
E-39		1.22	393.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
E-40		1.07	389.2	C

[1] Brosse, Nicolas et al., "Preparation of multiply protected alkylhydrazine derivatives by MITSUNOBU and PTC approaches"; *Europ. J. Org. Chem.* **2003**, 4757-4764;

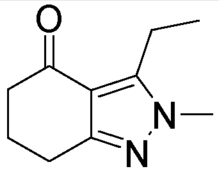
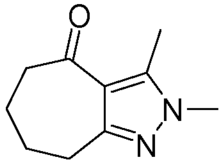
[2] Brosse, Nicolas et al., "New synthesis of 1,1-substituted hydrazines by alkylation of *N*-acyl or *N*-[(alkyloxycarbonyl)amino]phthalimide using the MITSUNOBU protocol"; *J. Org. Chem.* **2000**, 4370-4374.

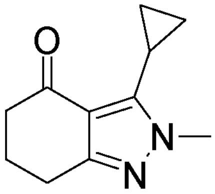
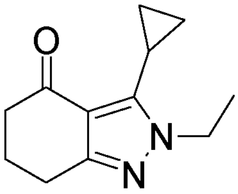
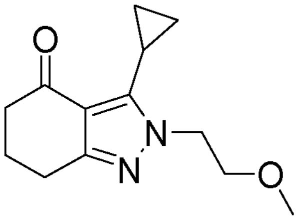
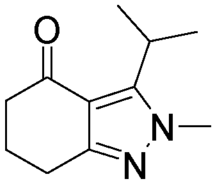
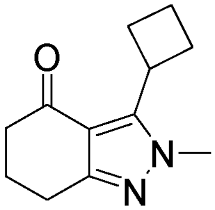
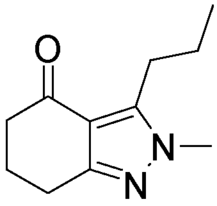
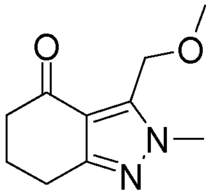
Preparation of B-13 by cyclisation (method E)

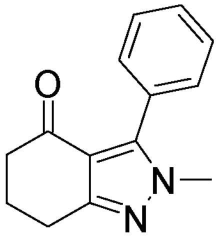
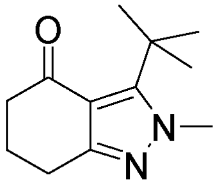
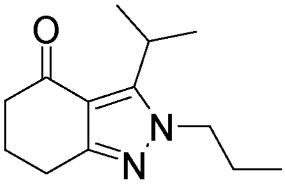
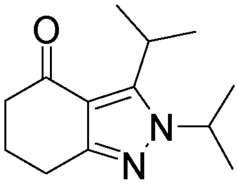
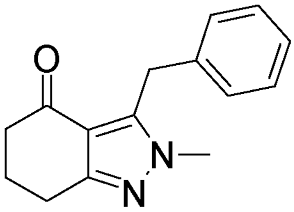
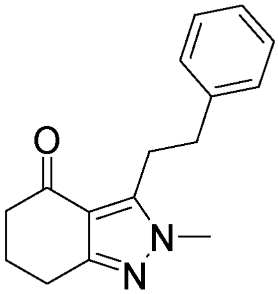
The protected hydrazine **E-01**(1.5 g, 5.06 mmol) in anhydrous dioxane (3 mL) is combined with 4 N HCl in dioxane (5 mL) and stirred for 1 h at RT. The reaction mixture is evaporated down, the residue is taken up in DCM, washed with saturated potassium carbonate solution and saturated sodium chloride solution, dried (Na_2SO_4), filtered and evaporated down. Optionally the crude product may be purified by chromatography.

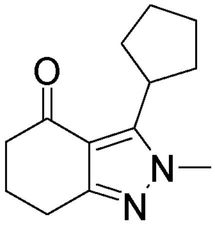
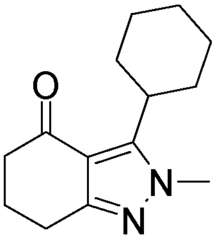
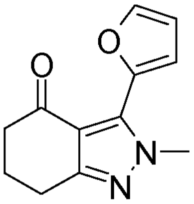
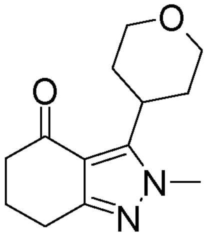
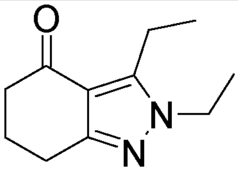
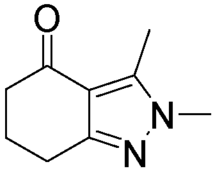
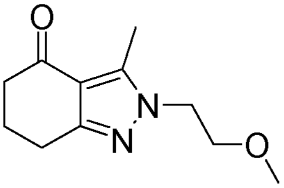
Analogously to **B-13** further intermediate compounds **E** are cyclised (Table 5).

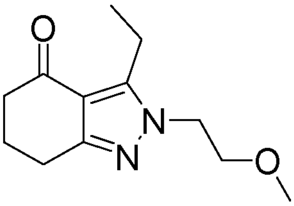
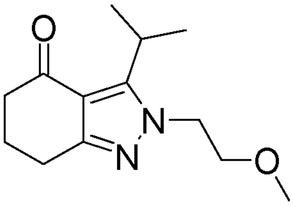
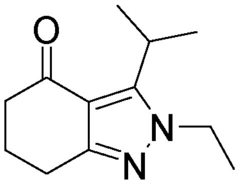
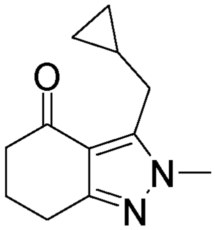
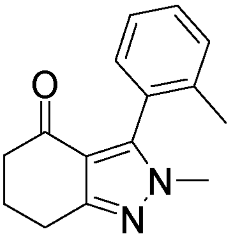
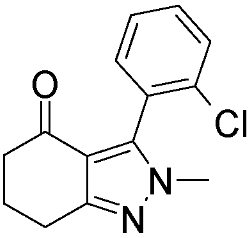
Table 5

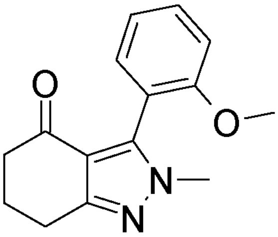
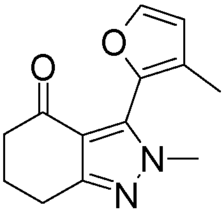
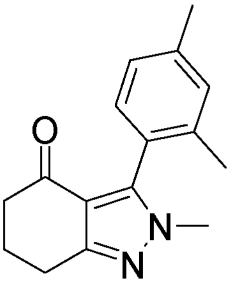
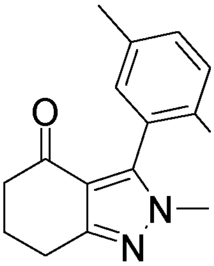
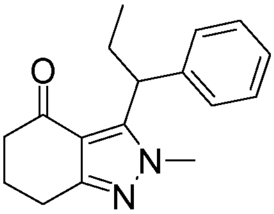
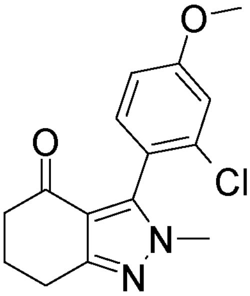
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-13		0.60	179.1	C
B-14		0.60	179.1	C

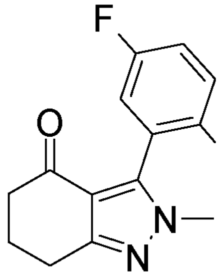
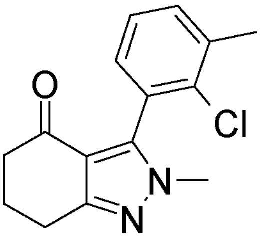
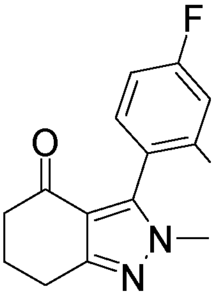
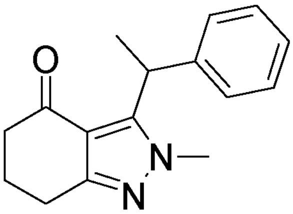
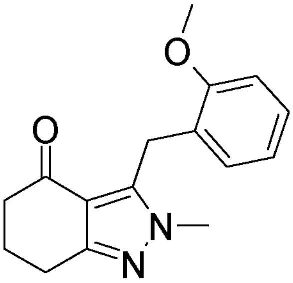
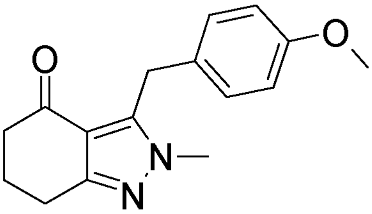
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-15		0.62	191.1	C
B-16		0.72	205.2	C
B-17		0.66	235.2	C
B-18		0.74	193.2	C
B-19		0.81	205.2	C
B-20		0.71	193.2	C
B-21		0.48	195.2	F

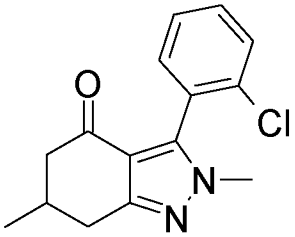
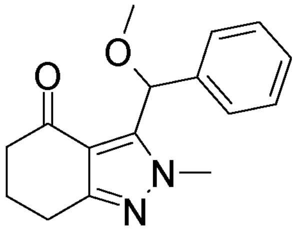
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-22		0.79	227.1	C
B-23		0.87	207.2	C
B-24		0.95	221.1	C
B-25		0.95	221.1	C
B-26		0.892	241.2	C
B-27		0.96	255.3	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-28		0.91	219.3	C
B-29		1.02	233.1	C
B-30		0.79	217.2	C
B-31		0.59	235.2	C
B-32		0.68	193.2	C
B-33		0.46	165.2	F
B-34		0.53	209.1	C

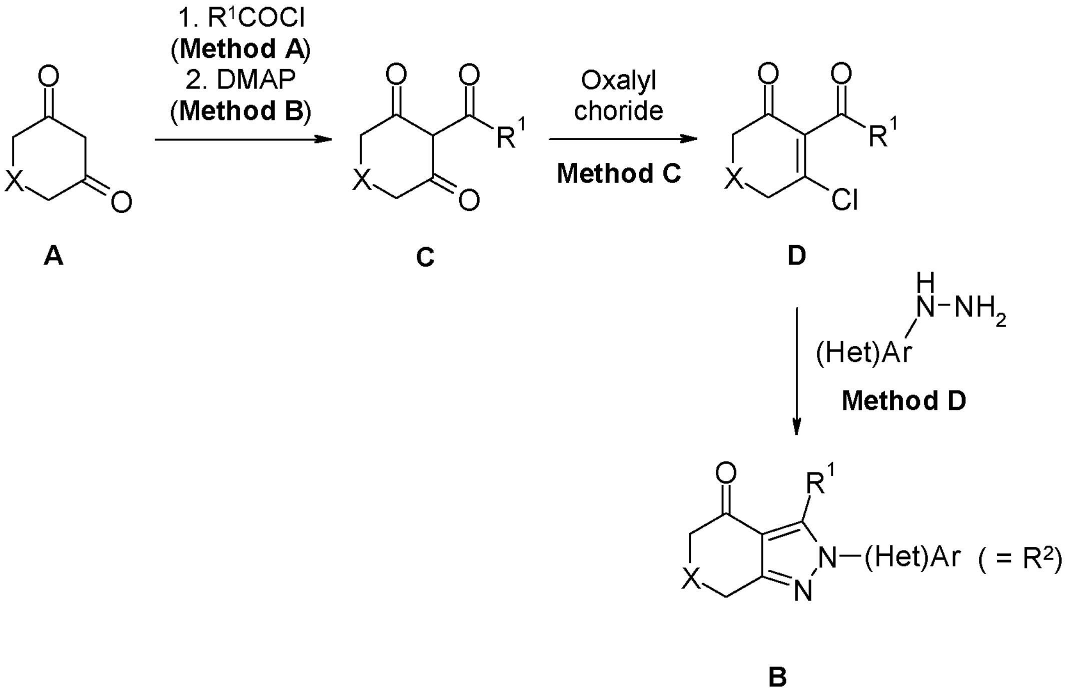
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-35		0.64	223.2	C
B-36		0.80	237.3	C
B-37		0.84	207.3	C
B-38		0.95	205.2	C
B-39		0.85	241.2	C
B-40		0.88	261.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-41		0.80	257.2	C
B-42		0.80	231.2	C
B-43		1.00	255.2	C
B-44		1.00	275.2	C
B-45		1.08	269.2	C
B-46		0.94	291.0	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-47		0.92	279.2	C
B-48		0.99	275.2	C
B-49		0.92	279.0	C
B-50		0.98	255.2	C
B-51		0.95	271.2	C
B-52		0.90	271.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-53		0.99	275.2	C
B-54		1.00	271.2	C

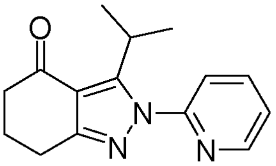
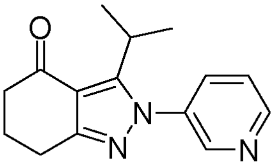
1.3. Preparation of (hetero)arylpyrazole fragments B via triketones C (Variant 2/2b)



Preparation of pyrazole fragment B-55 by cyclisation with (hetero)arylhydrazine (method D)

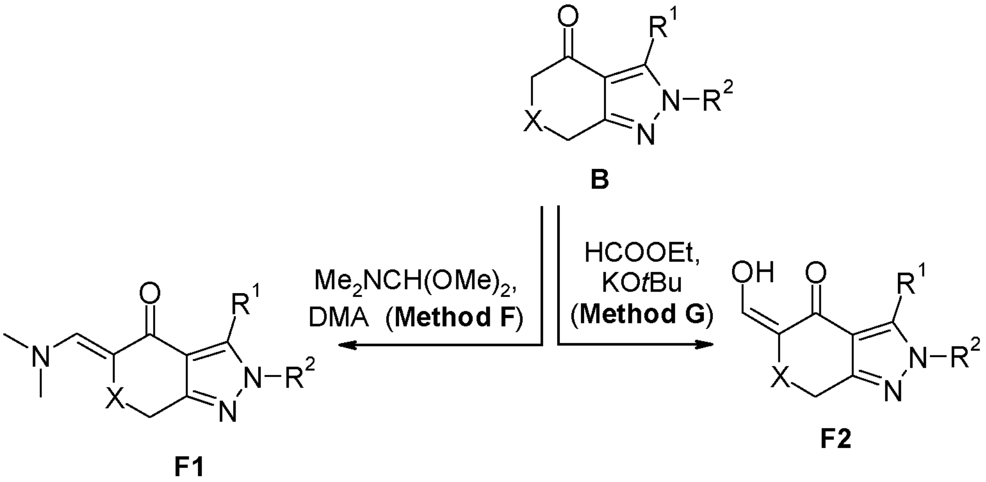
The reaction of the chlorinated diketones with (hetero)arylhydrazines is carried out according to method E and yields the corresponding (hetero)arylpyrazole fragment directly.

Table 6

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
B-55		0.93	256.2	C
B-56		0.85	256.2	C

2. Preparation of the starting compounds for the pyrimidine cyclisation reaction

2.1. Reaction of B to obtain intermediates F1 and F2

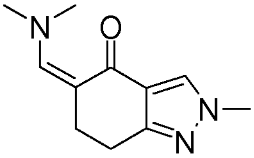
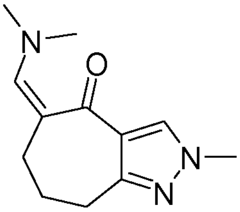
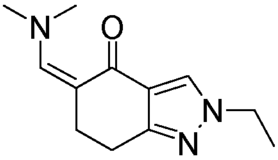
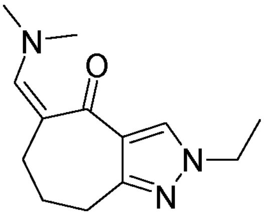
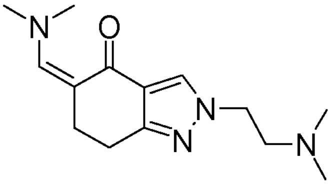
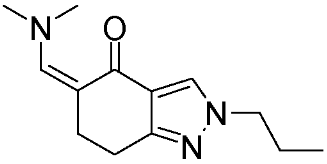
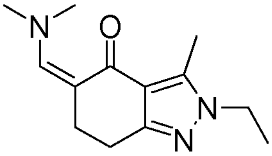


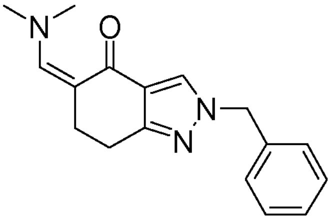
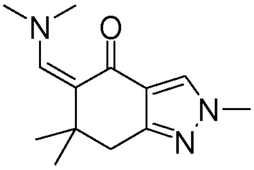
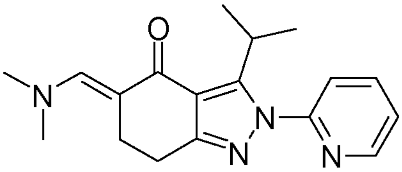
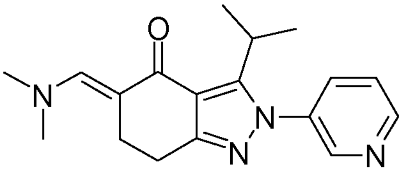
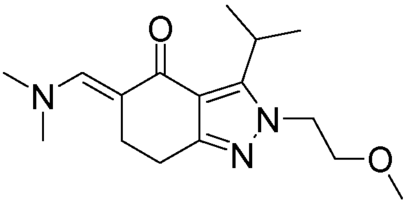
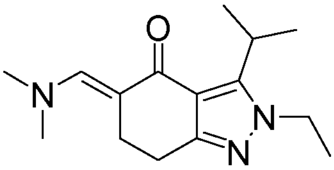
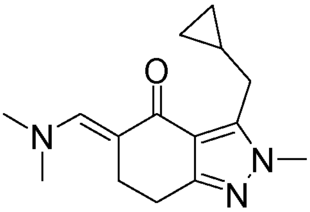
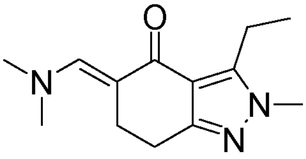
Preparation of F1-01: Condensation with dimethylformamide-dimethylacetal (method F)

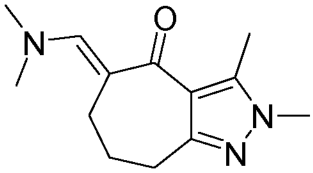
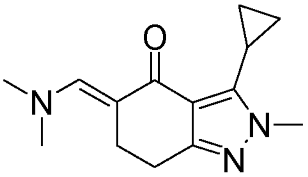
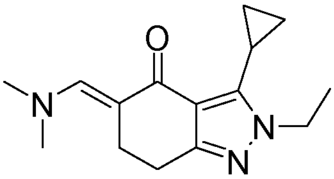
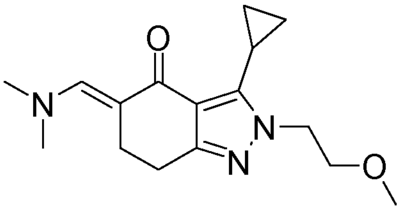
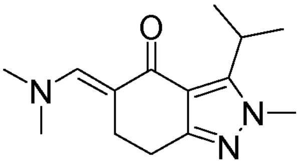
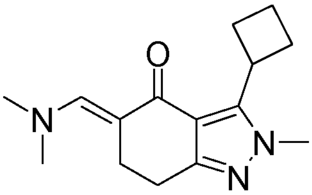
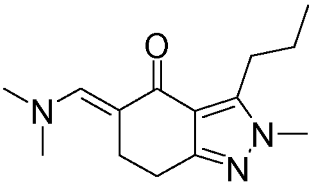
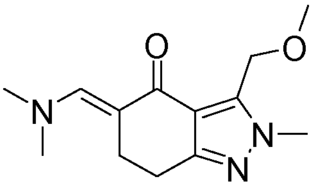
Pyrazole fragment **B-01** (7.5 g, 49.9 mmol) and DMF-DMA (15 mL, 113.3 mmol) in DMA (15 mL) are stirred in a microwave reactor for 30 min at 180°C. The solvent is spun off in vacuo and the residue is purified by chromatography.

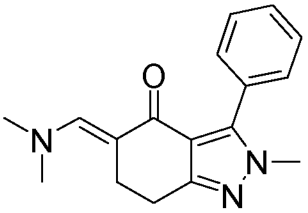
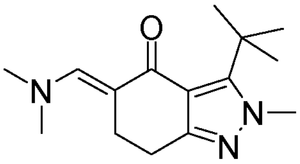
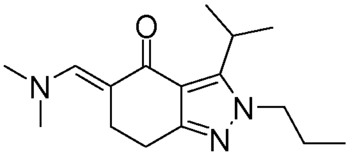
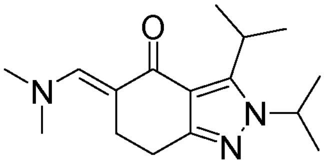
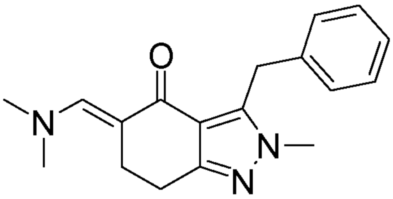
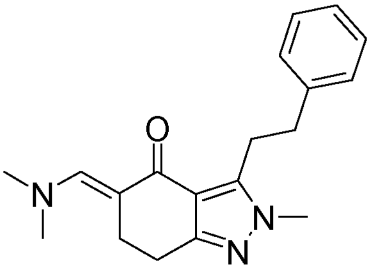
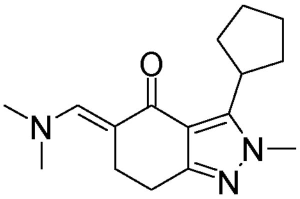
Analogously to **F1-01** further intermediate compounds **F1** are obtained by condensation of pyrazole fragments **B** with DMF-DMA (Table 7).

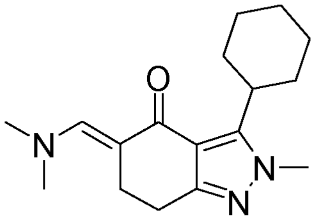
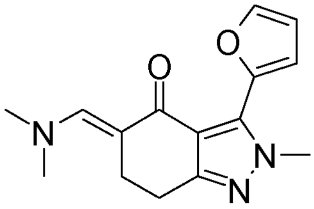
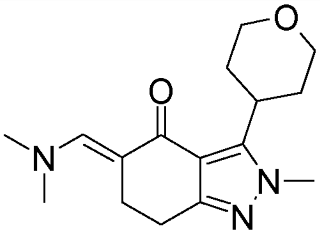
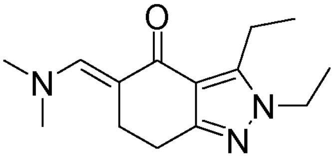
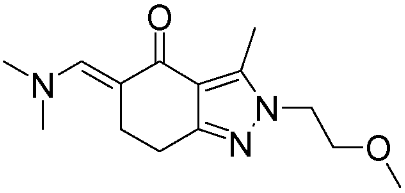
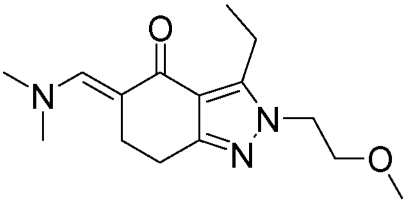
Table 7

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F1-01		0.45	179.0 (hydrolysis)	C
F1-02		0.74	193.1 (hydrolysis)	F
F1-03		0.34	220.2	E
F1-04		0.42	234.2	E
F1-05		0.33	263.2	E
F1-06		0.67	207.3	C
F1-07		0.39	234.2	E

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F1-08		0.56	282.0	A
F1-09		0.40	234.2	E
F1-10		0.81	311.2	B
F1-11		0.75	311.2	B
F1-12		0.53	292.2	A
F1-13		0.84	262.2	B
F1-14		0.74	260.2	B
F1-15		0.64	234.3	B

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F1-16		0.45	234.3	A
F1-17		0.41	246.2	A
F1-18		0.48	260.2	A
F1-19		0.45	290.2	A
F1-20		0.49	248.2	A
F1-21		0.76	260.2	B
F1-22		0.49	248.2	A
F1-23		0.34	250.2	A

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F1-24		0.52	282.2	A
F1-25		0.60	262.2	A
F1-26		0.64	276.2	A
F1-27		0.86	276.2	B
F1-28		0.82	296.2	B
F1-29		0.87	310.2	B
F1-30		1.11	247.2 (hydrolysis)	C

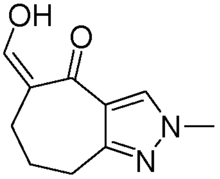
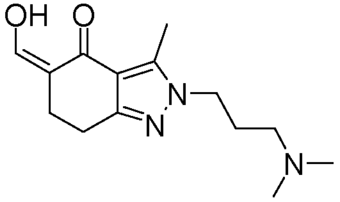
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F1-31		1.21	261.2 (hydrolysis)	C
F1-32		0.75	272.0	B
F1-33		0.66	290.2	B
F1-34		0.71	248.2	B
F1-35		0.37	264.2	A
F1-36		0.43	278.2	A

Preparation of F2-01: reaction with formic acid esters (method G)

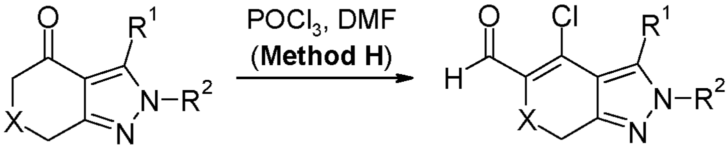
KO*t*Bu (100 mg, 0.89 mmol) is added at 0°C to pyrazole fragment **B-09** (100 mg, 0.43 mmol) in anhydrous dioxane (0.5 mL) and stirred for 5 min. Ethyl formate (60 µL) is added and the mixture is stirred until the starting compound is completely reacted. KO*t*Bu and ethyl formate are optionally metered in subsequently. The crude product may be reacted further directly in the next step.

Analogously to **F2-01** further intermediate compounds **F2** are obtained by reacting formic acid esters with pyrazole fragments **B** (Table 8).

Table 8

No.	product	t_{ret} [min]	$[M+H]^+$	Method of analysis
F2-01		0.84	207.3	C
F2-02		0.13	264.2	E

2.2. Formylation and chlorination of B to form intermediates F3



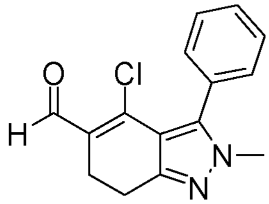
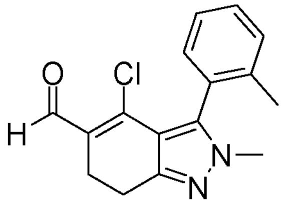
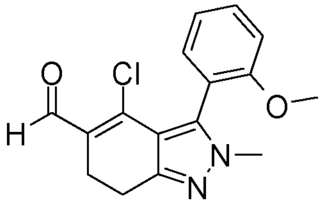
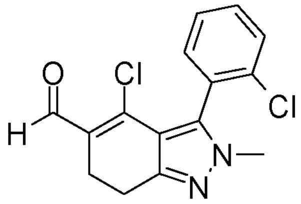
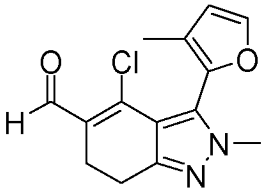
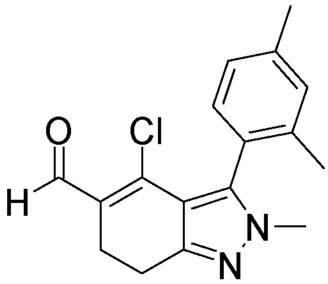
B **F3**

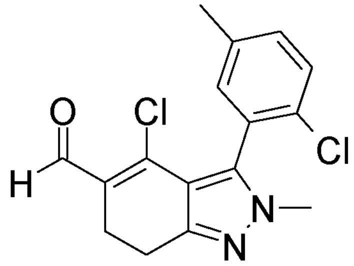
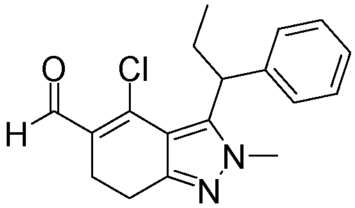
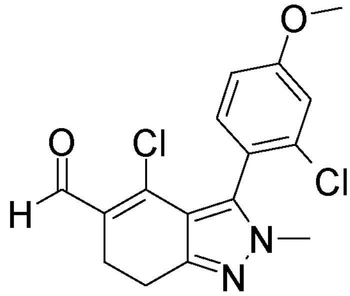
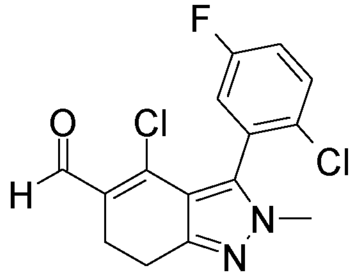
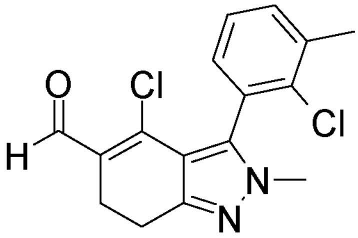
Preparation of F3-01 by reaction with phosphorus oxychloride/DMF (method H)

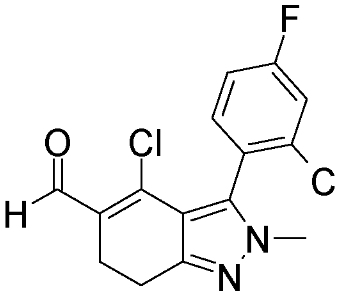
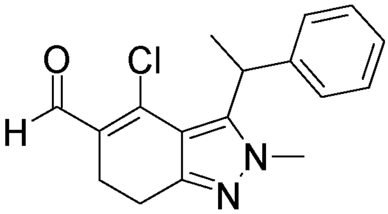
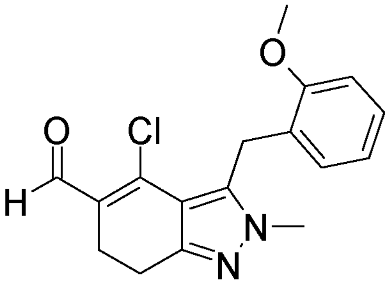
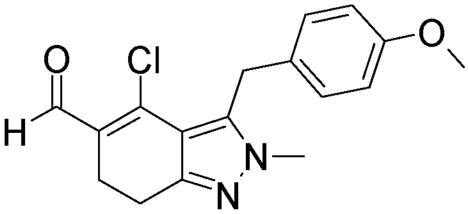
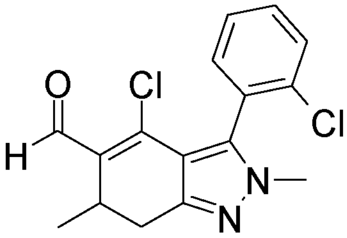
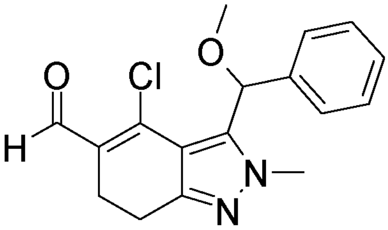
DMF (2.7 mL) is added at 0°C to $POCl_3$ (2.4 mL) in anhydrous DCM (10 mL) and stirred for 20 min. Pyrazole fragment **B-22** (2.0 g, 8.8 mmol) is added, the mixture is stirred for 20 min at RT and for 10 min at 100°C in a microwave reactor. The reaction mixture is added dropwise to semisaturated potassium carbonate solution and the product is extracted with DCM. The organic phase is washed with water, dried on sodium sulphate, filtered and evaporated down.

Analogously to **F3-01** further intermediate compounds **F3** are obtained by reacting pyrazole fragments **B** with $POCl_3$/DMF (Table 9).

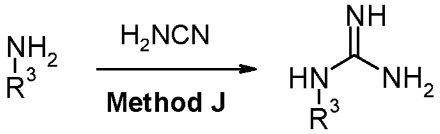
Table 9

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F3-01		1.15	273.2	C
F3-02		1.22	287.2	C
F3-03		1.11	303.2	C
F3-04		1.20	307.0	C
F3-05		1.14	277.2	C
F3-06		1.32	301.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F3-07		1.32	321.0	C
F3-08		1.36	315.2	C
F3-09		1.24	337.0	C
F3-10		1.23	325.0	C
F3-11		1.30	321.0	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
F3-12		1.24	325.0	C
F3-13		1.25	301.0	C
F3-14		1.21	317.2	C
F3-15		1.16	317.2	C
F3-16		1.26	321.0	C
F3-17		1.27	317.2	C

3. Guanidine syntheses



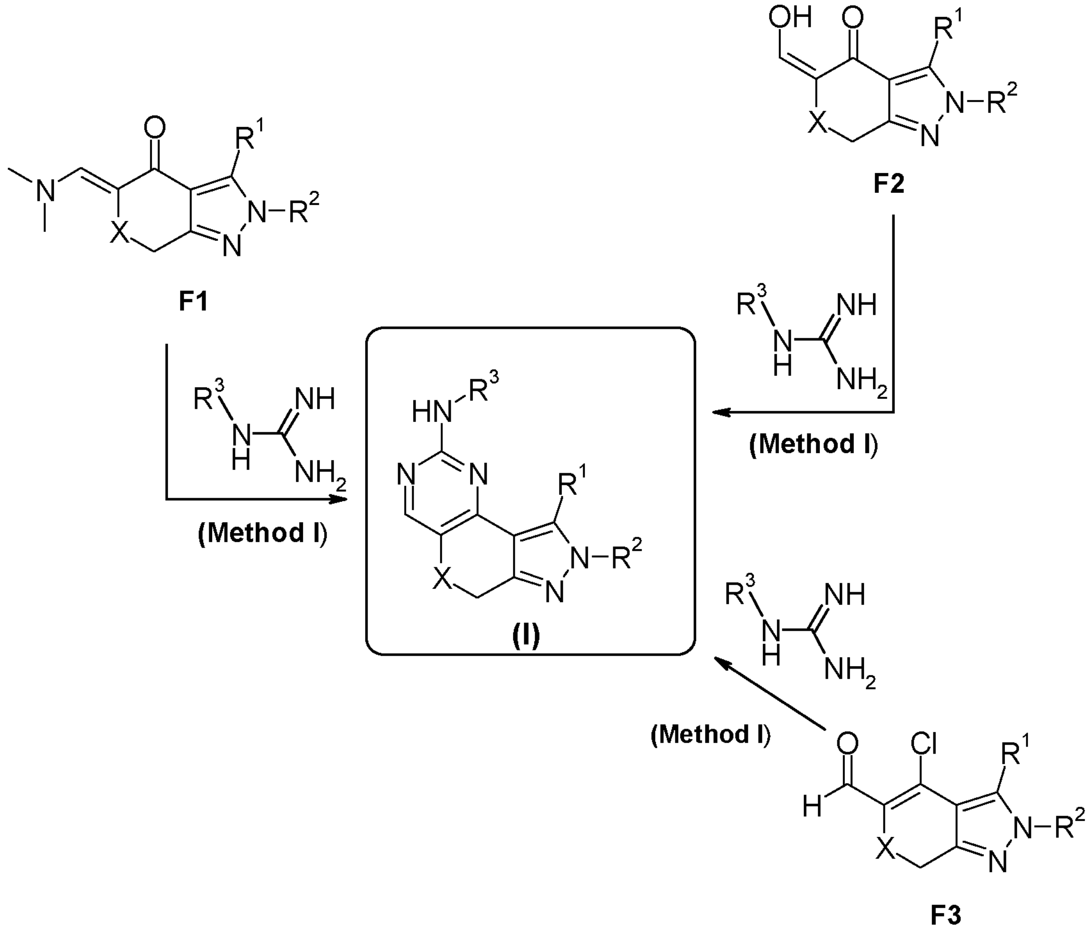
The preparation of the guanidine compounds (**method J**) takes place in the Parallel Synthesis Microwave Reactor (Synthos 3000, Anton Paar GmbH). The aniline (0.5 mmol) in dioxane (300 µL) is combined with cyanamide (1.5 mmol) in dioxane (125 µL) and HCl (4 N in dioxane, 188 µL) and stirred for 1 h at 120°C.

The reaction solutions are used in the next step without any further purification.

Complexly substituted guanidines are prepared analogously to or using the methods of C. E. Stephens, *J. Med. Chem.* **2001**, 1741–1748 and H. Ube, *J. Organomet. Chem.* **2007**, 545-549 using isothiourea components.

4. Preparation of novel compounds (I) by pyrimidine cyclisation and optionally derivatisation

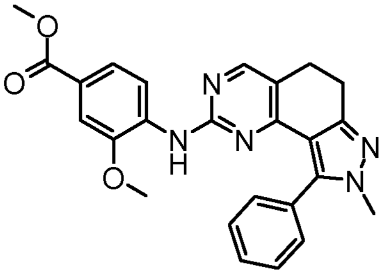
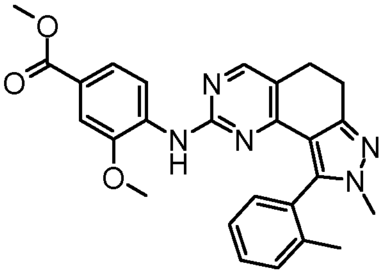
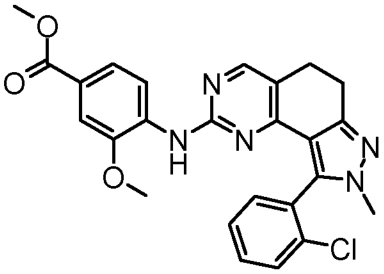
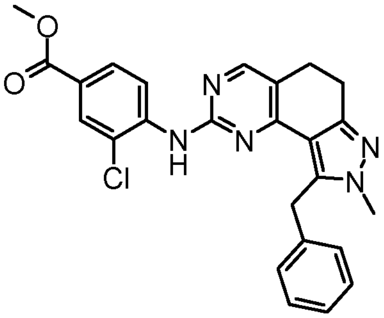
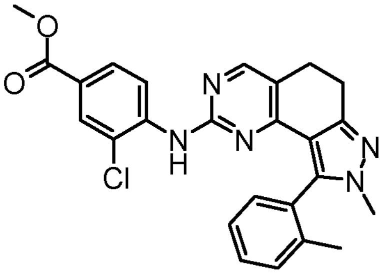
4.1. Pyrimidine cyclisation on intermediates F1, F2 and F3 using guanidine (method I, type I)

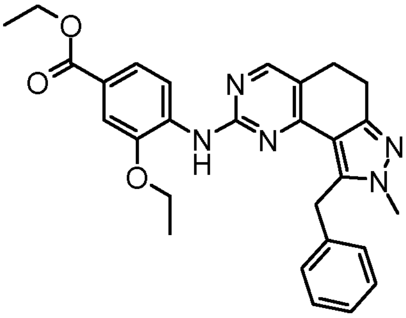
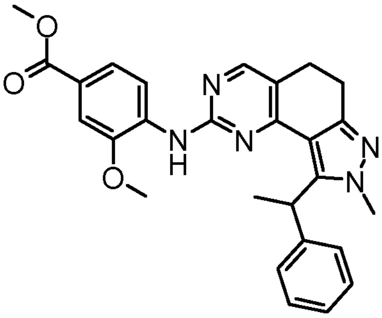
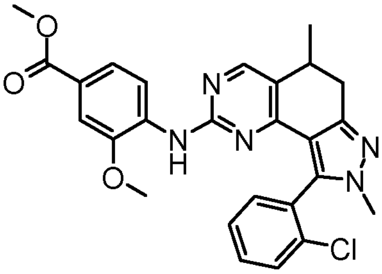
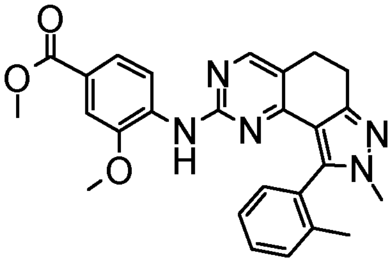
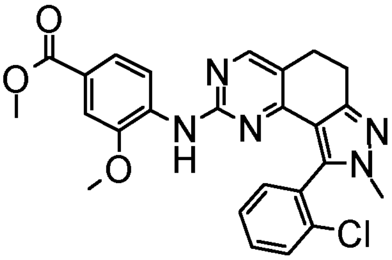


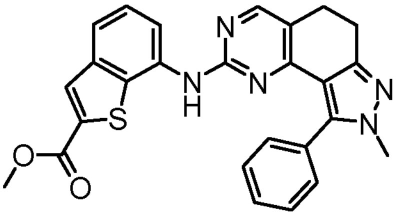
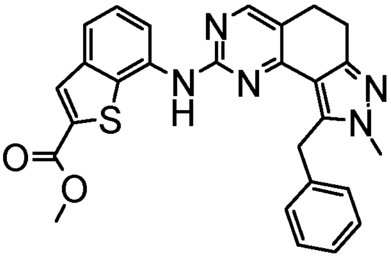
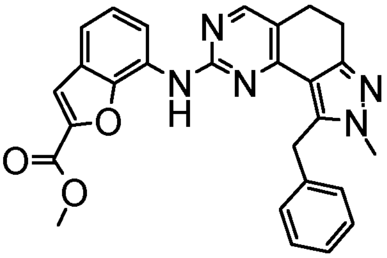
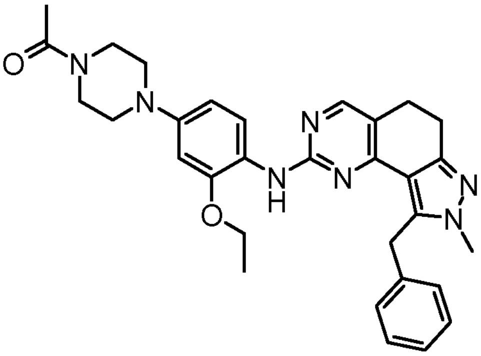
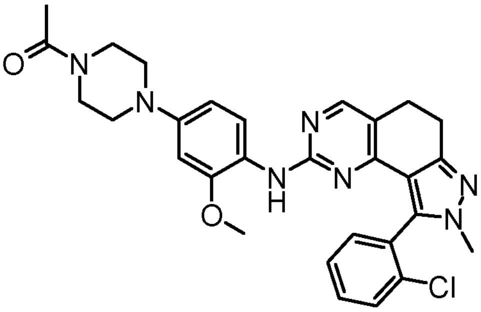
Method I: The reaction mixture of the guanidine synthesis is combined with pyridine (200 µL) and the corresponding pyrazole component **F1**, **F2** or **F3** (0.5 mmol) in dioxane (150 µL) and stirred for 1 h at 120°C in a parallel synthesis microwave reactor. The reaction mixture is purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried. The compounds **I-1** to **I-295** according to the invention (Table 10) are prepared in this way.

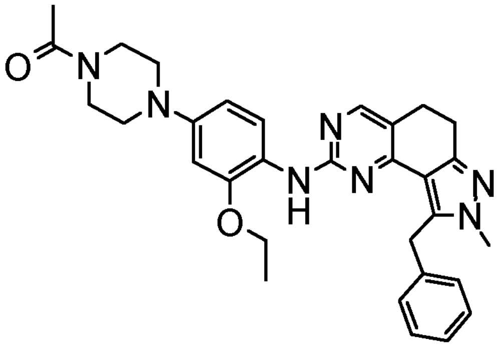
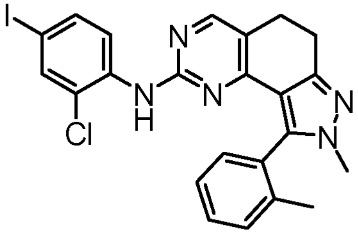
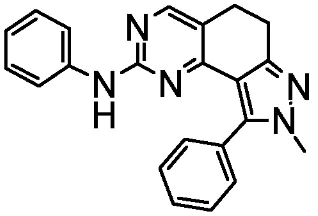
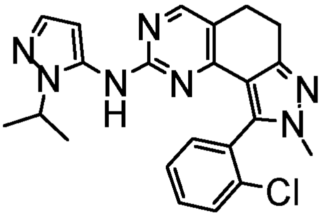
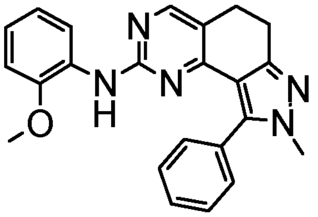
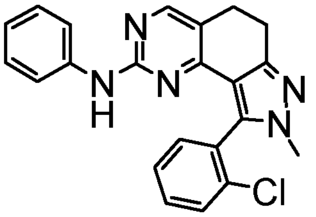
Protected intermediate stages or guanidine intermediates intended for further derivatisation are prepared analogously and purified by conventional methods. The synthesis components required for this are synthesised from commercial reactants using standard methods.

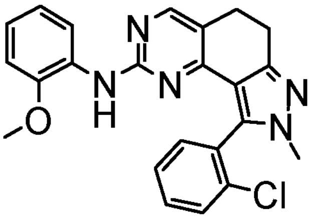
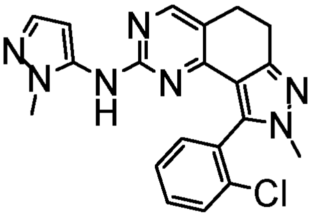
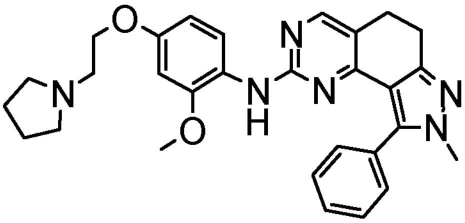
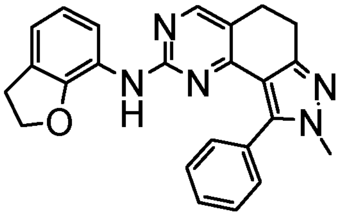
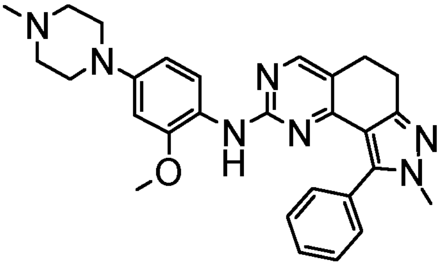
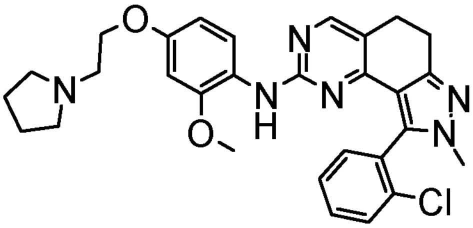
Table 10

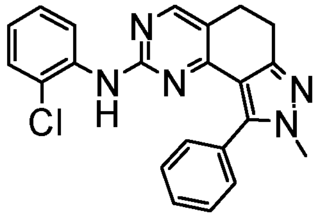
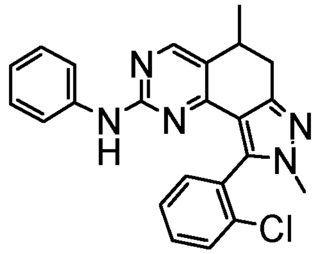
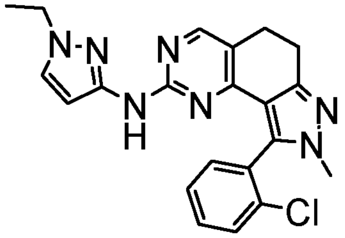
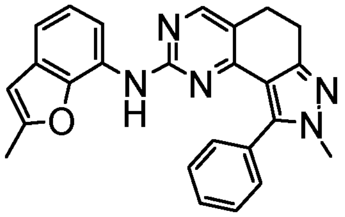
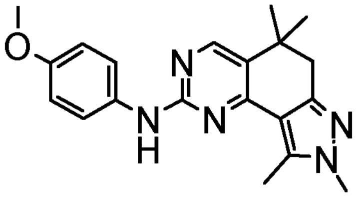
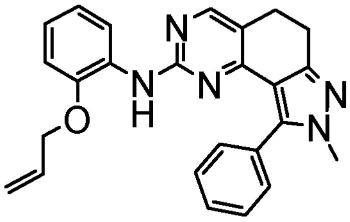
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-1		1.33	442.2	C
I-2		1.39	456.2	C
I-3		1.36	476.2	C
I-4		1.50	460.2	C
I-5		1.54	460.2	C

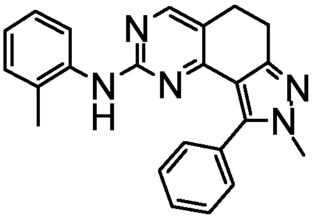
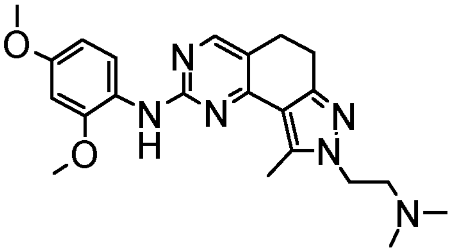
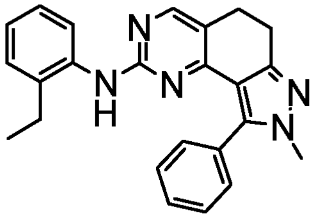
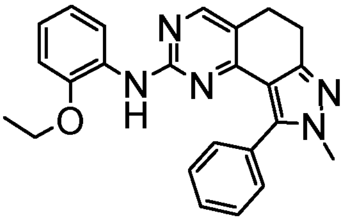
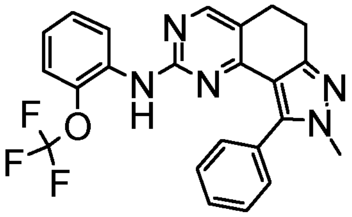
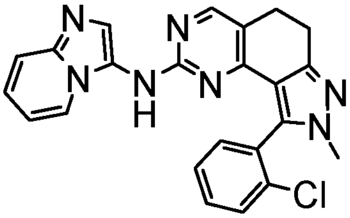
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-6		1.53	484.2	C
I-7		1.46	470.2	C
I-8*		1.40	490.2	C
I-9		2.07	456.3	G
I-10		2.05	476.3	G

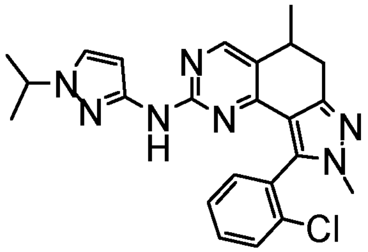
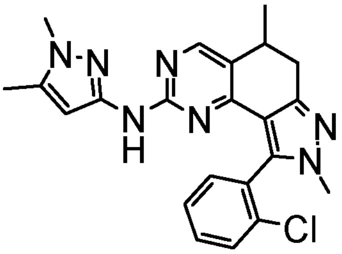
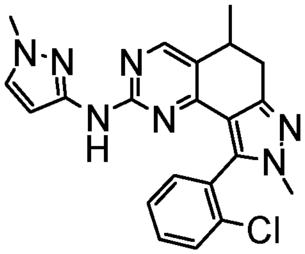
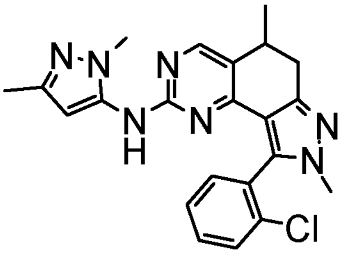
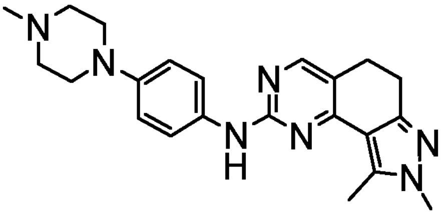
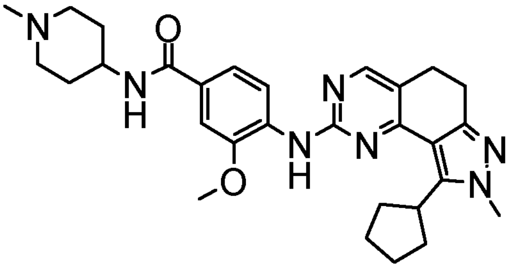
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-11		1.25	482.2	C
I-12		2.04	482.0	G
I-13		2.05	466.0	G
I-14		0.90	538.4	C
I-15		0.93	544.2	C

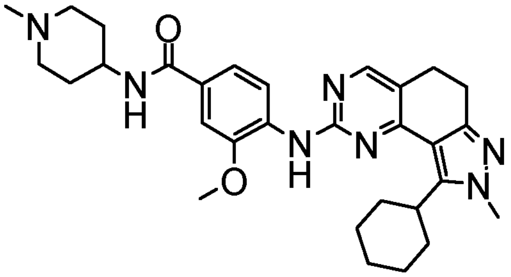
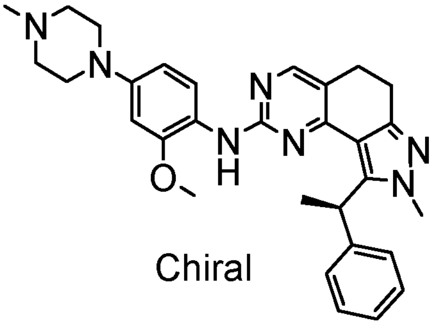
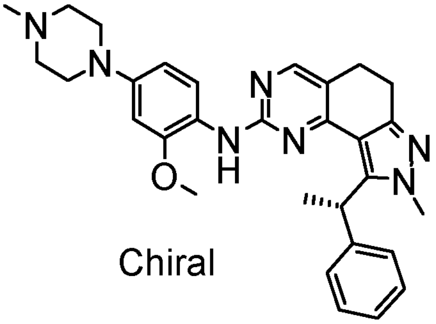
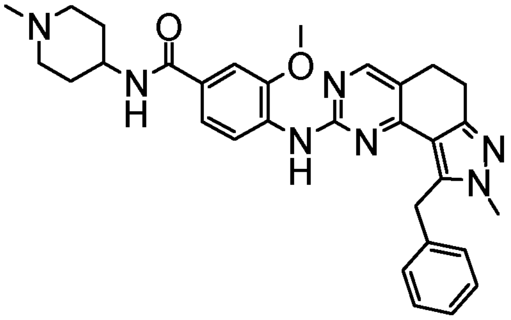
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-16		1.84	538.3	G
I-17		1.66	528.2	C
I-18		1.88	354.3	G
I-19		1.66	420.3	G
I-20		1.99	384.3	G
I-21		1.91	388.3	G

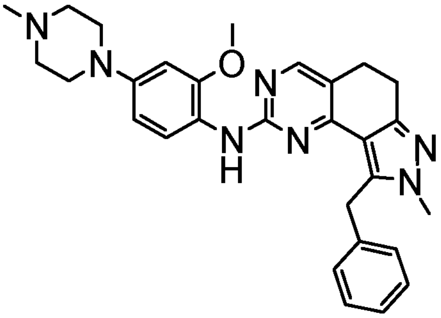
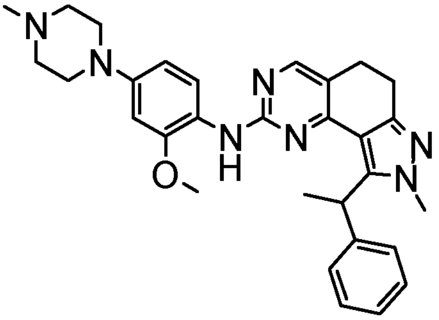
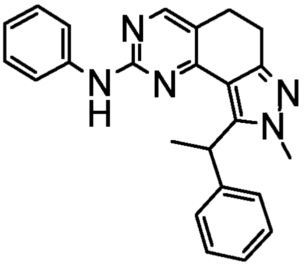
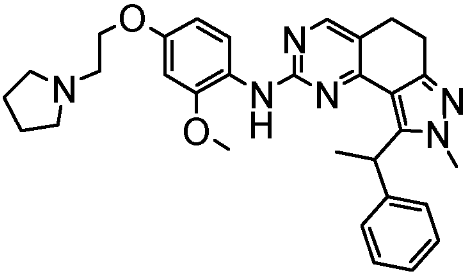
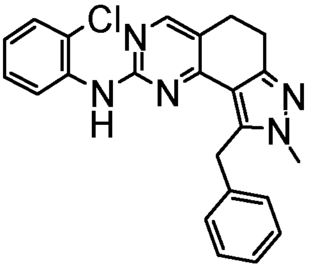
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-22		2.04	418.3	G
I-23		1.54	392.3	G
I-24		2.05	497.3	G
I-25		1.97	396.0	G
I-26		1.83	482.3	G
I-27		2.11	531.2	G

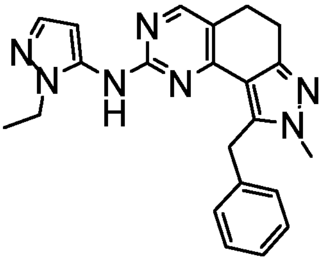
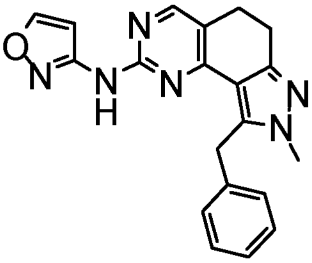
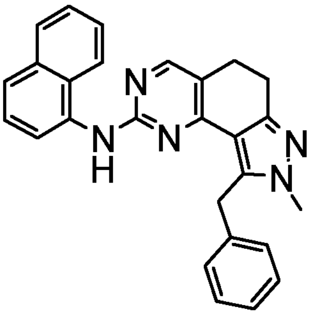
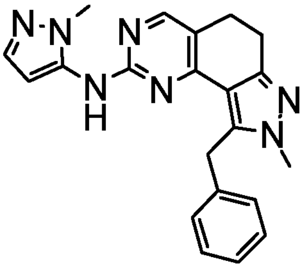
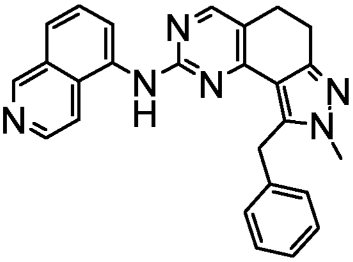
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-28		2.14	388.0	G
I-29*		1.96	402.3	G
I-30		1.65	406.3	G
I-31		2.11	408.0	G
I-32		1.79	350.3	G
I-33		2.15	410.3	G

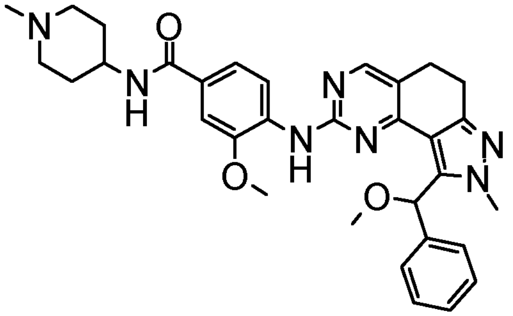
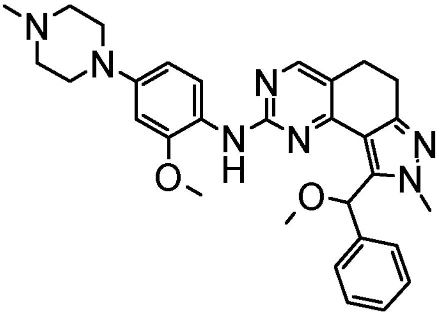
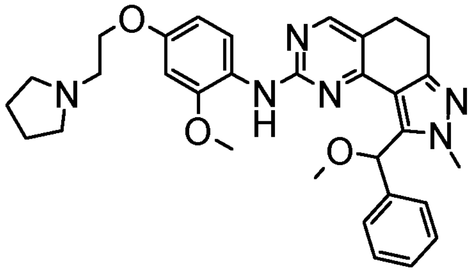
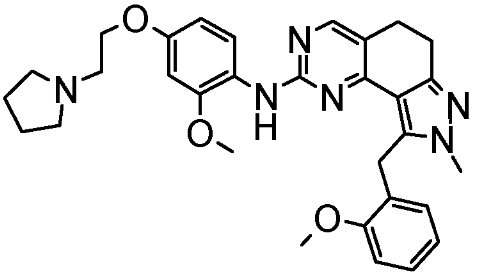
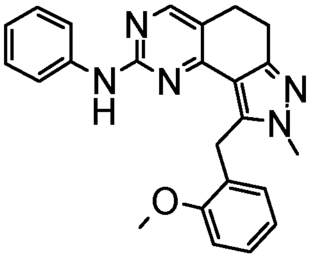
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-34		1.97	368.0	G
I-35		1.83	409.3	G
I-36		2.08	382.0	G
I-37		2.13	398.0	G
I-38		2.21	438.0	G
I-39		1.51	428.3	G

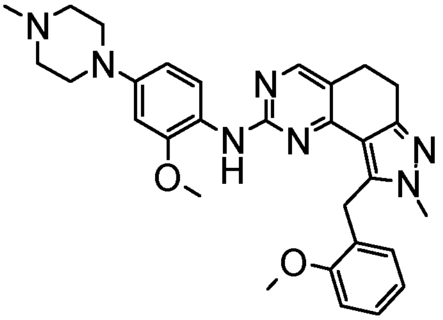
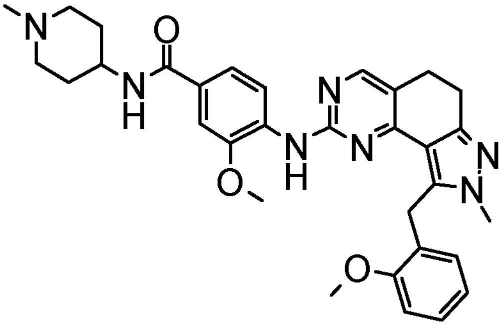
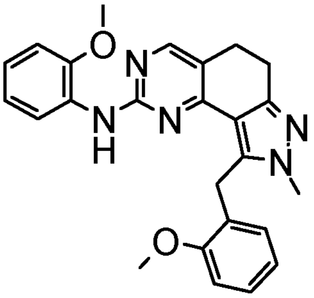
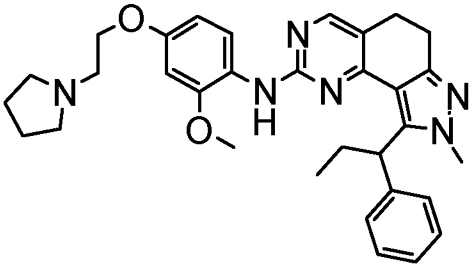
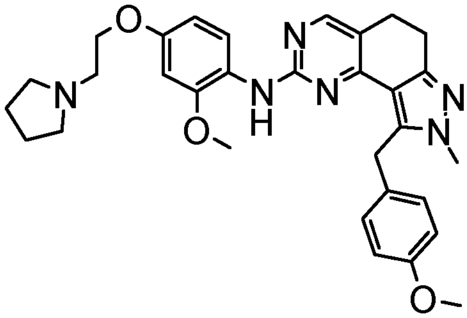
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-40*		1.82	434.3	G
I-41*		1.69	420.3	G
I-42*		1.64	406.3	G
I-43*		1.64	420.3	G
I-44		1.53	390.3	G
I-45		2.16	516.3	G

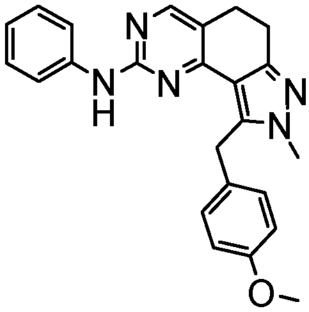
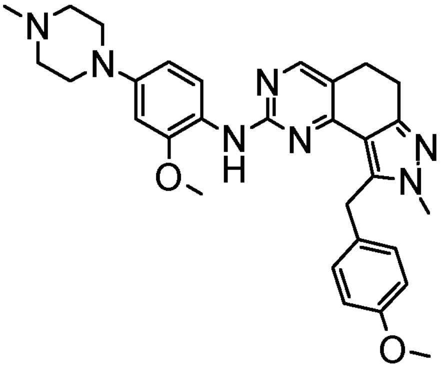
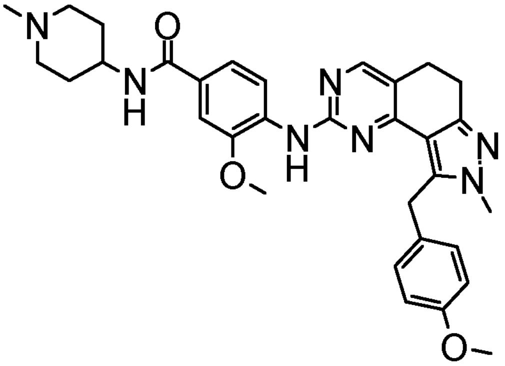
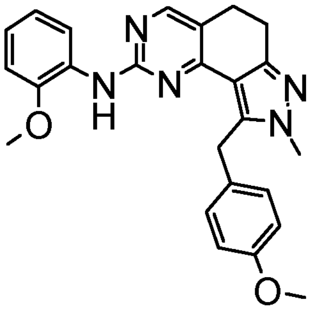
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-46		2.28	530.5	G
I-47	 Chiral	1.78	510.5	G
I-48	 Chiral	1.94	510.3	G
I-49		1.77	538.3	G

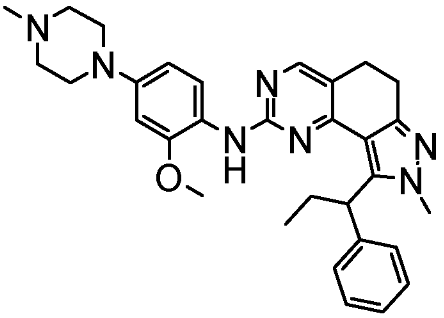
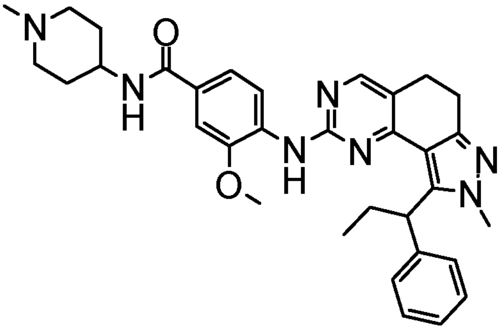
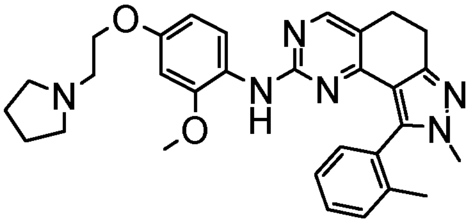
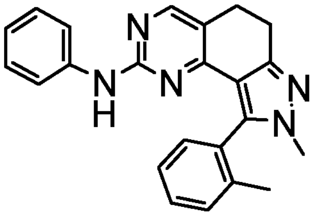
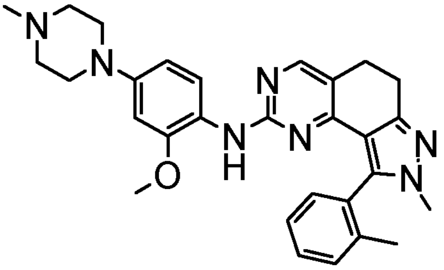
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-50		1.86	496.3	G
I-51		1.94	510.3	G
I-52		2.05	382.3	G
I-53		2.16	525.3	G
I-54		2.01	402.2	G

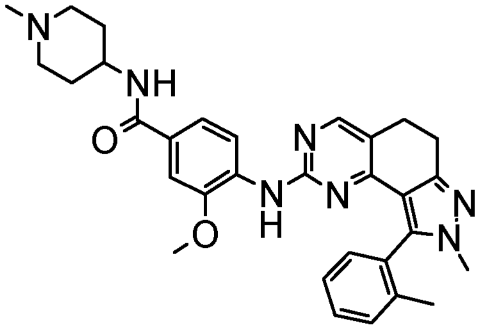
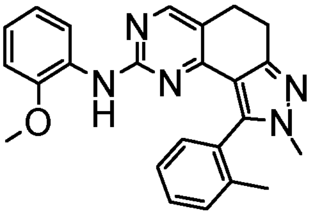
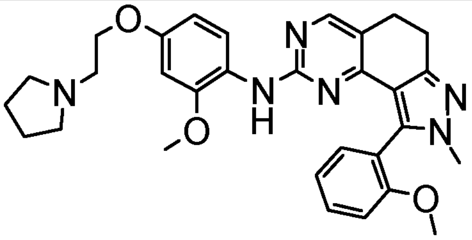
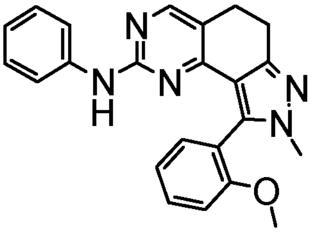
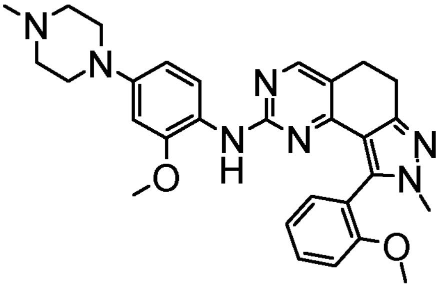
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-55		1.64	386.0	G
I-56		1.67	359.0	G
I-57		2.11	418.0	G
I-58		1.56	372.3	G
I-59		1.77	419.0	G

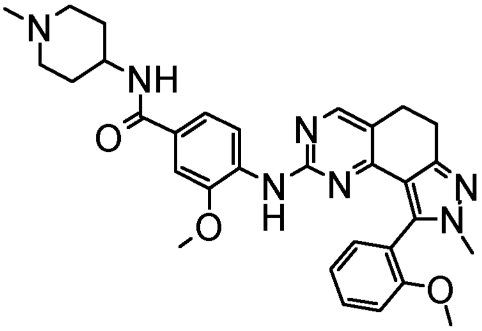
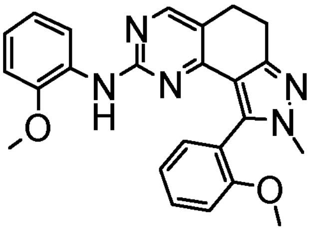
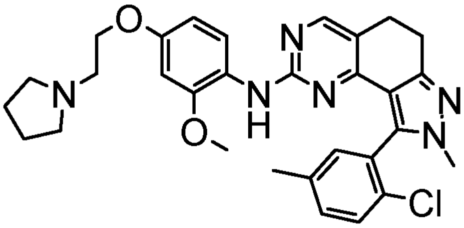
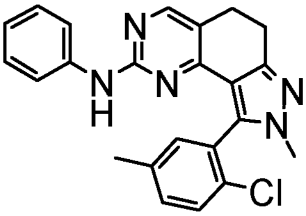
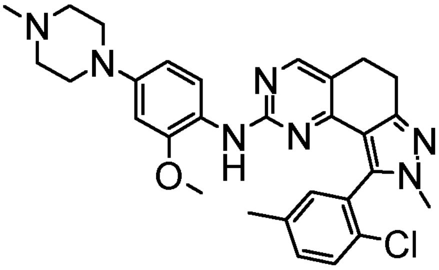
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-60		1.90	568.2	G
I-61		1.94	526.2	G
I-62		2.16	541.3	G
I-63		2.01	541.5	G
I-64		1.77	398.3	G

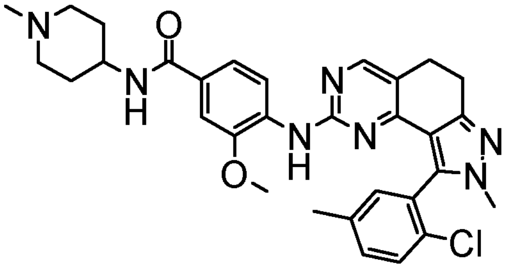
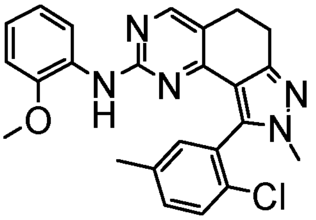
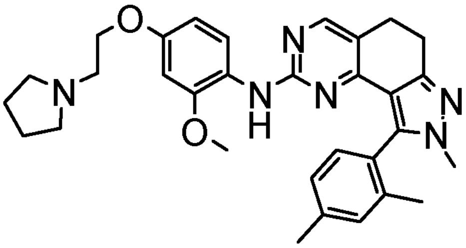
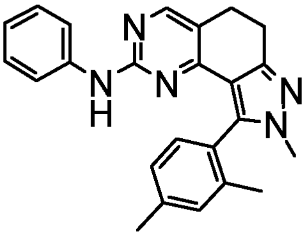
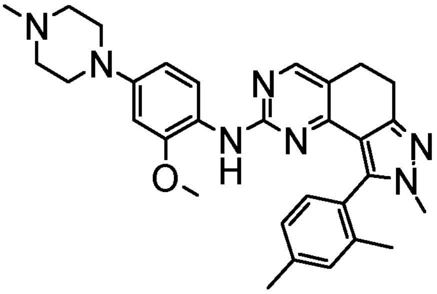
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-65		1.73	526.5	G
I-66		1.80	568.5	G
I-67		1.87	428.5	G
I-68		2.21	539.2	G
I-69		2.07	541.3	G

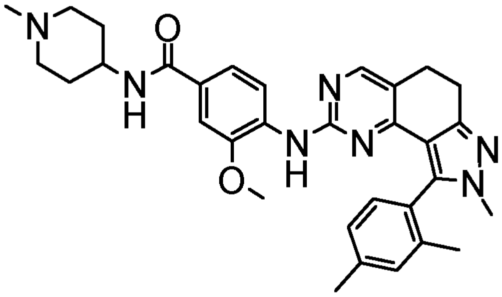
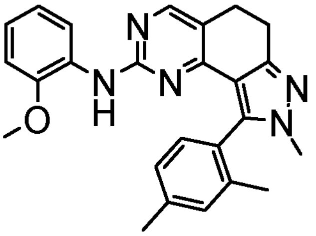
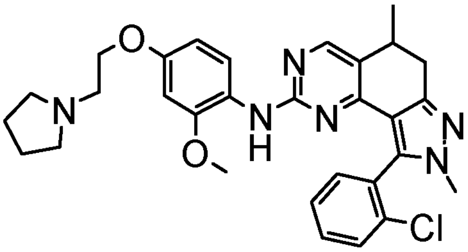
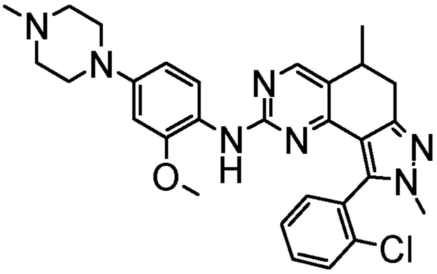
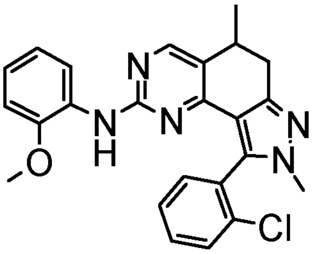
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-70		1.93	398.3	G
I-71		1.86	526.2	G
I-72		1.81	568.2	G
I-73		2.02	428.3	G

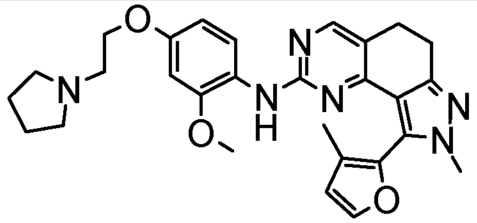
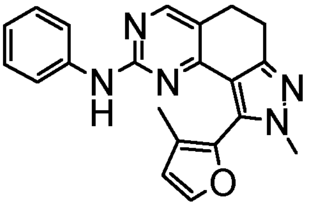
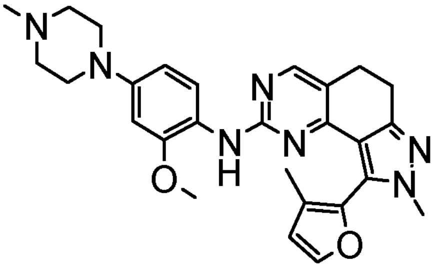
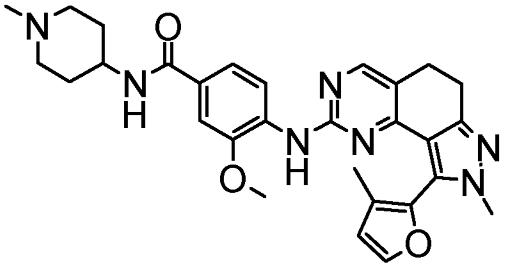
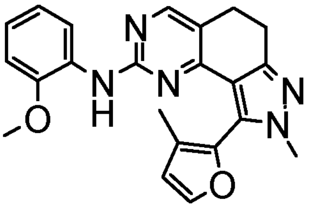
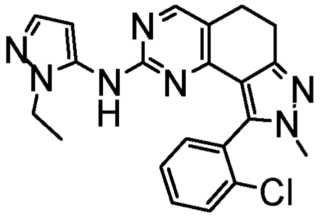
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-74		2.00	524.3	G
I-75		1.95	566.2	G
I-76		2.14	511.3	G
I-77		1.97	368.0	G
I-78		1.91	496.3	G

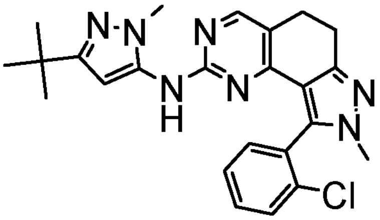
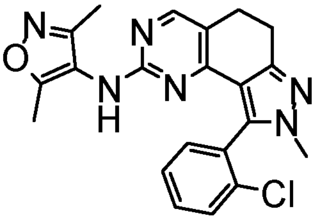
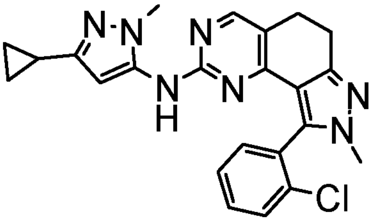
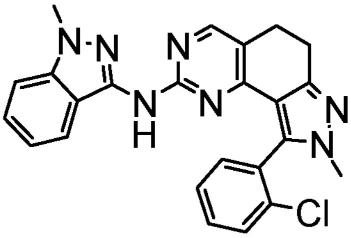
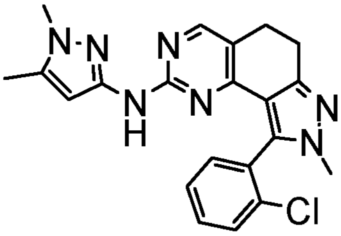
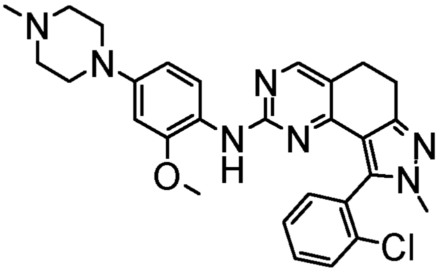
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-79		1.84	538.3	G
I-80		2.08	398.3	G
I-81		2.05	527.2	G
I-82		1.87	384.3	G
I-83		1.82	512.3	G

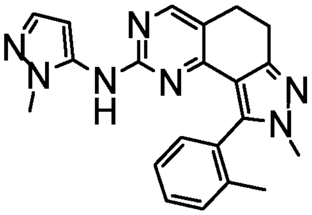
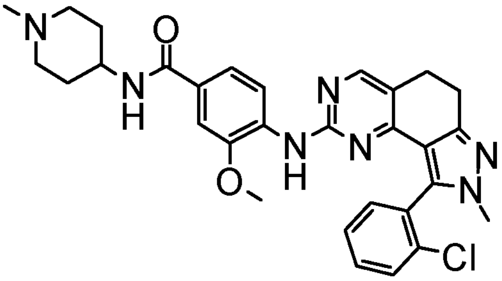
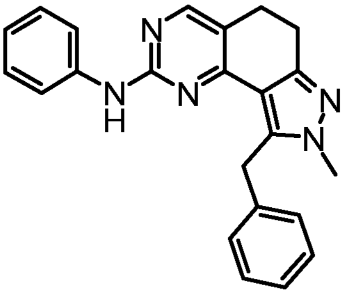
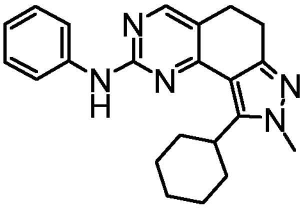
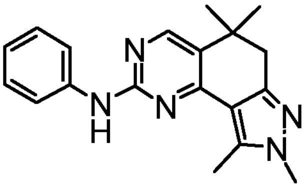
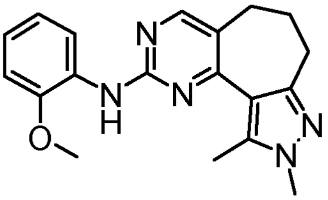
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-84		1.76	554.2	G
I-85		1.98	414.0	G
I-86		2.12	545.3	G
I-87		1.98	402.0	G
I-88		1.92	530.2	G

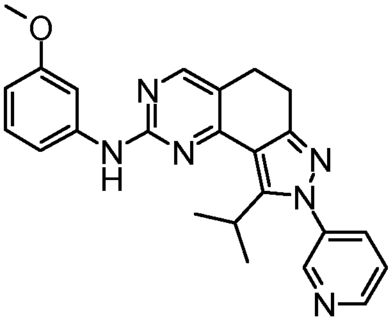
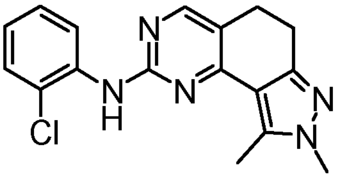
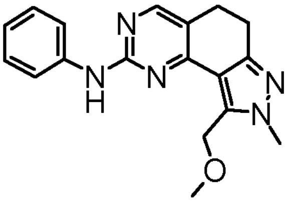
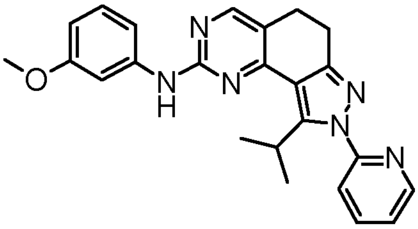
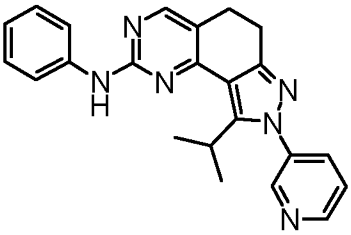
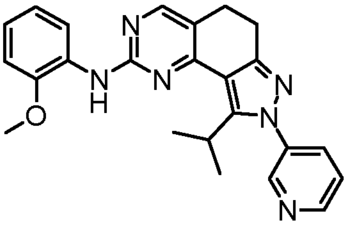
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-89		1.82	572.3	G
I-90		2.09	432.3	G
I-91		2.25	525.3	G
I-92		2.01	382.3	G
I-93		1.94	510.3	G

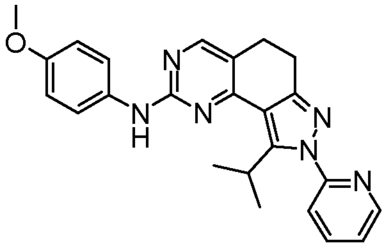
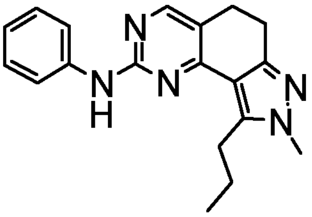
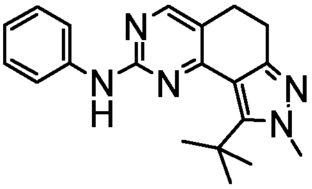
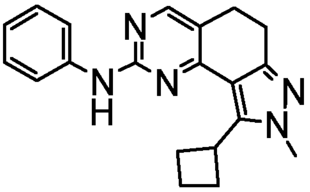
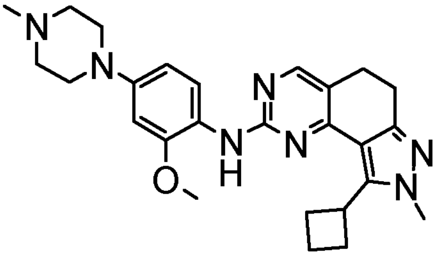
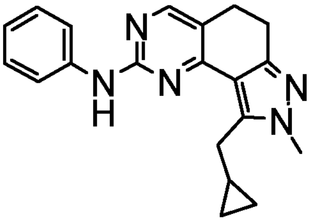
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-94		1.82	552.2	G
I-95		2.12	412.3	G
I-96*		2.12	545.3	G
I-97*		1.91	530.2	G
I-98*		2.08	432.3	G

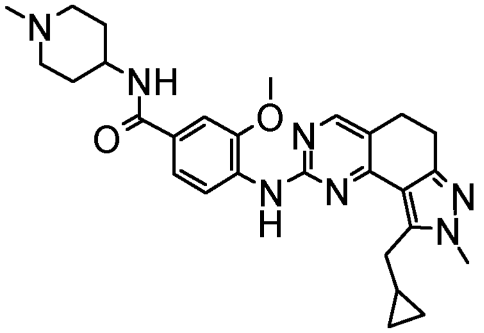
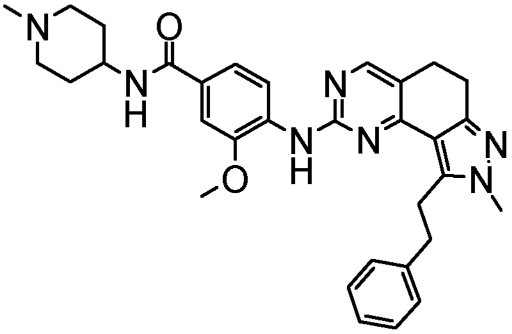
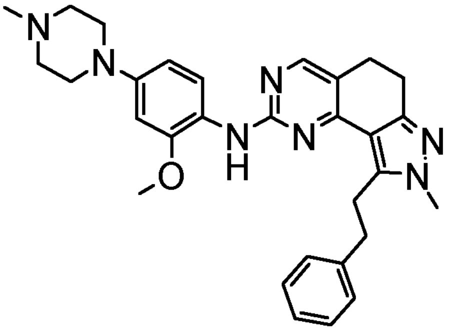
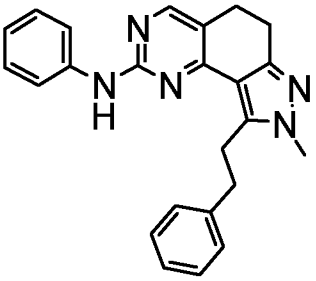
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-99		2.04	501.3	G
I-100		1.86	358.3	G
I-101		1.81	486.3	G
I-102		1.73	528.3	G
I-103		1.99	388.3	G
I-104		1.58	406.3	G

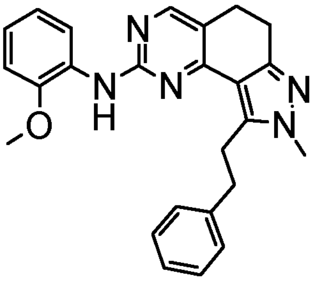
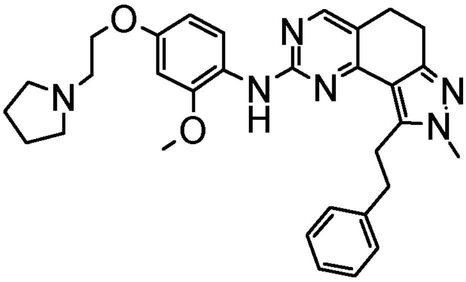
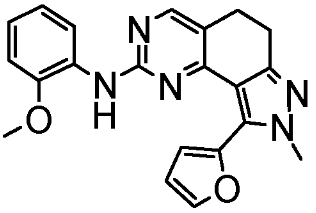
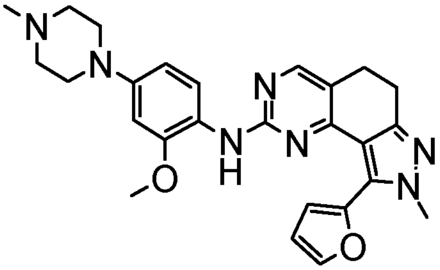
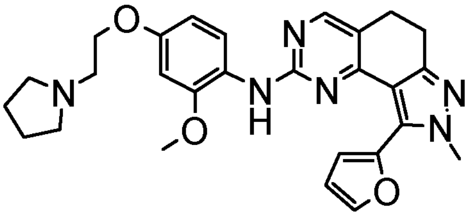
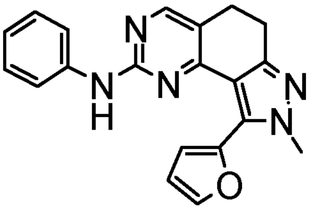
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-105		1.89	448.3	G
I-106		1.62	407.3	G
I-107		1.69	432.3	G
I-108		1.75	442.3	G
I-109		1.62	406.3	G
I-110		1.88	516.3	G

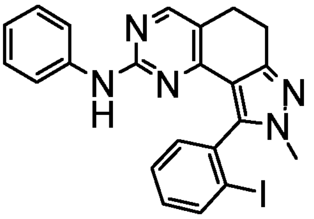
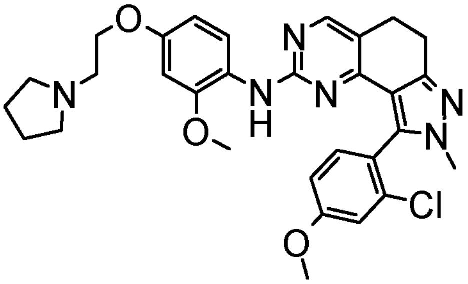
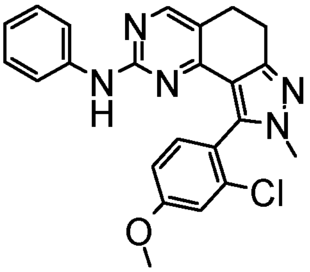
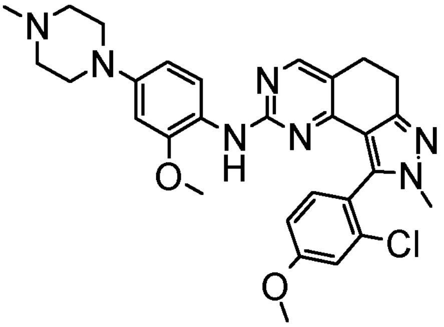
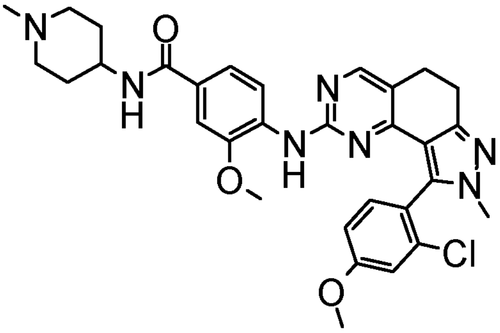
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-111		1.55	372.3	G
I-112		1.80	558.5	G
I-113		1.94	368.3	G
I-114		2.13	360.3	G
I-115		1.85	320.3	G
I-116		1.90	336.3	G

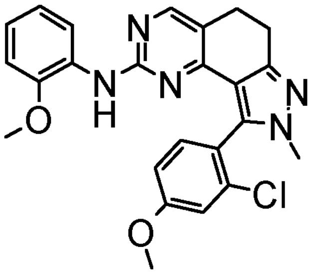
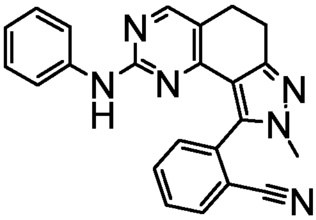
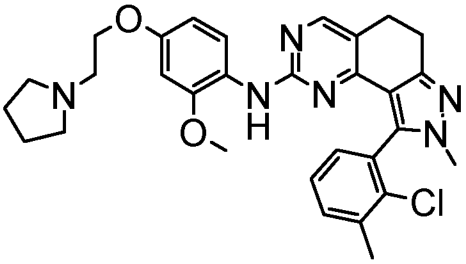
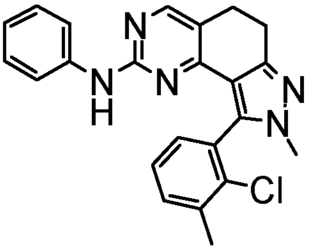
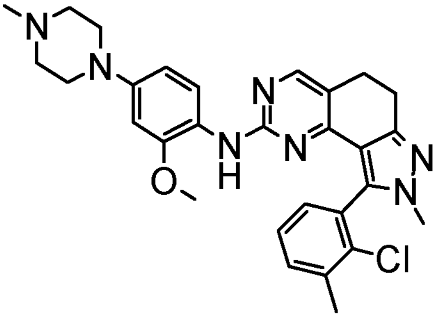
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-117		1.88	413.0	G
I-118		1.89	326.3	G
I-119		1.66	322.3	G
I-120		2.04	413.0	G
I-121		1.88	383.0	G
I-122		1.97	413.0	G

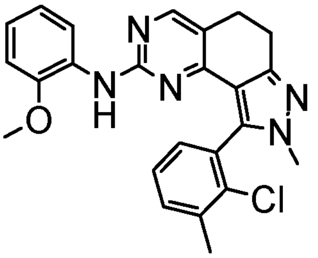
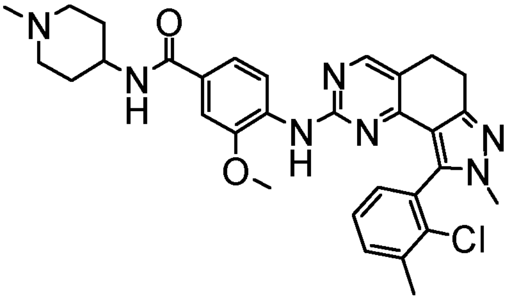
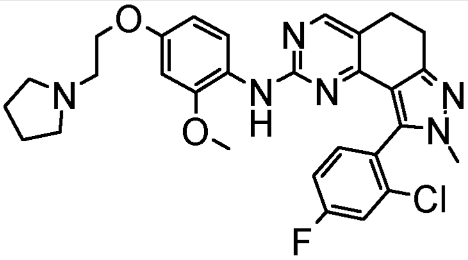
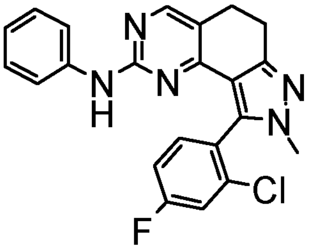
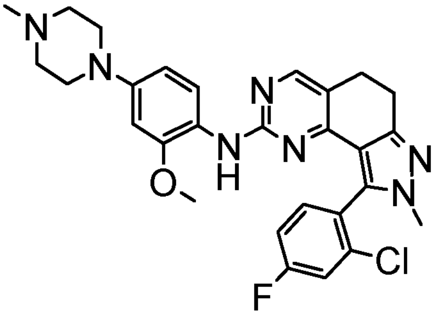
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-123		1.98	413.0	G
I-124		1.97	320.3	G
I-125		1.94	334.3	G
I-126		1.90	332.3	G
I-127		1.82	460.3	G
I-128		1.87	332.0	G

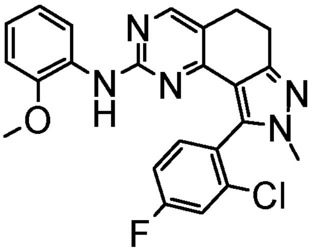
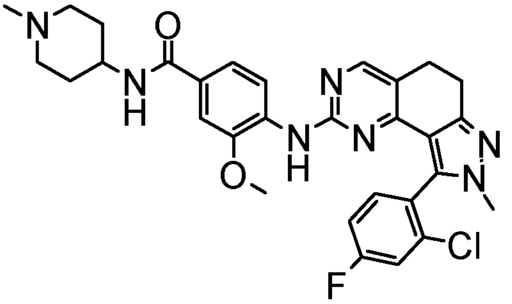
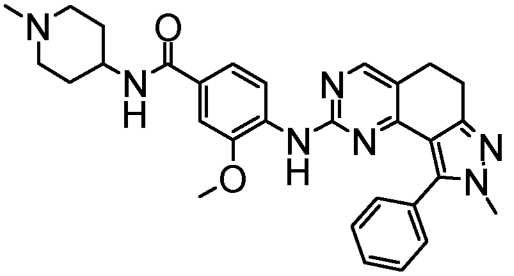
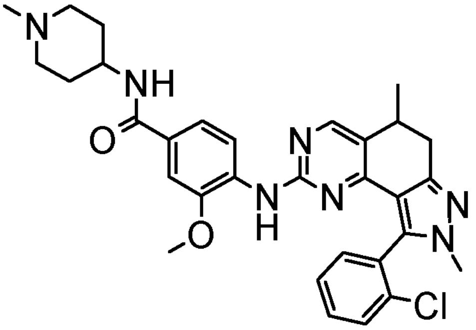
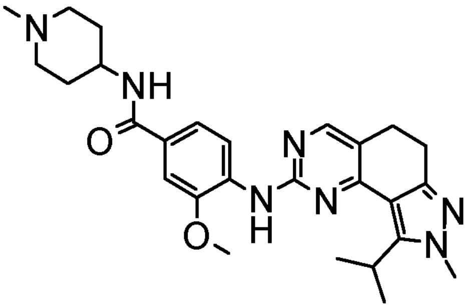
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-129		1.74	502.0	G
I-130		2.15	552.5	G
I-131		2.03	510.20	G
I-132		2.06	382.3	G

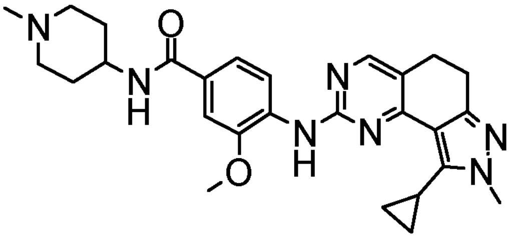
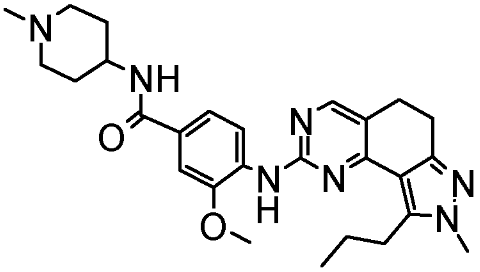
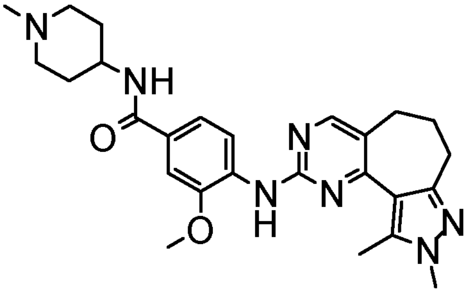
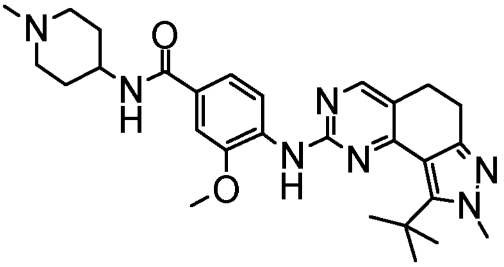
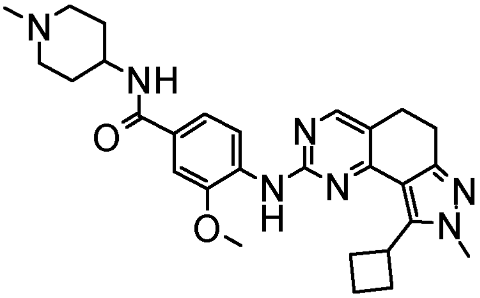
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-133		2.19	412.3	G
I-134		2.14	525.5	G
I-135		1.97	374.2	G
I-136		1.81	472.30	G
I-137		2.04	487.3	G
I-138		1.87	344.0	G

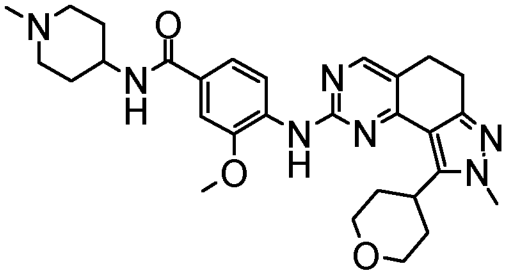
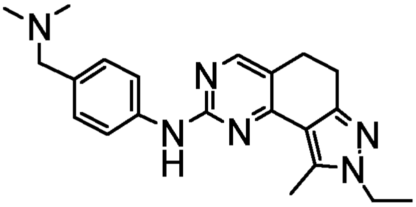
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-139		1.93	480.0	G
I-140		2.08	561.3	G
I-141		1.89	418.3	G
I-142		1.86	546.3	G
I-143		1.78	588.3	G

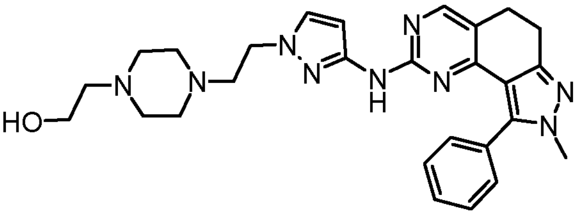
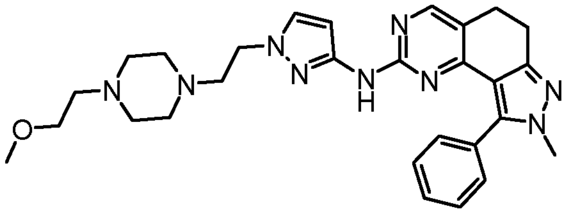
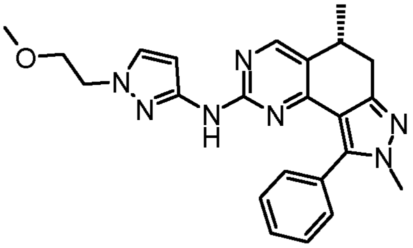
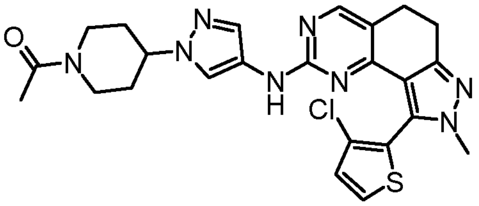
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-144		2.00	448.3	G
I-145		1.68	379.0	G
I-146		2.02	545.3	G
I-147		1.84	402.2	G
I-148		1.77	530.5	G

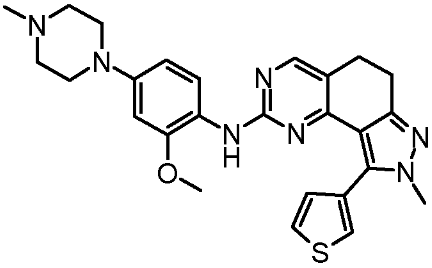
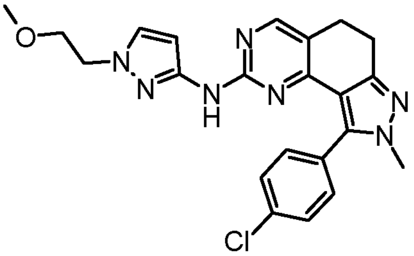
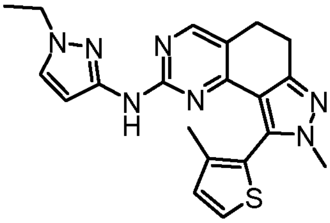
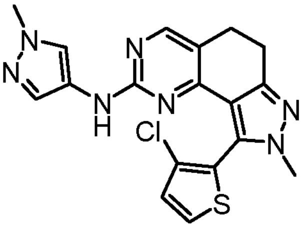
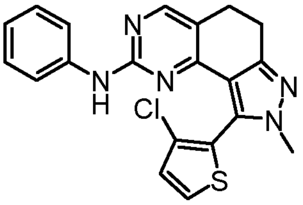
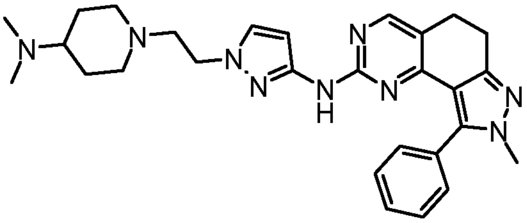
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-149		1.93	432.0	G
I-150		1.69	572.3	G
I-151		1.94	549.3	G
I-152		1.76	406.2	G
I-153		1.71	534.5	G

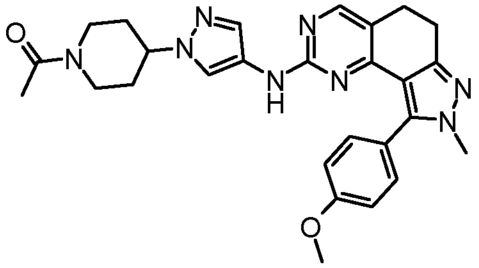
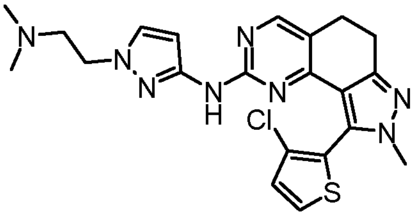
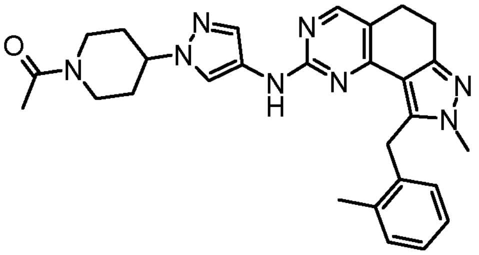
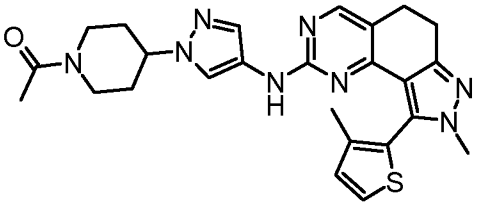
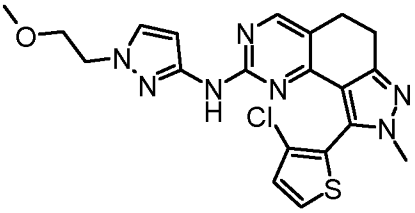
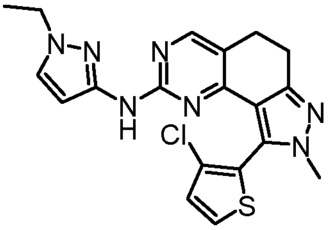
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-154		1.87	436.2	G
I-155		1.64	576.2	G
I-156		1.75	524.3	G
I-157*		1.82	572.3	G
I-158		1.72	490.3	G

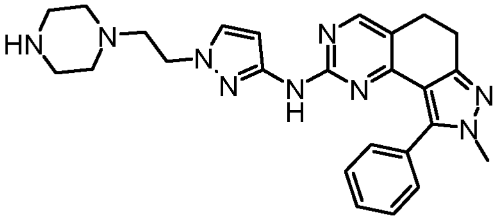
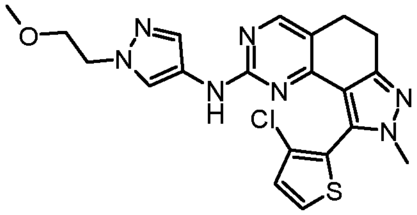
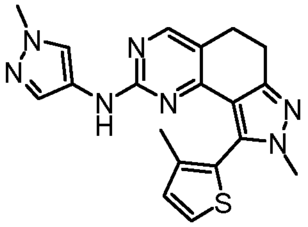
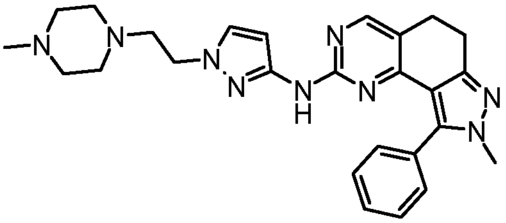
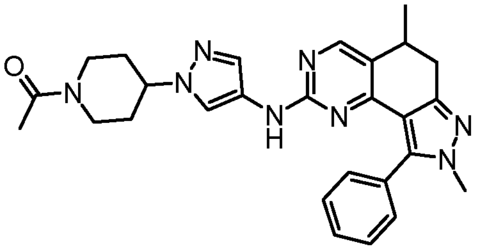
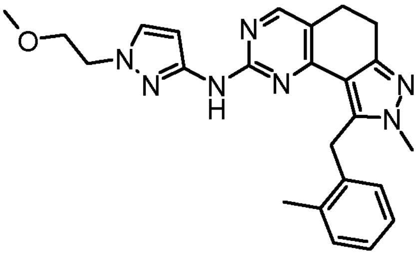
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-159		1.70	488.3	G
I-160		1.72	490.3	G
I-161		1.72	476.3	G
I-162		1.80	504.3	G
I-163		1.78	502.3	G

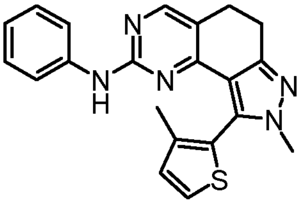
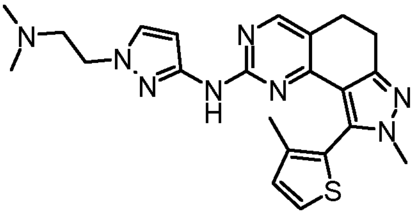
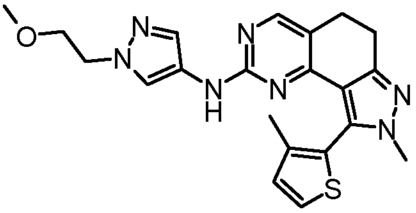
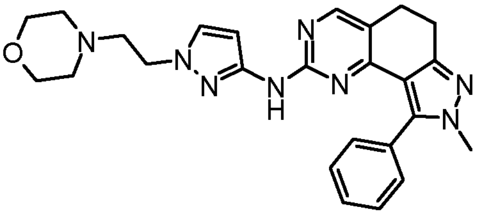
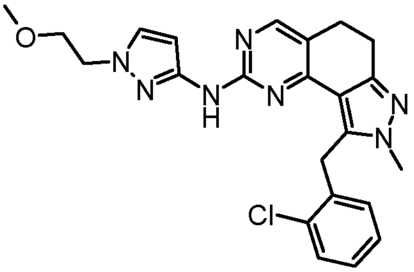
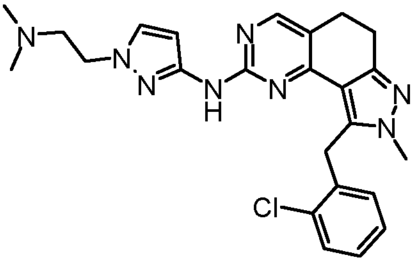
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
I-164		1.66	532.3	G
I-165		1.76	363.3	G

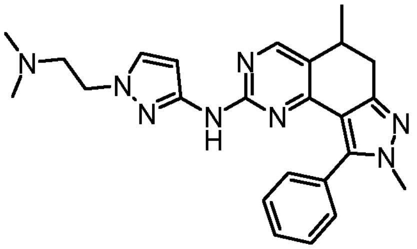
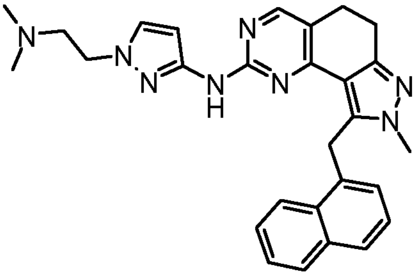
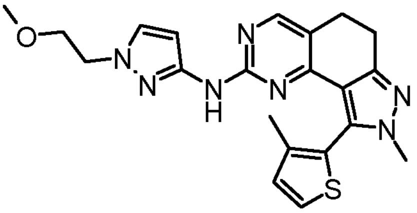
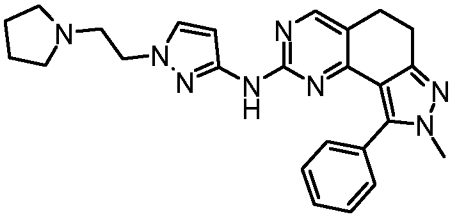
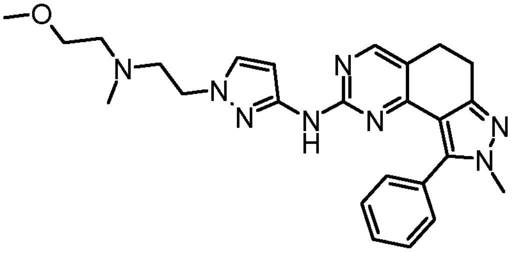
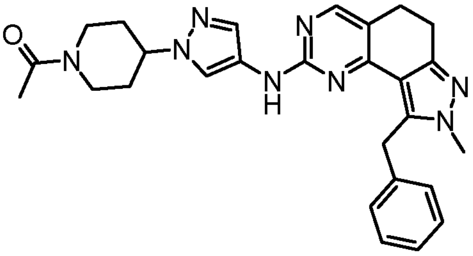
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-166		1.07	500	G
I-167		1.17	514	G
I-168		1.67	416	G
I-169		1.25	509	G

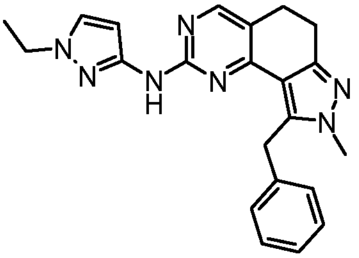
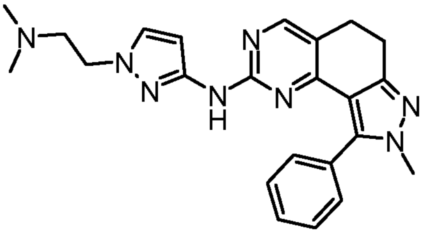
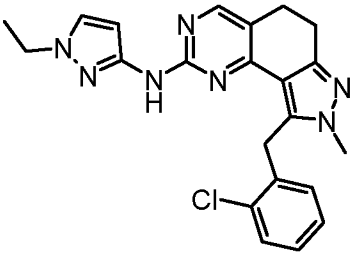
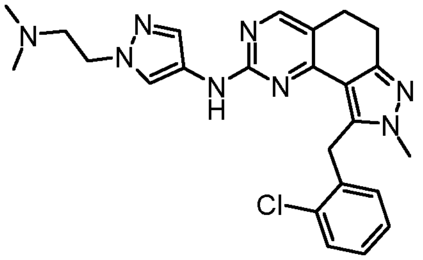
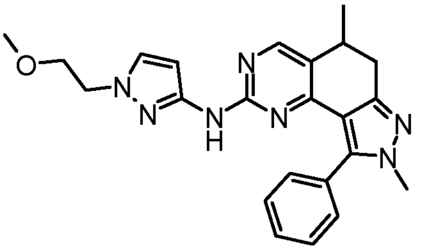
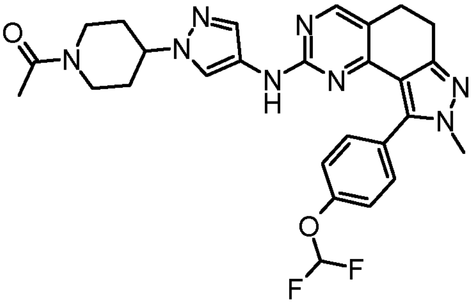
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-170		1.76	488	G
I-171		1.29	436	G
I-172		1.37	392	G
I-173		1.25	398	G
I-174		1.54	394	G
I-175		1.29	498	G

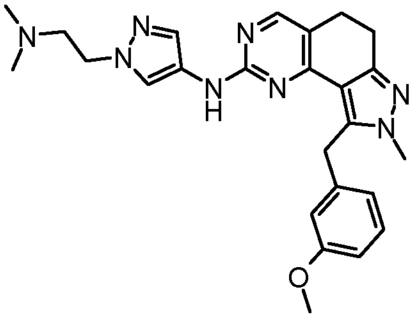
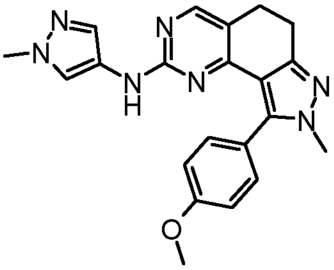
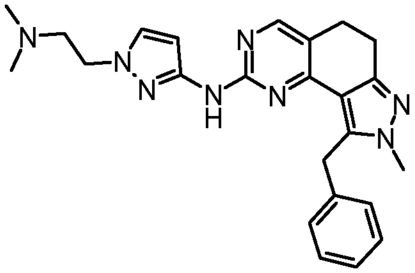
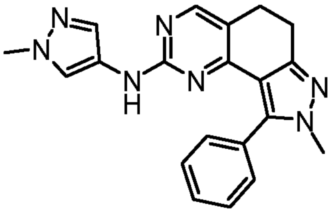
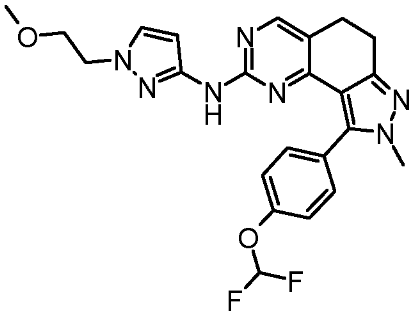
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-176		1.14	499	G
I-177		1.35	455	G
I-178		1.19	497	G
I-179		1.24	489	G
I-180		1.33	442	G
I-181		1.37	412	G

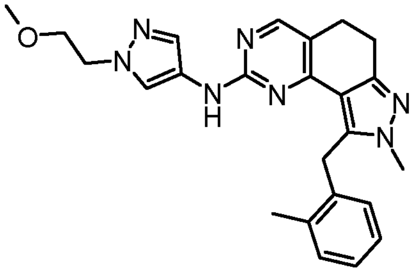
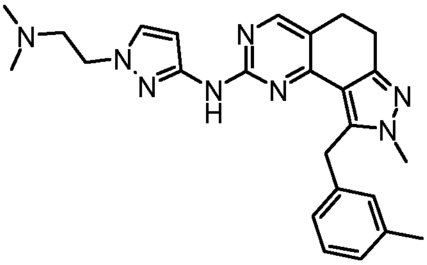
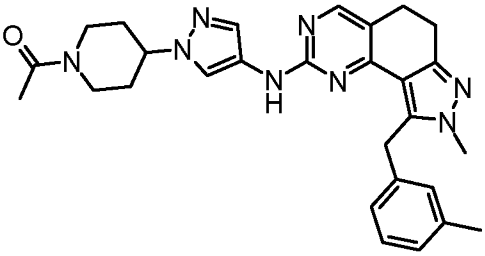
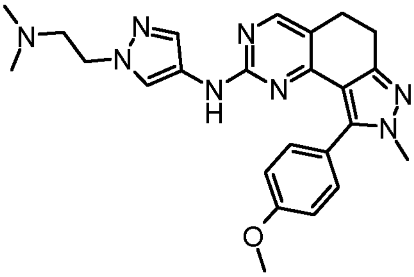
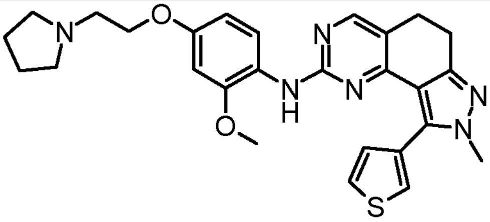
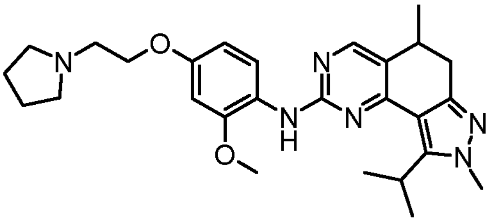
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-182		1.10	456	G
I-183		1.28	442	G
I-184		1.24	378	G
I-185		1.14	470	G
I-186*		1.18	483	G
I-187		1.29	430	G

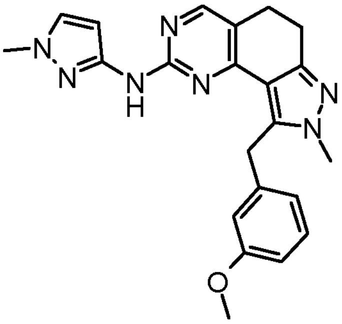
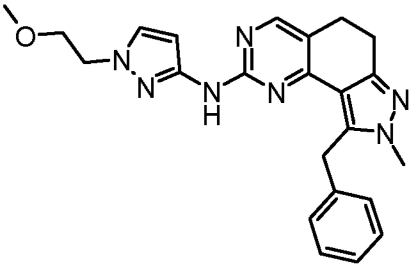
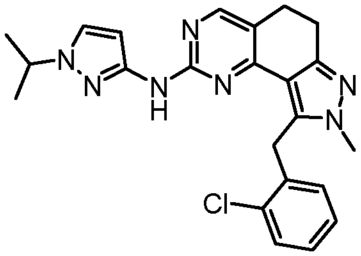
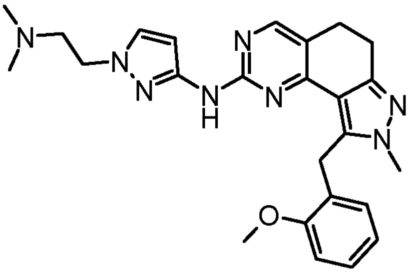
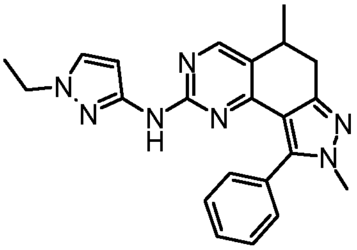
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-188		1.55	374	G
I-189		1.34	435	G
I-190		1.28	422	G
I-191		1.16	457	G
I-192		1.30	450/452	G
I-193		1.29	463	G

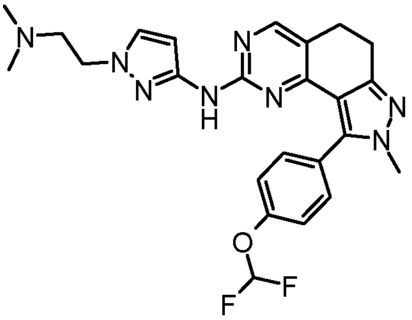
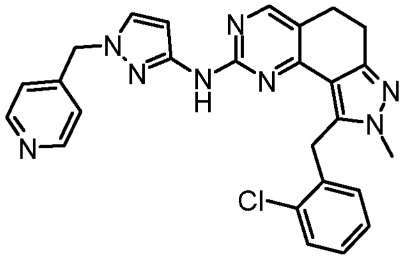
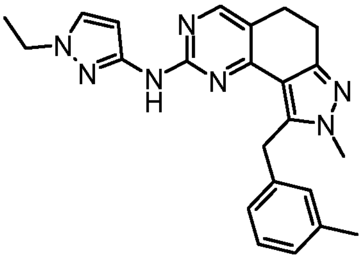
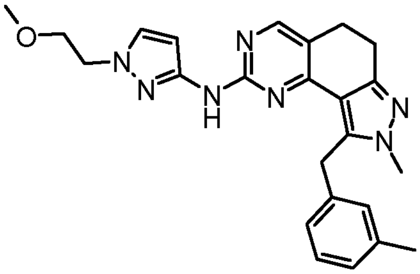
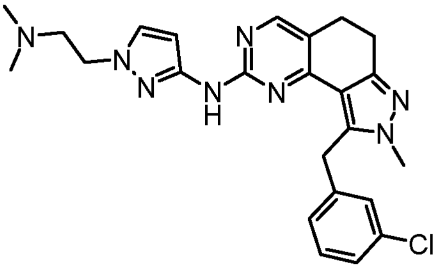
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-194*		1.25	429	G
I-195		1.32	479	G
I-196		1.32	422	G
I-197		1.26	441	G
I-198		1.22	459	G
I-199		1.16	483	G

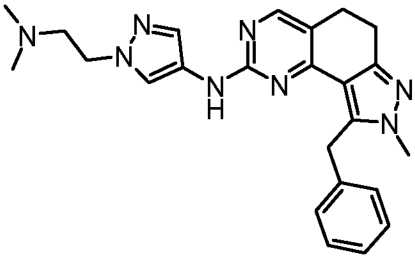
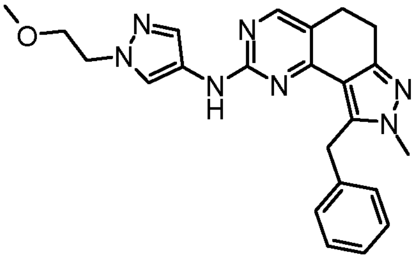
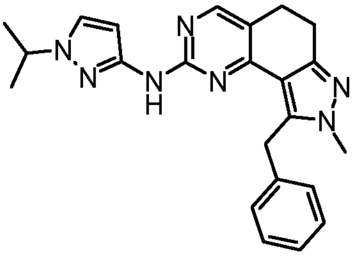
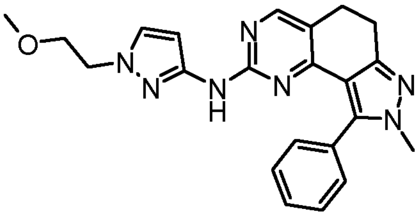
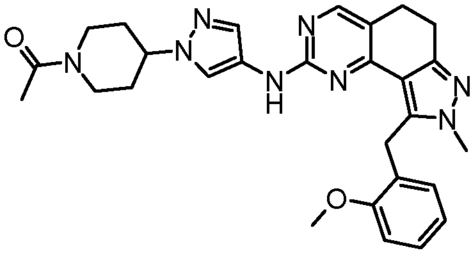
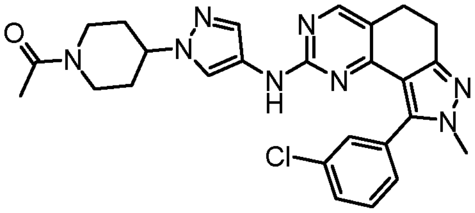
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-200		1.30	386	G
I-201		1.19	415	G
I-202		1.34	420/422	G
I-203		1.27	463/465	G
I-204*		1.25	416	G
I-205		1.65	535	G

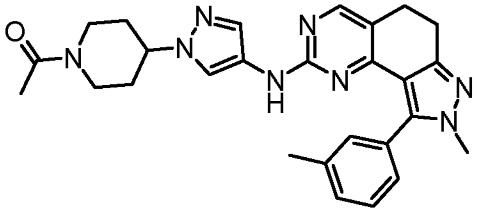
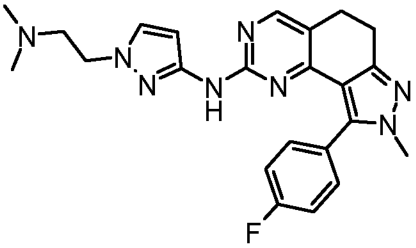
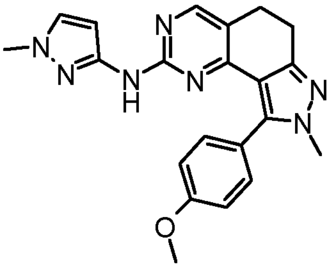
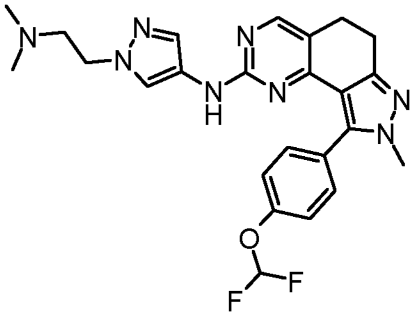
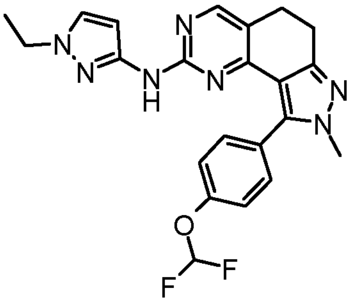
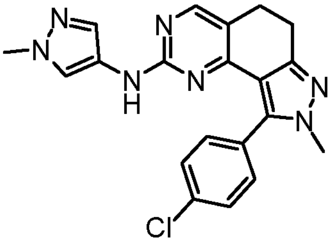
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-206		1.19	459	G
I-207		1.14	388	G
I-208		1.26	429	G
I-209		1.12	358	G
I-210		1.72	468	G

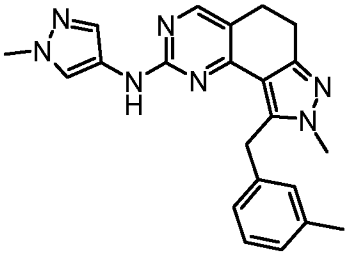
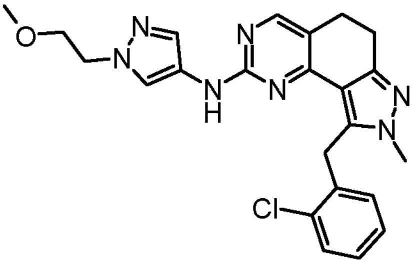
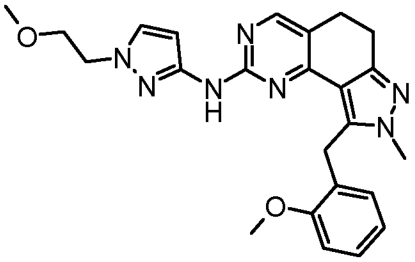
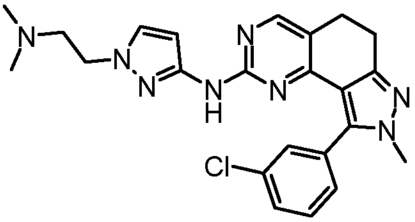
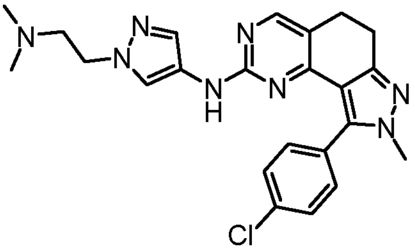
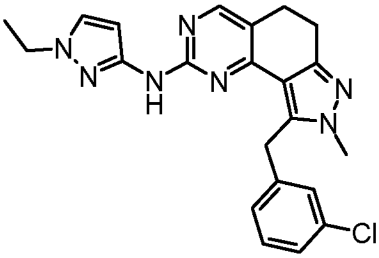
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-211		1.26	430	G
I-212		1.52	443	G
I-213		1.35	497	G
I-214		1.18	445	G
I-215		1.99	503	G
I-216*		2.05	477	G

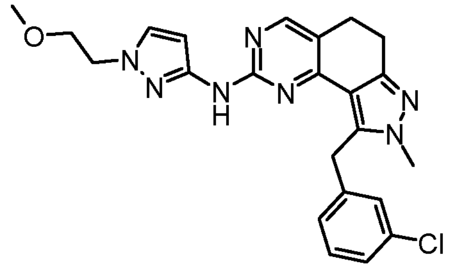
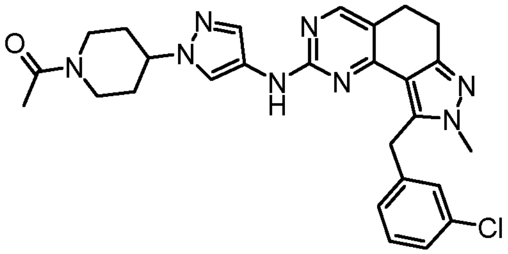
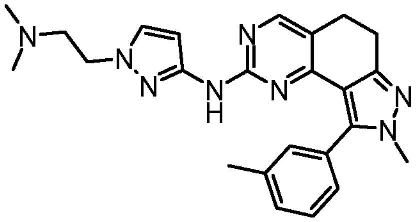
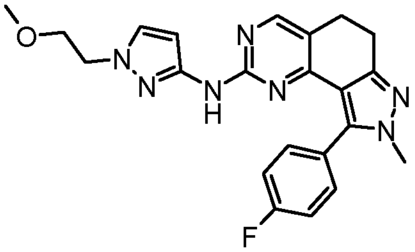
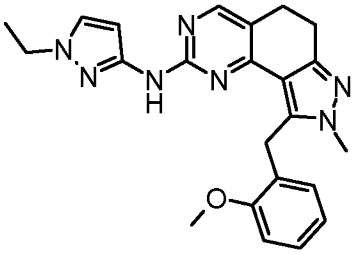
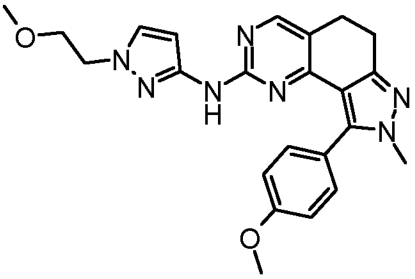
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-217		1.20	402	G
I-218		1.26	416	G
I-219		1.41	434/436	G
I-220		1.25	459	G
I-221*		1.27	386	G

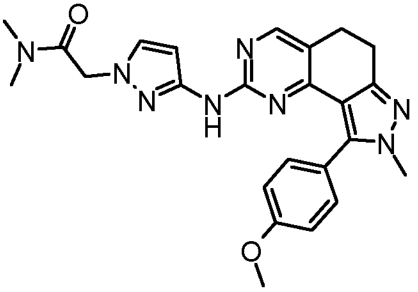
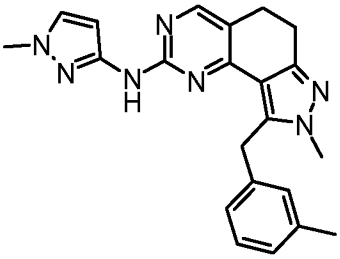
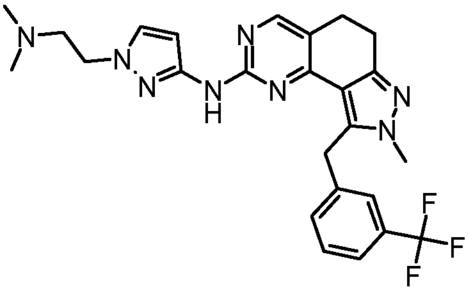
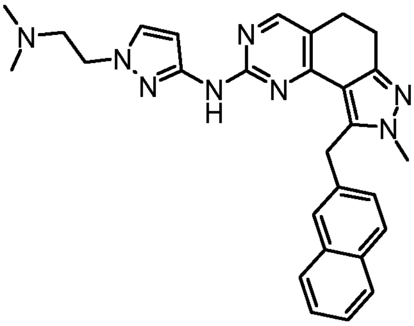
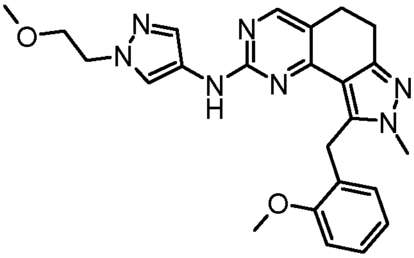
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-222		1.72	481	G
I-223		1.25	483	G
I-224		1.57	400	G
I-225		1.54	430	G
I-226		1.54	463	G

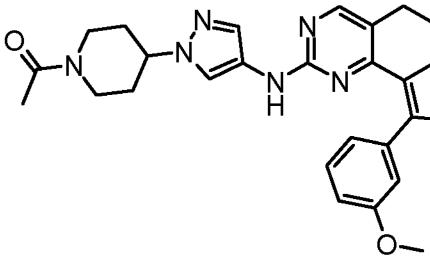
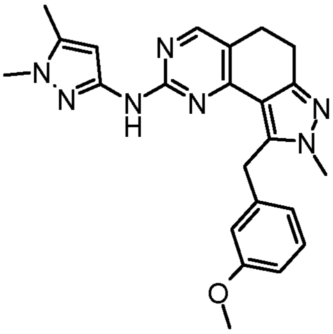
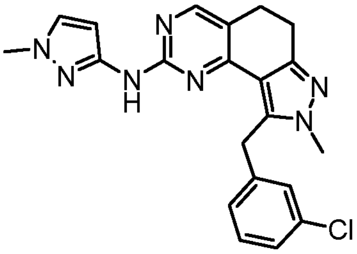
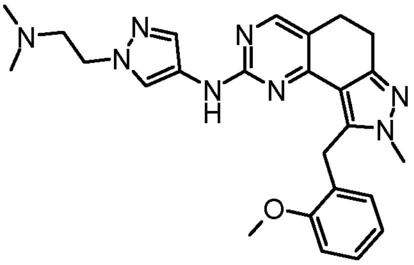
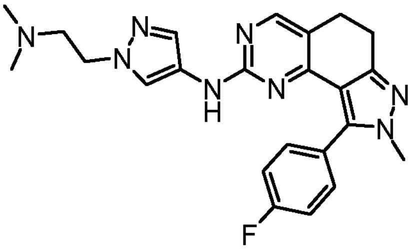
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-227		1.24	429	G
I-228		1.25	416	G
I-229		1.37	400	G
I-230		1.19	402	G
I-231		1.16	513	G
I-232		1.19	503/505	G

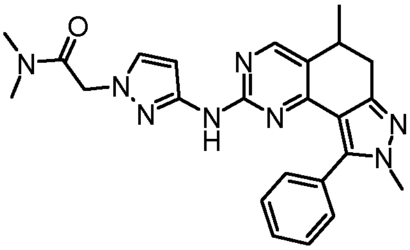
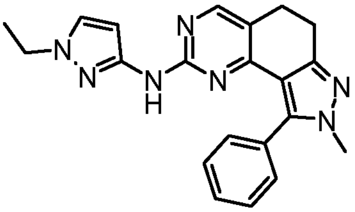
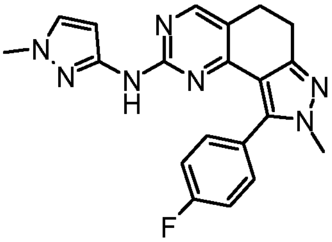
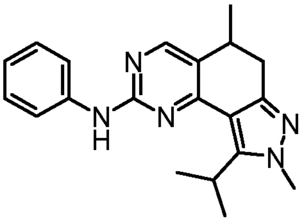
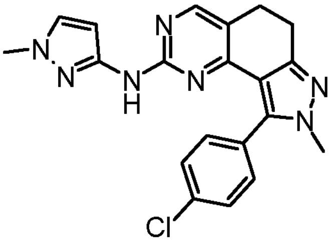
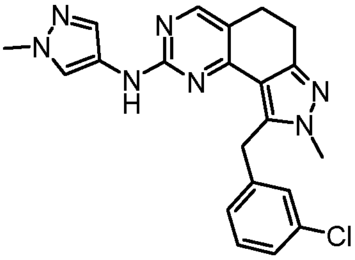
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-233		1.17	483	G
I-234		1.24	433	G
I-235		1.16	388	G
I-236		1.71	481	G
I-237		1.76	438	G
I-238		1.21	392	G

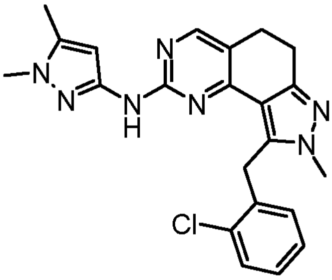
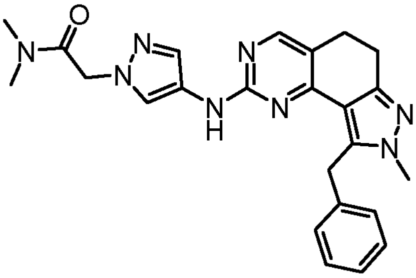
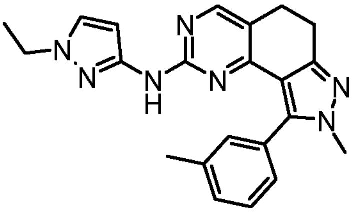
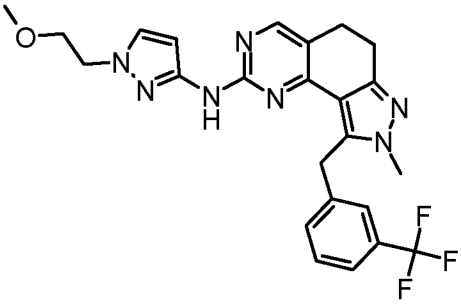
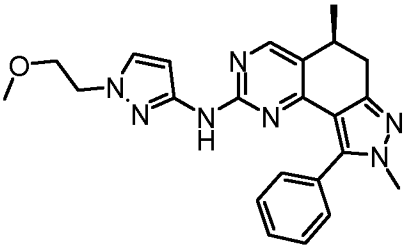
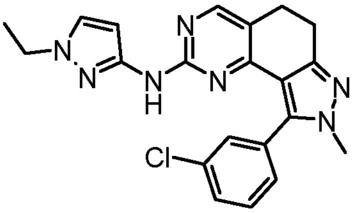
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-239		1.44	386	G
I-240		1.27	450/452	G
I-241		1.25	446	G
I-242		1.26	449/451	G
I-243		1.24	449	G
I-244		1.58	420	G

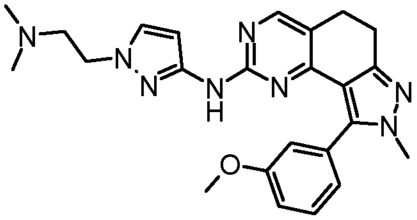
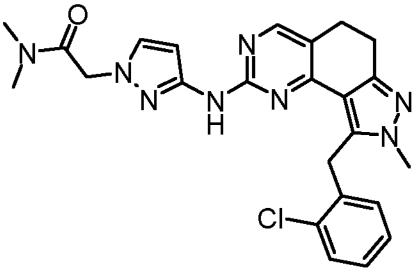
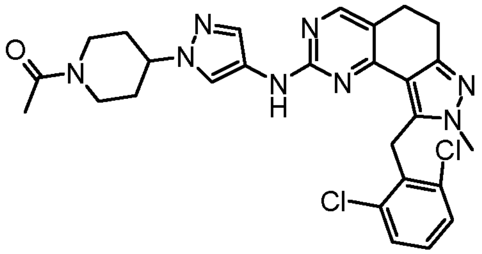
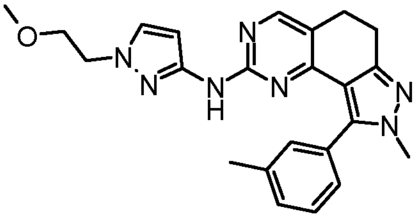
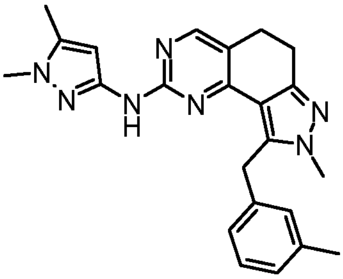
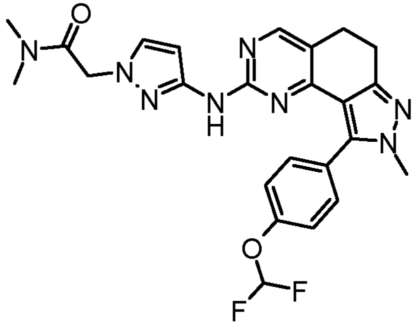
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-245		1.54	450	G
I-246		1.39	517	G
I-247		1.24	429	G
I-248		1.23	420	G
I-249		1.31	416	G
I-250		1.20	432	G

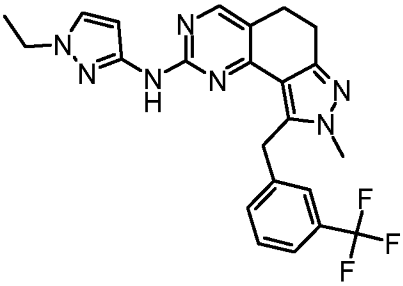
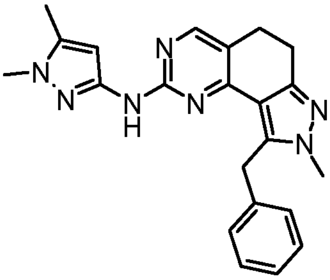
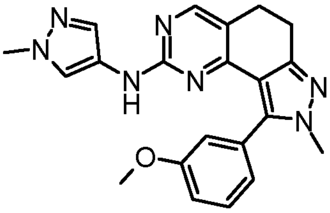
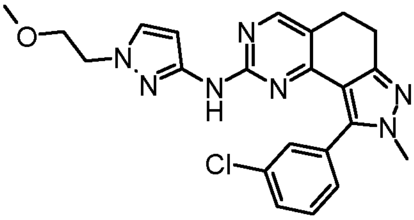
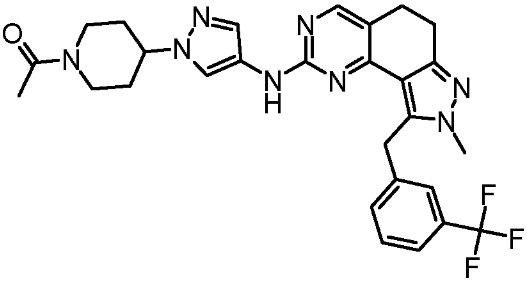
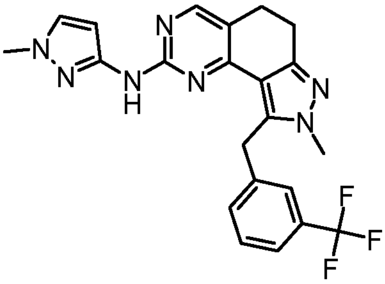
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-251		1.11	459	G
I-252		1.49	386	G
I-253		1.61	497	G
I-254		1.33	479	G
I-255		1.22	446	G

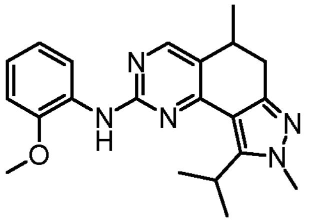
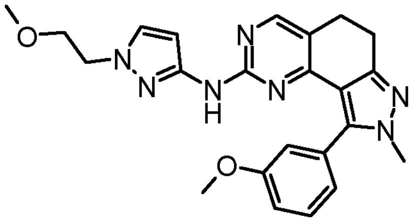
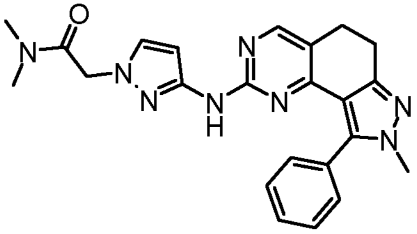
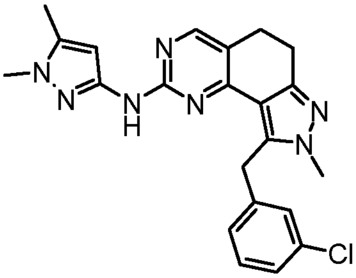
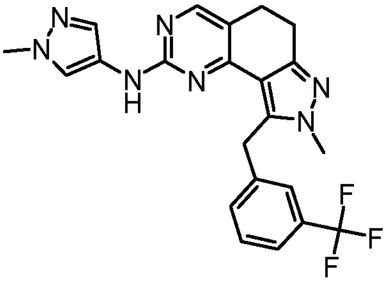
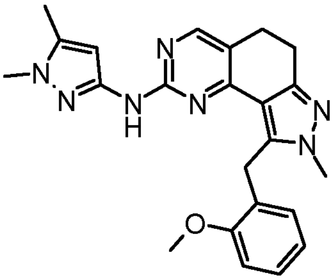
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-256		1.13	499	G
I-257		1.71	416	G
I-258		1.49	406	G
I-259		1.22	459	G
I-260		1.22	433	G

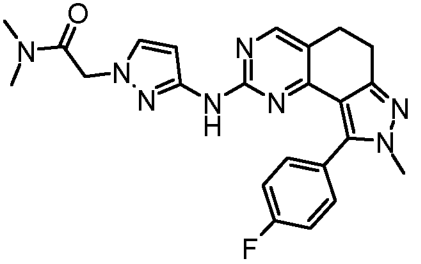
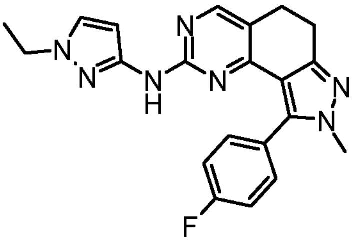
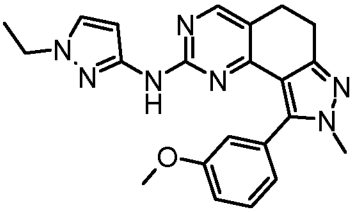
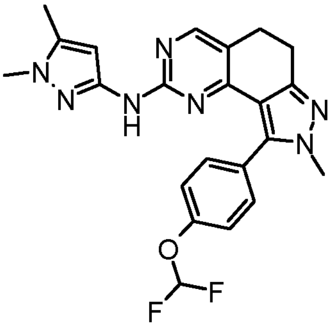
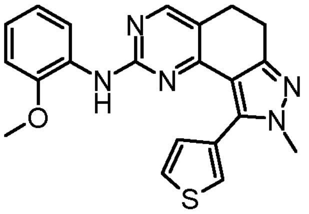
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-261*		1.15	443	G
I-262		1.22	372	G
I-263		1.20	376	G
I-264*		1.92	334	G
I-265		1.25	392	G
I-266		1.45	406	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-267		1.33	420	G
I-268		1.08	443	G
I-269		1.29	386	G
I-270		1.58	484	G
I-271		1.67	416	G
I-272		1.30	406/408	G

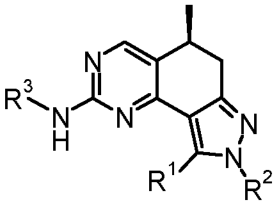
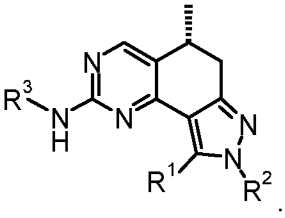
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-273		1.20	445	G
I-274		1.18	477	G
I-275		1.26	551	G
I-276		1.25	416	G
I-277		1.55	400	G
I-278		1.60	495	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-279		1.64	454	G
I-280		1.28	386	G
I-281		1.13	388	G
I-282		1.26	436/438	G
I-283		1.45	551	G
I-284		1.57	440	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-285*		2.04	364	G
I-286		1.19	432	G
I-287		1.09	429	G
I-288		1.55	420	G
I-289		1.52	440	G
I-290		1.29	416	G

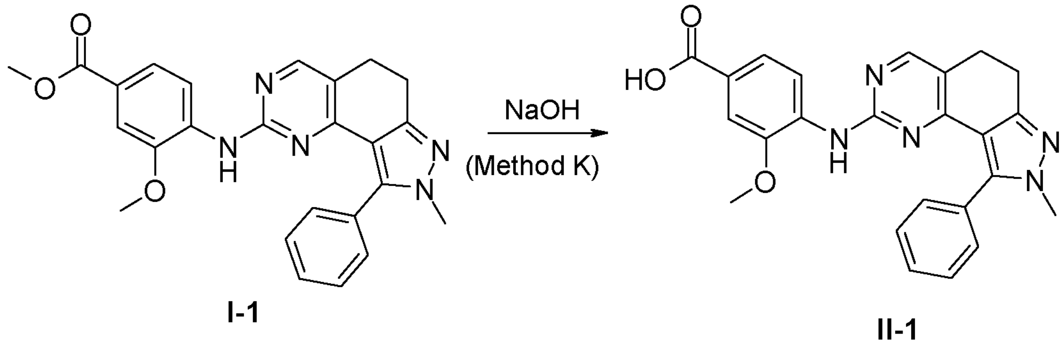
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
I-291		1.13	447	G
I-292		1.26	390	G
I-293		1.22	402	G
I-294		1.73	438	G
I-295		1.94	390	G

* Structure includes both enantiomers in each case, i.e.

 and .

4.2. Preparation of other novel compounds (I) by derivatisation of carboxylic acids (method K/method L)

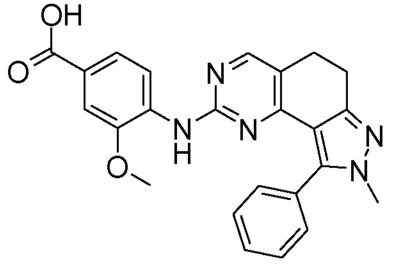
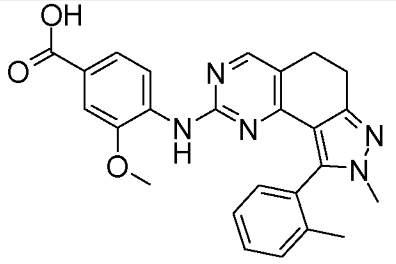
Preparation of compound II-1 by ester cleaving

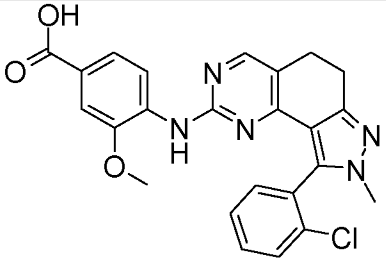
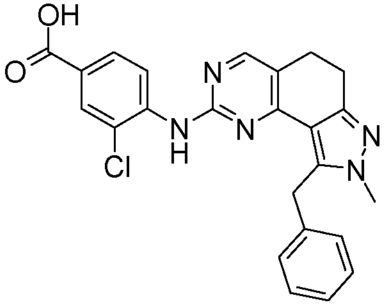
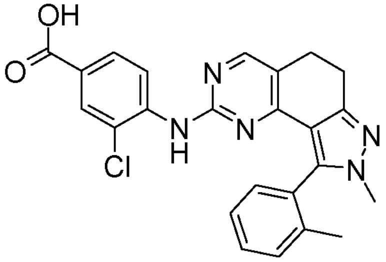
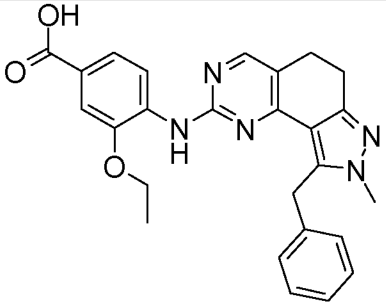
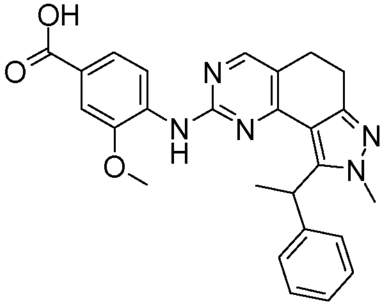


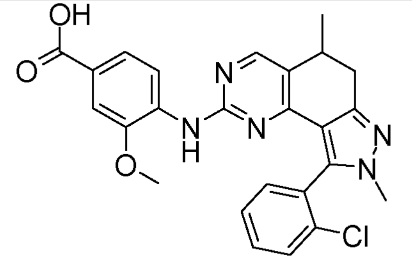
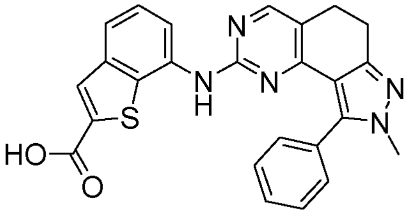
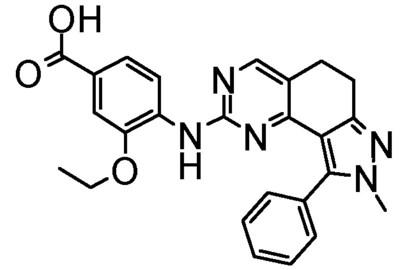
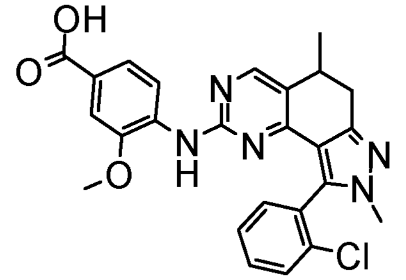
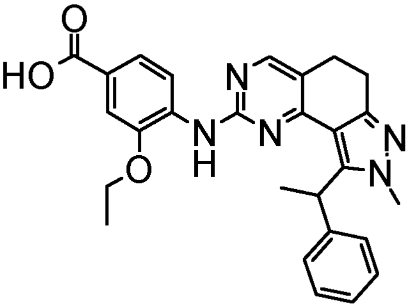
Ester cleaving (method K). Compound **I-1** (2.5 g, 5.66 mmol) in MeOH (25 mL) is combined with 10 N NaOH (2.8 mL, 28 mmol) and stirred at 50°C until the reaction is complete. The reaction mixture is acidified with conc. hydrochloric acid (pH = 3). The precipitated solid is isolated by filtration, digested several times with water and dried.

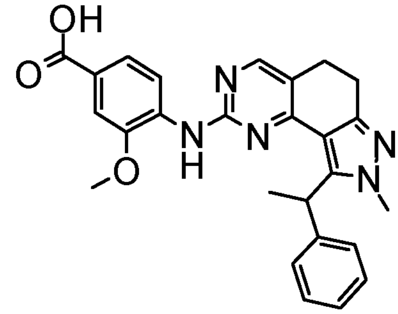
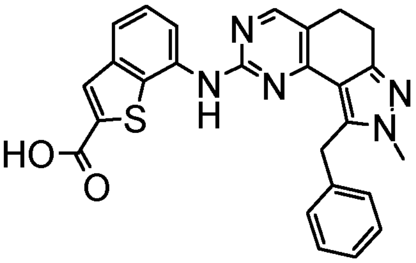
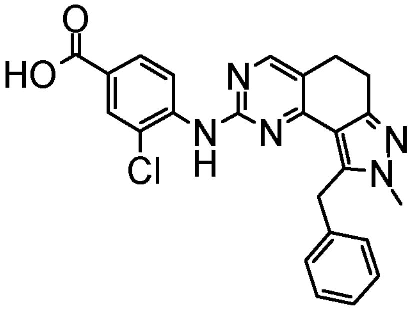
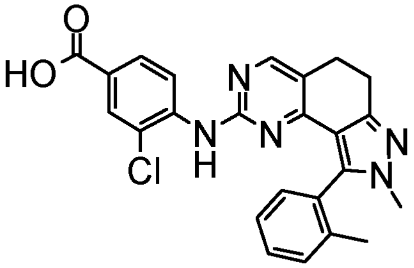
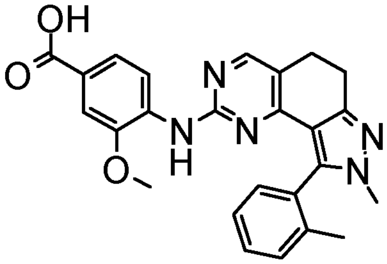
Analogously to **II-1** further free acids are obtained by ester cleaving (Table 11). The product may optionally be isolated by extraction and purified by chromatography.

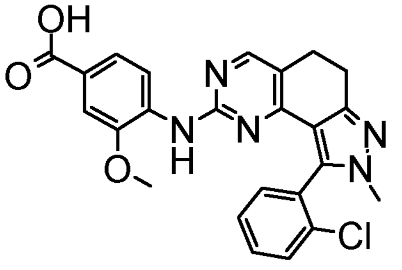
Table 11

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
II-1		1.06	428.2	C
II-2		1.10	442.2	C

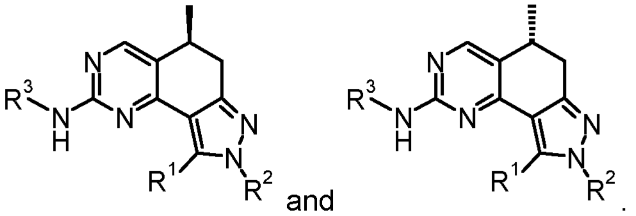
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
II-3		1.11	462.2	C
II-4		1.21	446.2	C
II-5		1.25	446.2	C
II-6		1.17	456.3	C
II-7		1.18	456.2	C

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
II-8*		1.14	476.2	C
II-9		0.97	468.2	C
II-10		1.13	442.0	G
II-11*		1.16	476.3	G
II-12		1.29	470.3	G

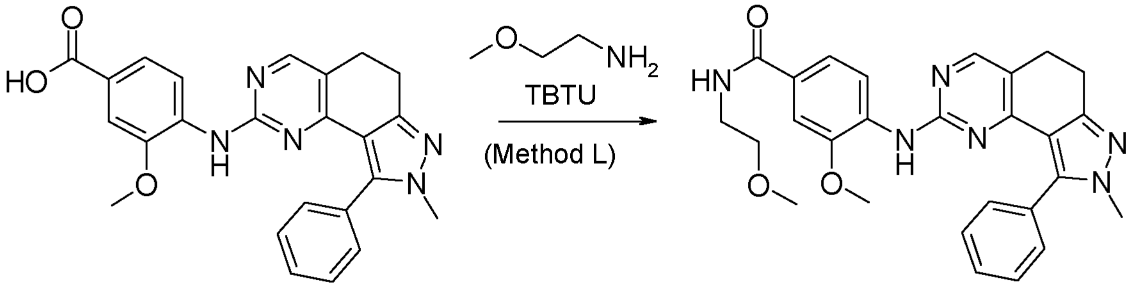
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
II-13		1.24	456.3	G
II-14		1.21	468.3	G
II-15		1.20	446.0	G
II-16		1.18	446.3	G
II-17		1.06	442.3	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
II-18		1.07	462.0	G

* Structure includes both enantiomers in each case, i.e.



Preparation of compound III-1 by amidation

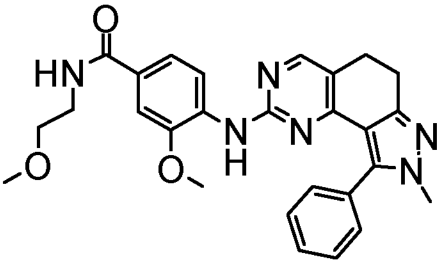
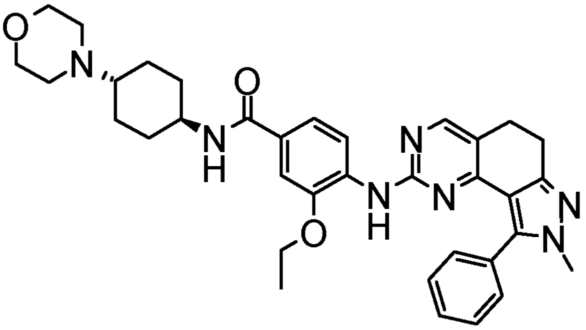
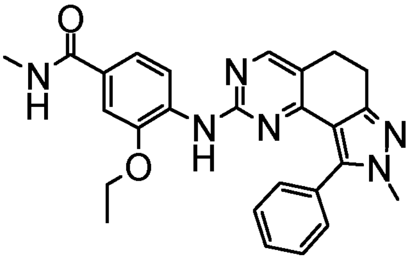
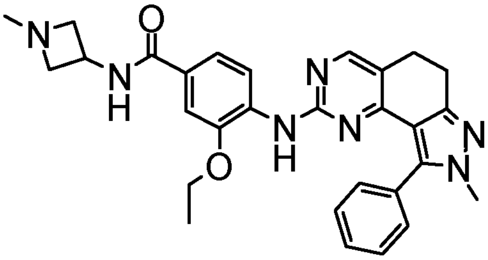
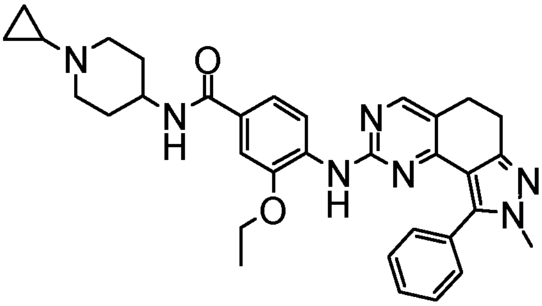


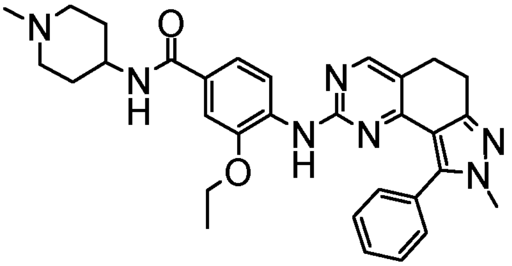
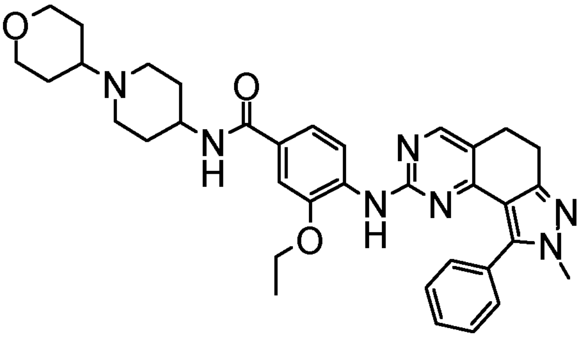
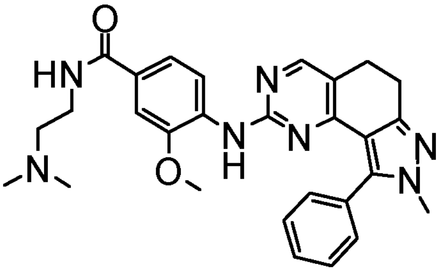
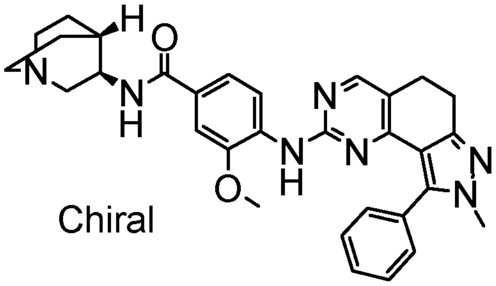
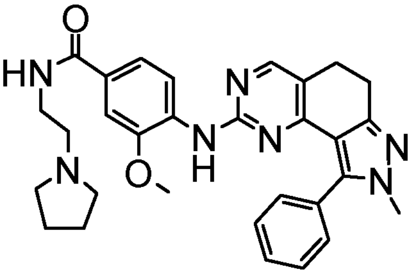
II-1 **III-1**

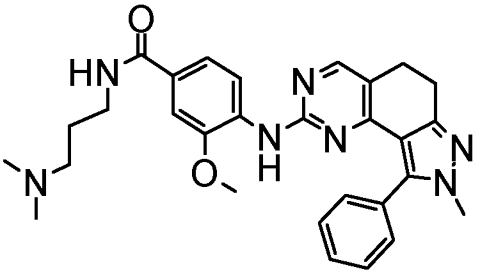
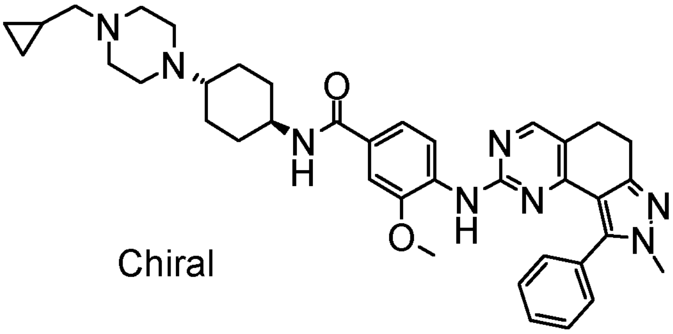
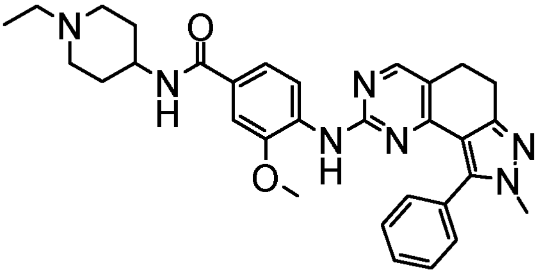
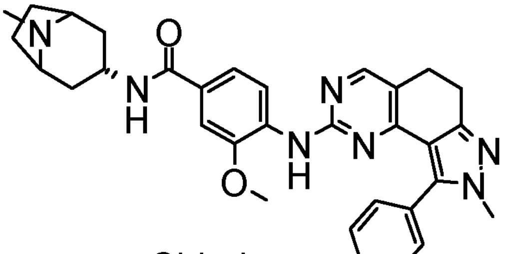
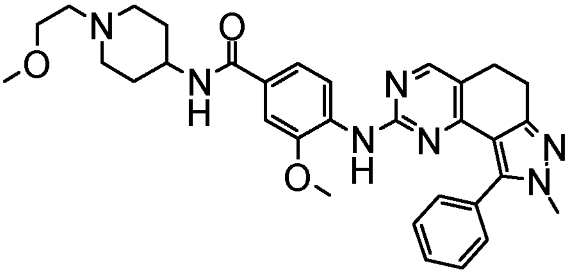
Amide formation (method L). The starting compound **II-1** (75 mg, 0.18 mmol) and TBTU (87 mg, 0.27 mmol) in anhydrous DMSO (0.5 mL) are combined with triethylamine (124 µL, 0.90 mmol) and 2-methoxyethylamine (17 mg, 0.23 mmol) and stirred at RT until the reaction is complete. The reaction mixture is purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried.

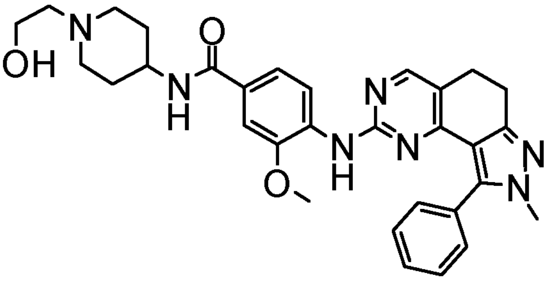
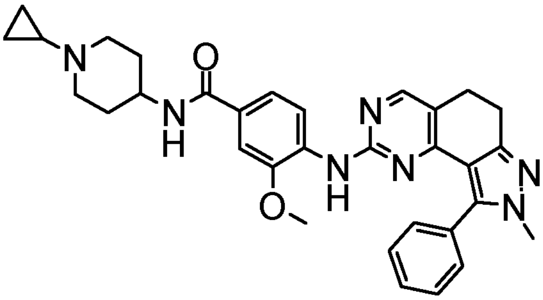
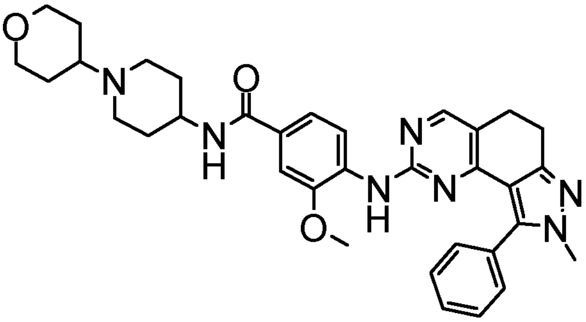
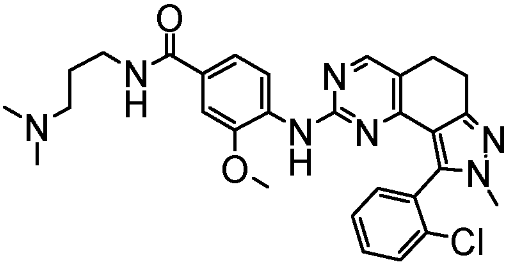
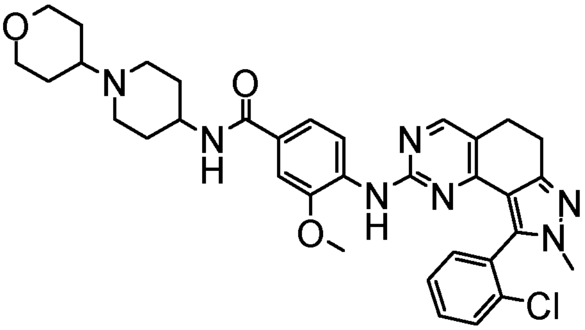
Analogously to **III-1** further novel compounds are obtained by amidation or esterification (Table 12).

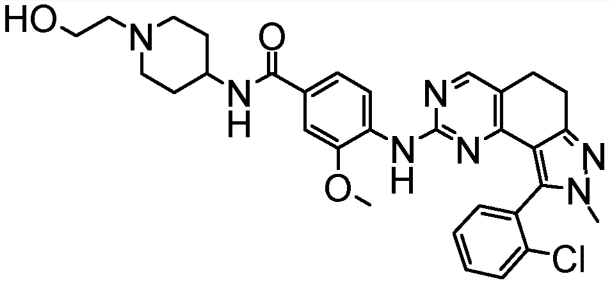
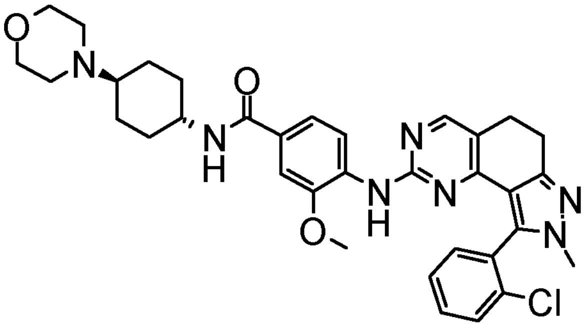
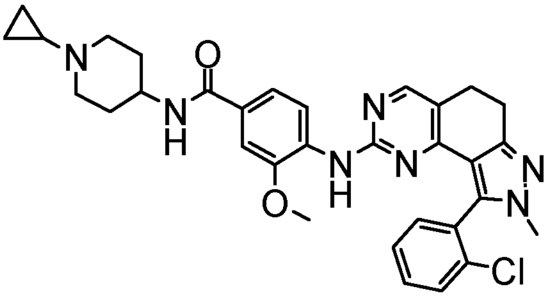
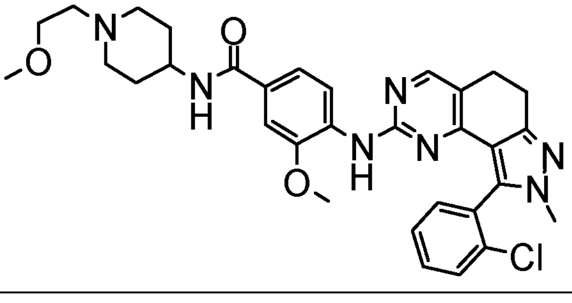
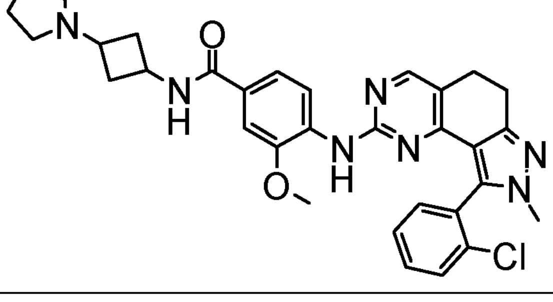
Table 12

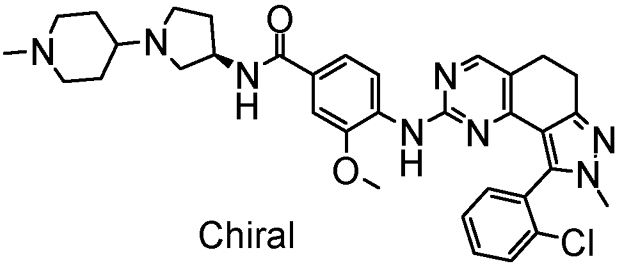
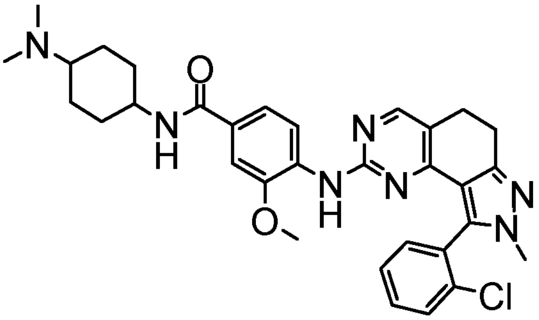
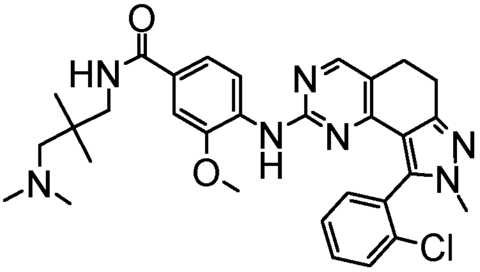
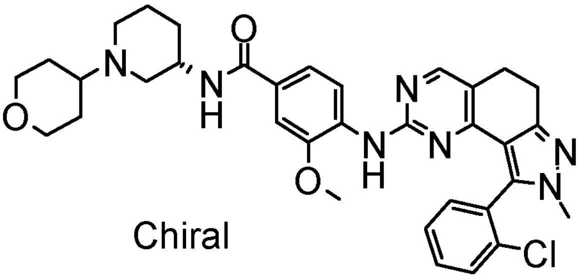
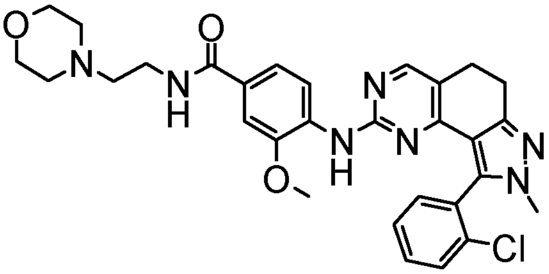
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-1		1.73	485.3	G
III-2		1.89	608.0	G
III-3		1.76	455.0	G
III-4		1.81	510.3	G
III-5		2.00	564.3	G

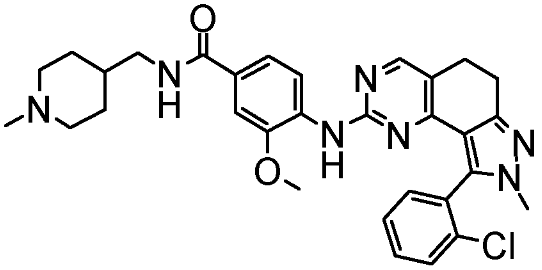
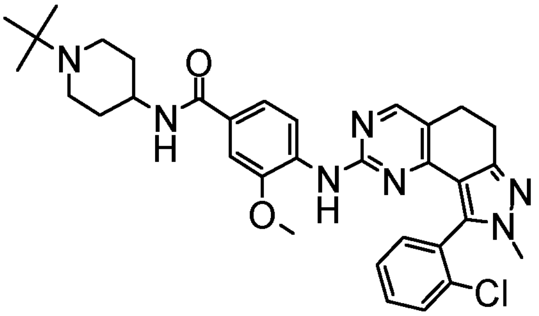
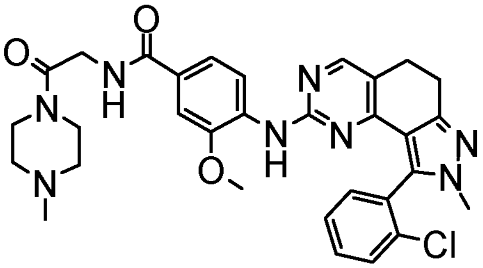
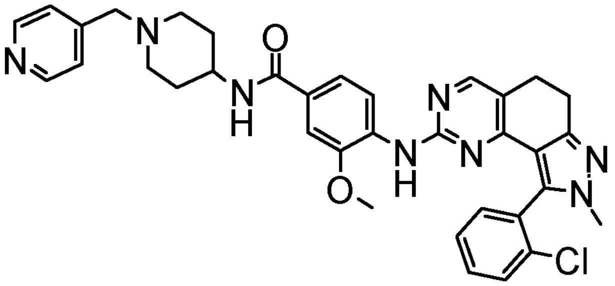
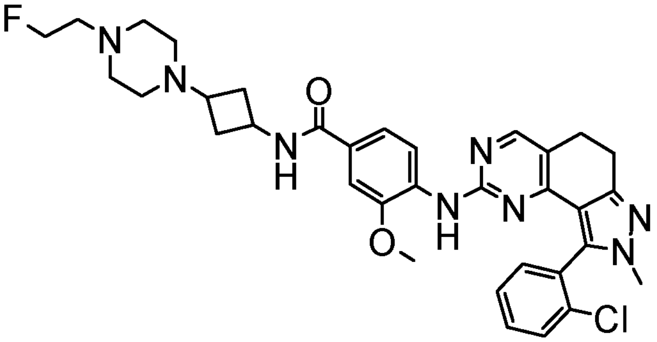
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-6		1.85	538.0	G
III-7		1.86	608.3	G
III-8		1.78	498.3	G
III-9	 Chiral	1.84	536.2	G
III-10		1.91	524.3	G

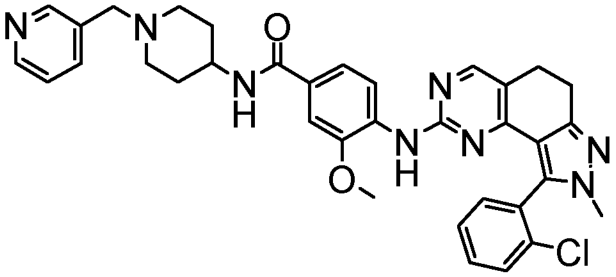
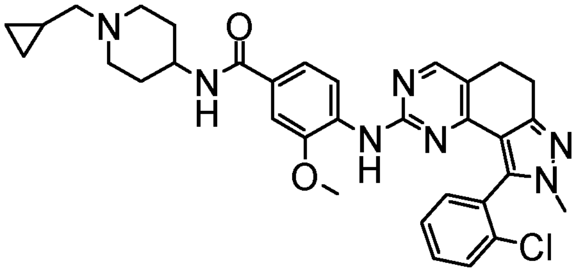
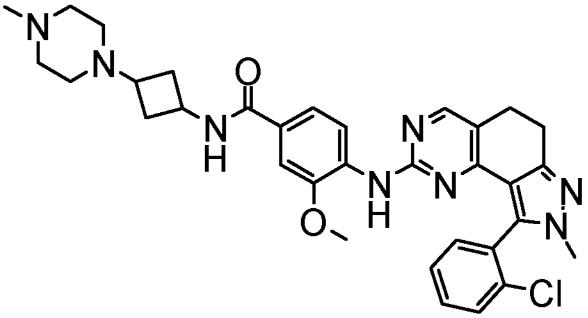
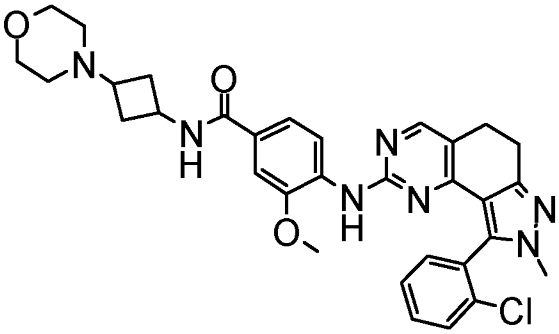
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-11		1.85	512.3	G
III-12	 Chiral	1.96	647.5	G
III-13		1.86	538.3	G
III-14	 Chiral	1.93	550.2	G
III-15		1.79	568.2	G

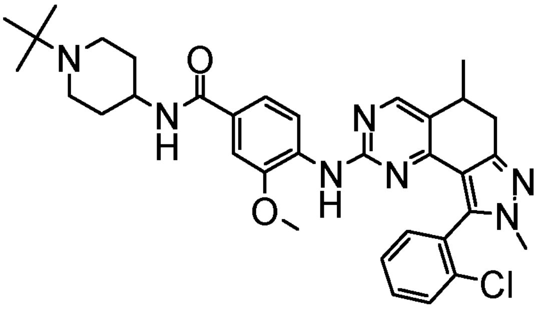
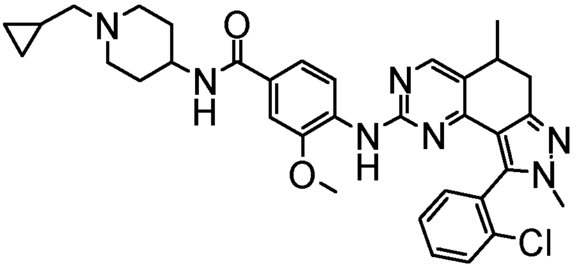
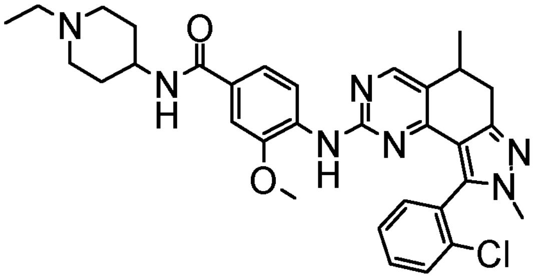
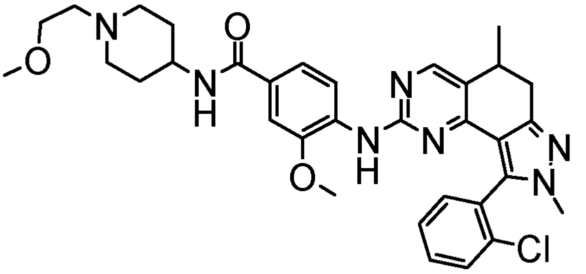
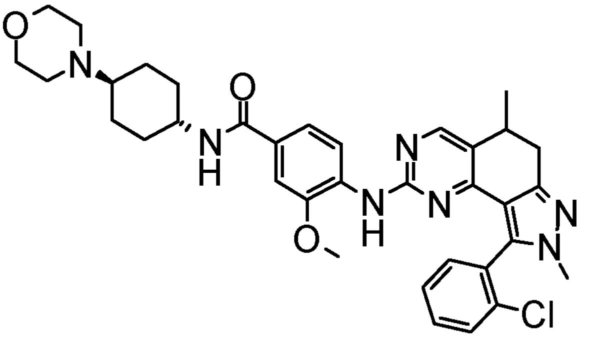
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-16		1.66	554.2	G
III-17		1.92	550.2	G
III-18		1.78	594.2	G
III-19		1.87	546.5	G
III-20		1.81	628.7	G

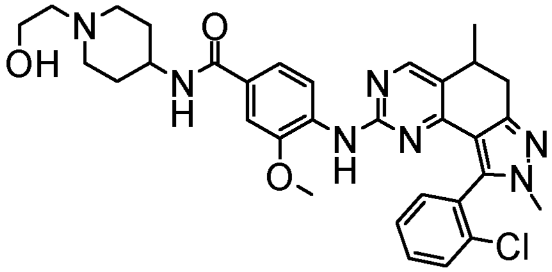
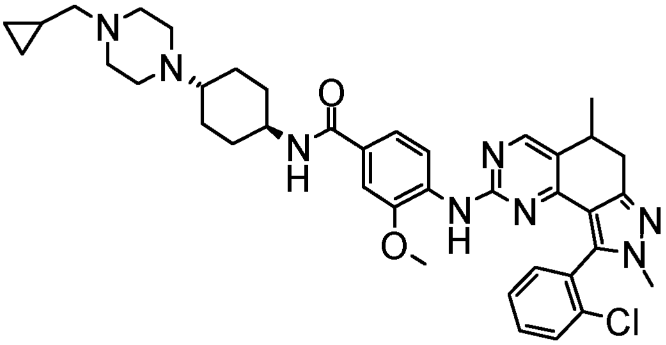
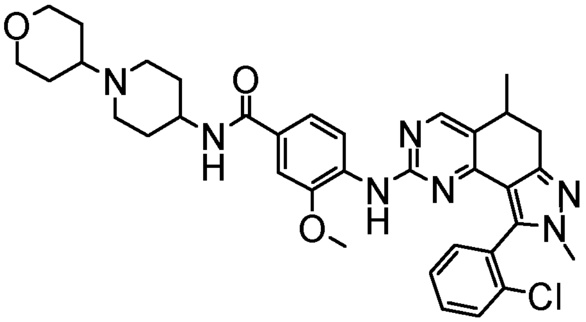
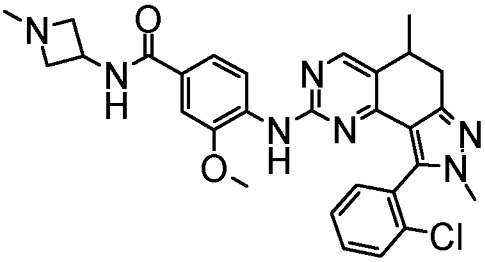
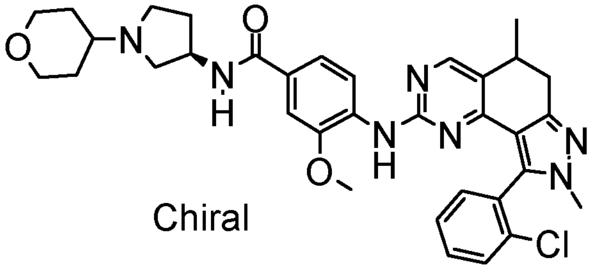
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-21		1.68	588.5	G
III-22		1.84	628.5	G
III-23		1.95	584.5	G
III-24		1.81	602.5	G
III-25		1.91	584.2	G

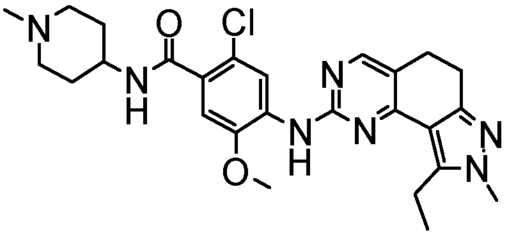
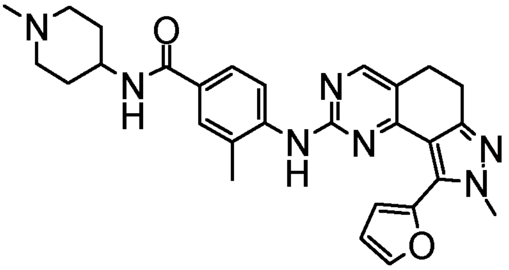
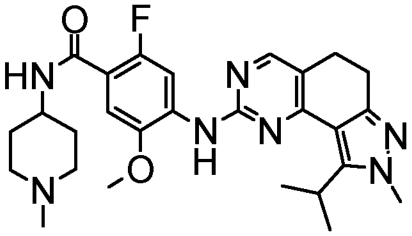
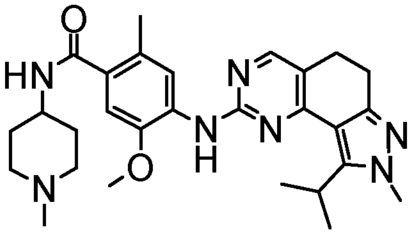
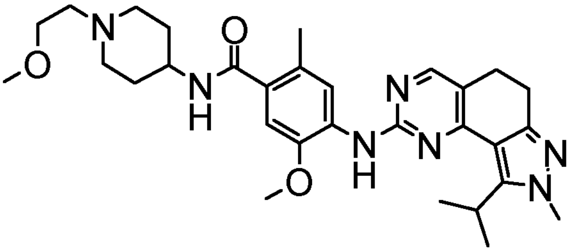
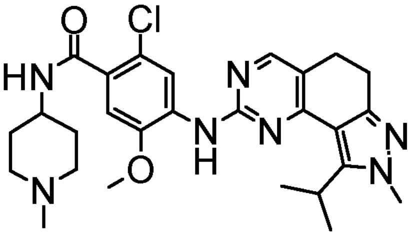
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-26	 Chiral	1.83	627.2	G
III-27		1.92	586.2	G
III-28		2.10	574.2	G
III-29	 Chiral	1.88	628.3	G
III-30		1.71	574.2	G

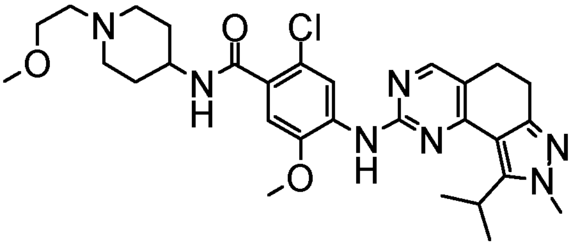
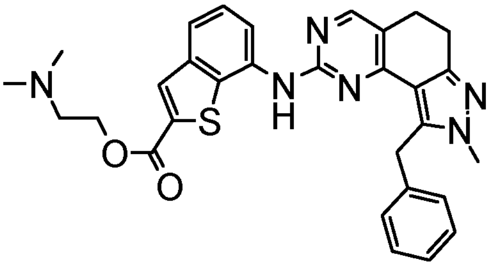
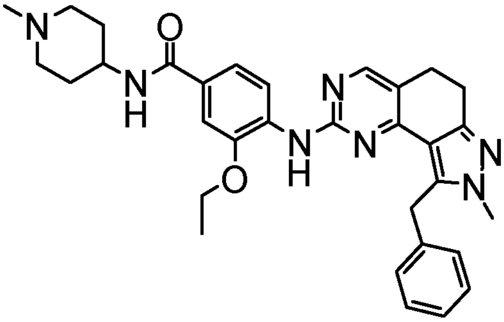
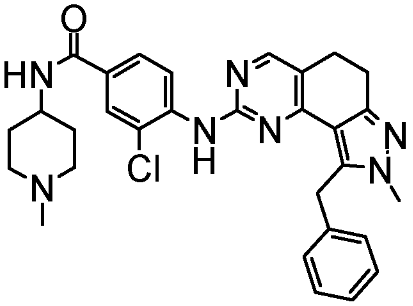
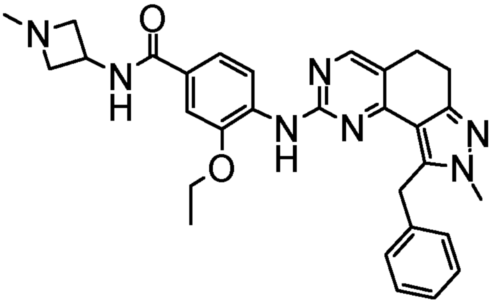
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-31		1.83	572.3	G
III-32		2.01	600.2	G
III-33		1.68	601.3	G
III-34		1.82	635.2	G
III-35		1.74	645.3	G

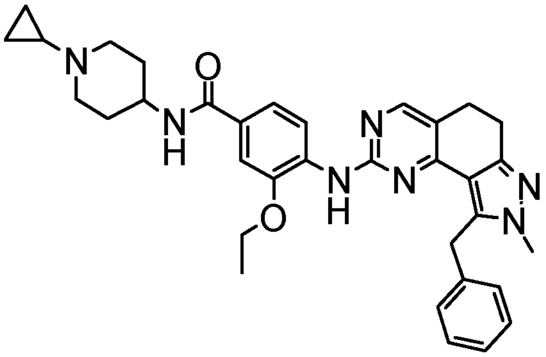
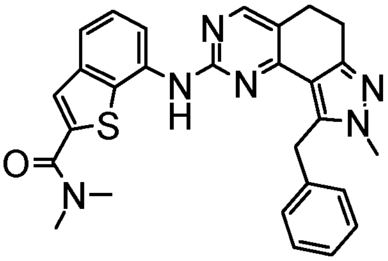
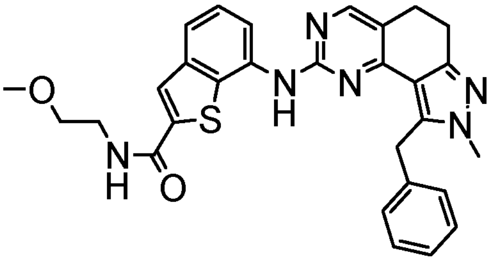
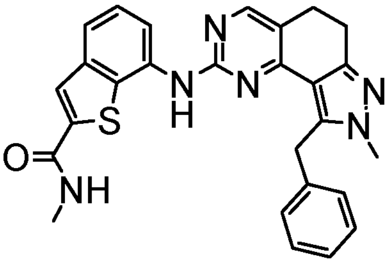
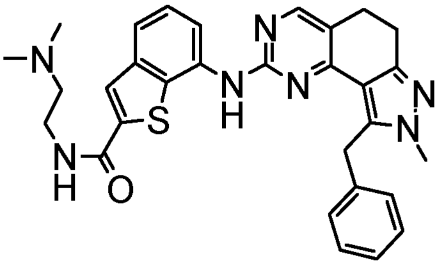
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-36		1.81	635.2	G
III-37		1.95	598.2	G
III-38		1.71	613.3	G
III-39		1.74	600.2	G

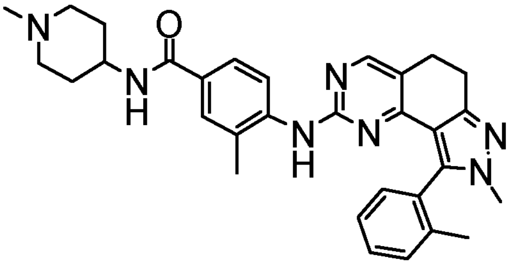
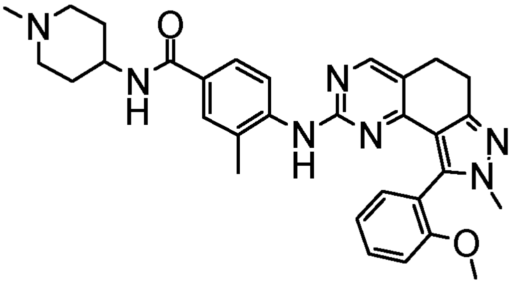
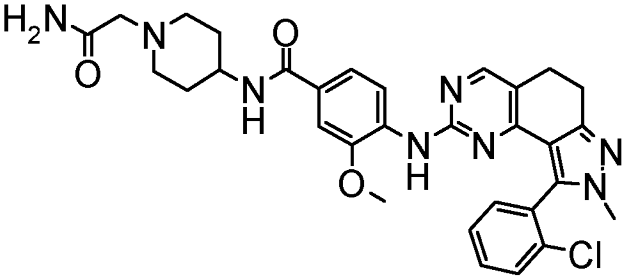
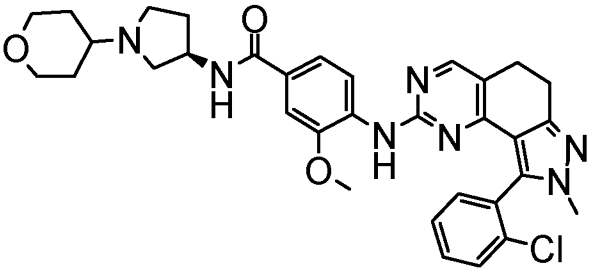
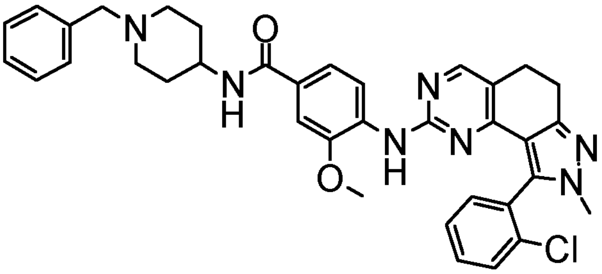
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-40*		2.07	614.2	G
III-41*		2.20	612.3	G
III-42*		1.91	586.2	G
III-43*		1.85	616.2	G
III-44*		1.88	642.3	G

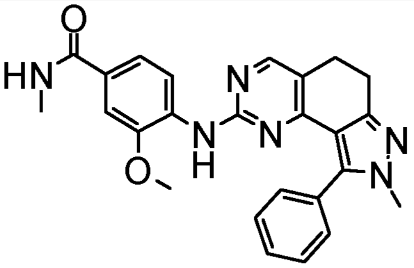
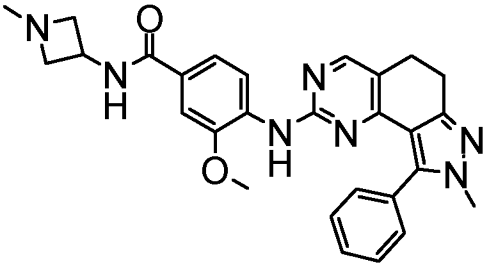
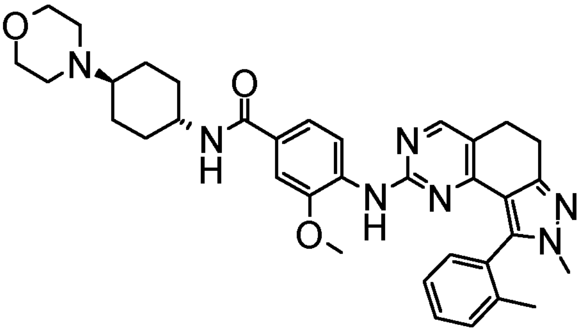
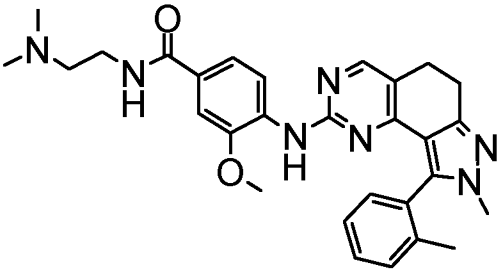
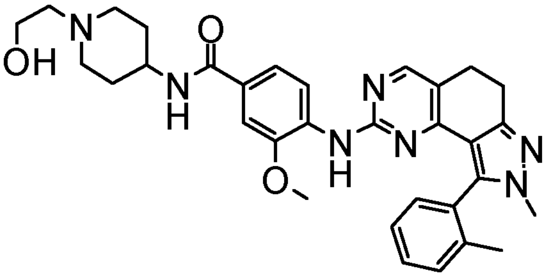
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-45*		1.72	602.2	G
III-46*		2.00	696.3	G
III-47*		1.84	642.3	G
III-48*		1.78	544.2	G
III-49*		1.84	628.3	G

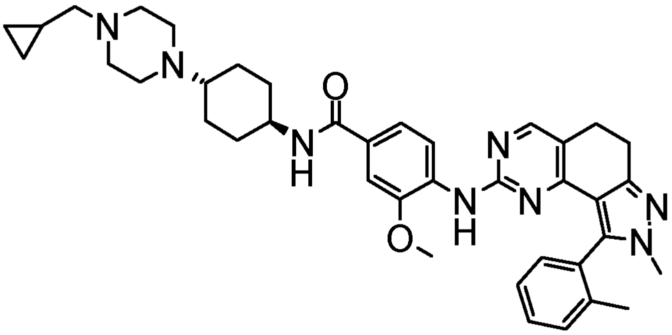
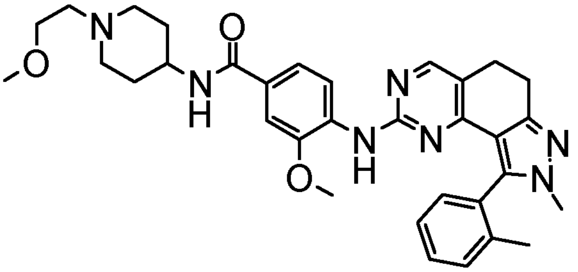
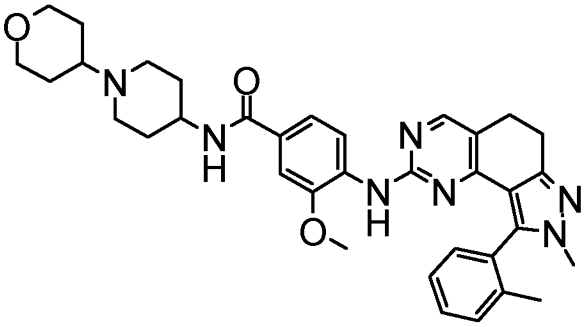
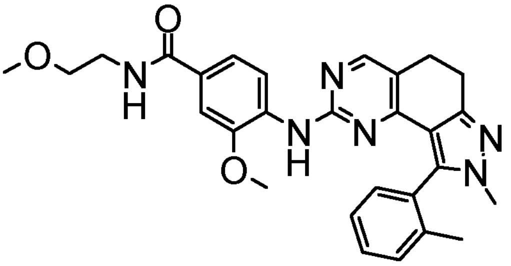
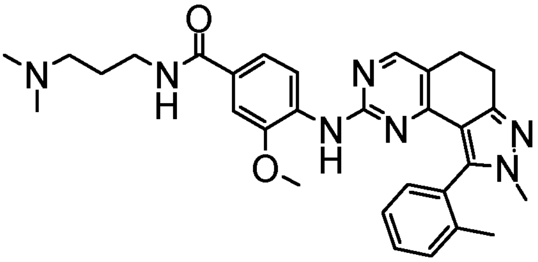
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-50		1.73	510.3	G
III-51		1.69	498.3	G
III-52		1.86	508.0	G
III-53		1.72	504.3	G
III-54		1.74	548.3	G
III-55		1.79	524.3	G

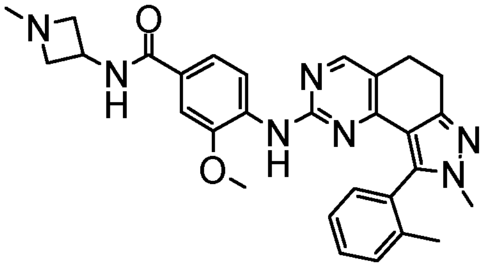
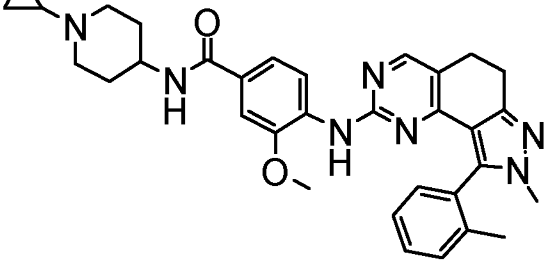
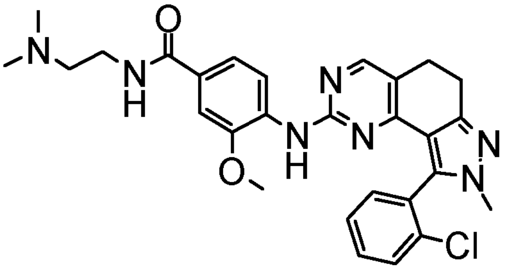
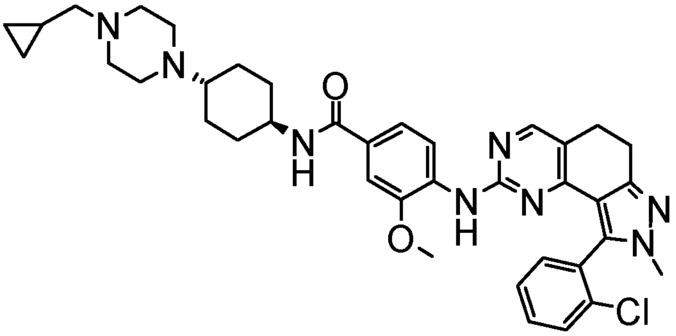
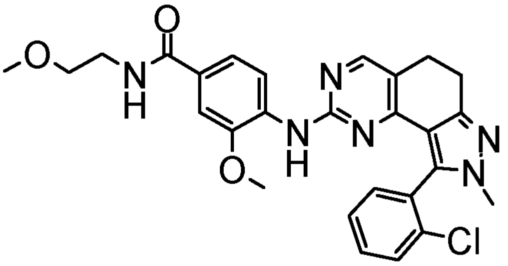
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-56		1.81	568.3	G
III-57		2.13	539.2	G
III-58		1.86	552.2	G
III-59		1.96	542.0	G
III-60		1.86	524.3	G

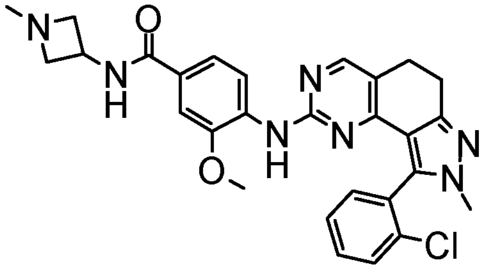
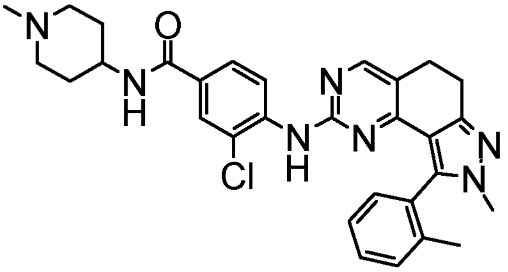
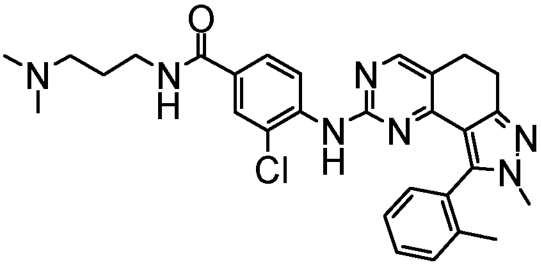
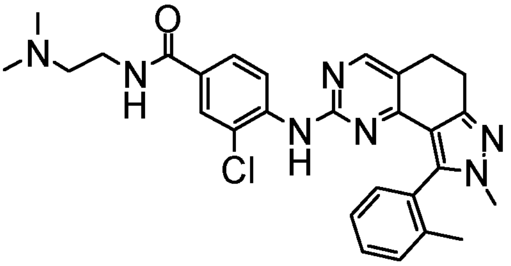
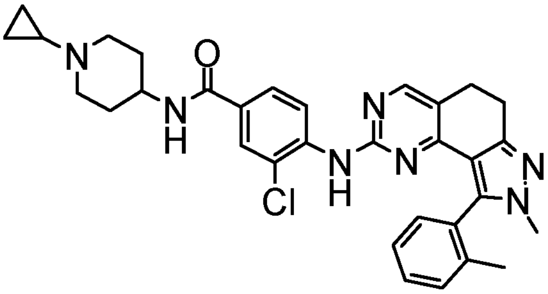
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-61		2.02	578.3	G
III-62		1.86	495.0	G
III-63		1.81	525.0	G
III-64		1.76	481.0	G
III-65		1.84	538.3	G

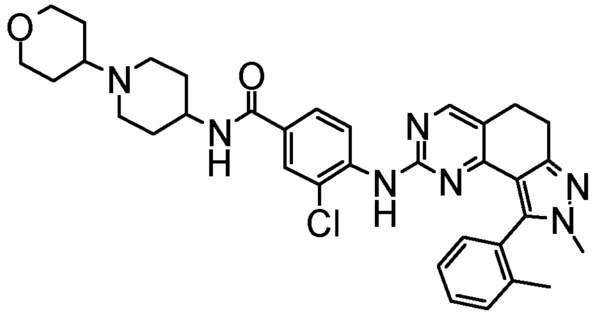
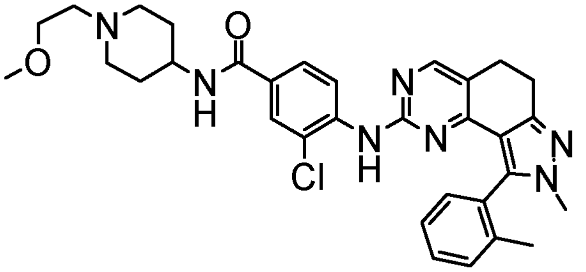
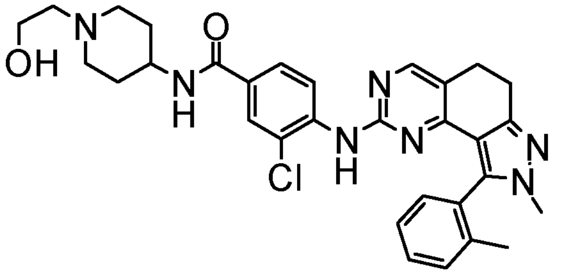
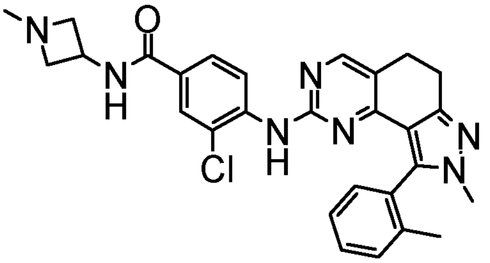
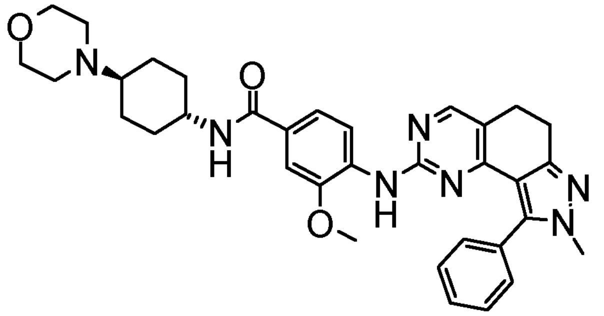
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-66		1.78	522.2	G
III-67		1.71	538.3	G
III-68		1.65	601.3	G
III-69		1.78	614.2	G
III-70		2.09	634.2	G

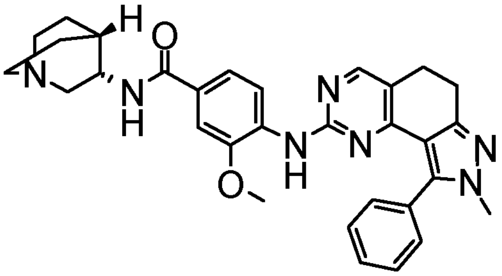
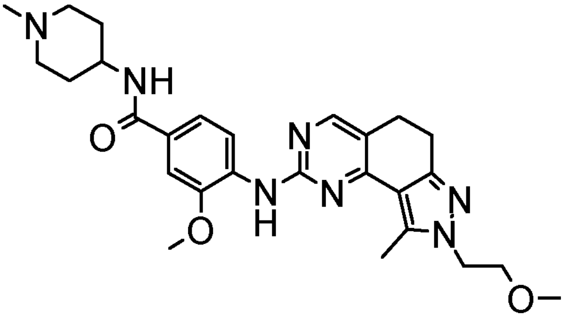
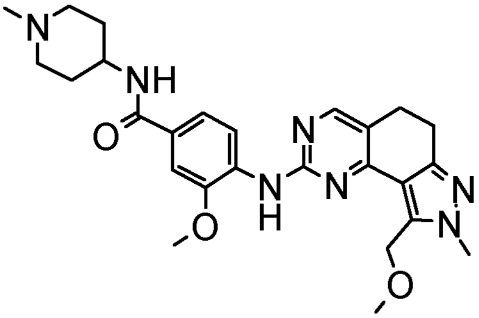
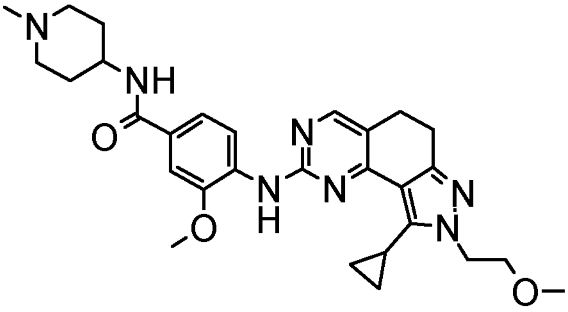
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-71		1.67	441.3	G
III-72		1.75	496.3	G
III-73		1.84	608.5	G
III-74		1.82	512.5	G
III-75		1.68	568.5	G

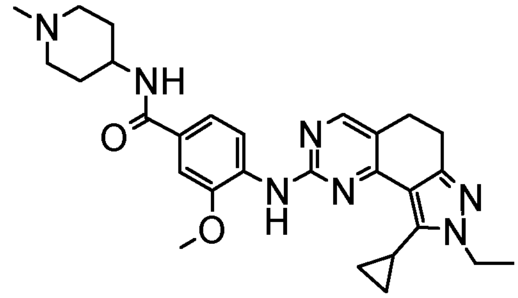
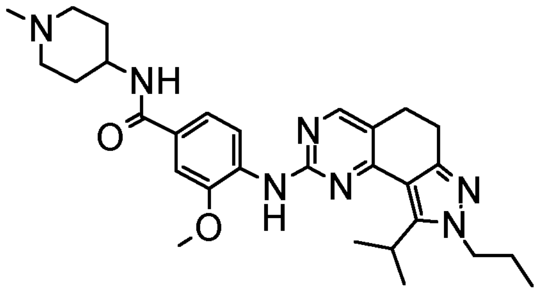
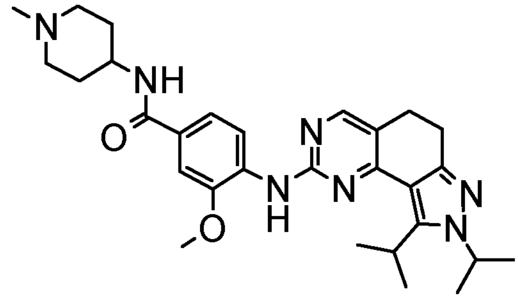
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-76		1.98	661.5	G
III-77		1.82	582.5	G
III-78		1.81	608.5	G
III-79		1.78	499.5	G
III-80		1.87	526.5	G

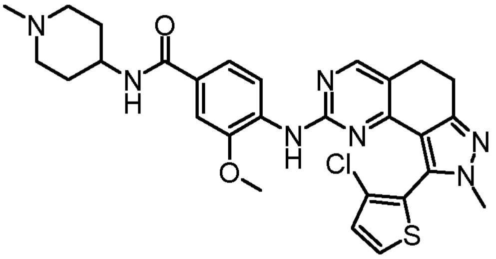
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-81		1.76	510.5	G
III-82		1.96	564.5	G
III-83		1.81	532.5	G
III-84		1.98	681.7	G
III-85		1.78	519.5	G

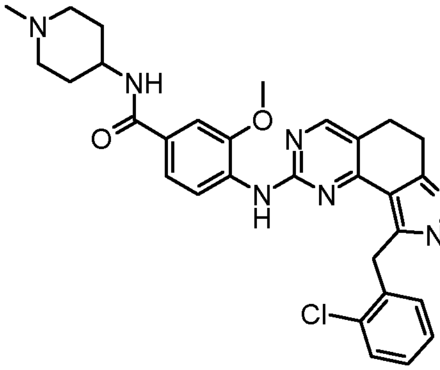
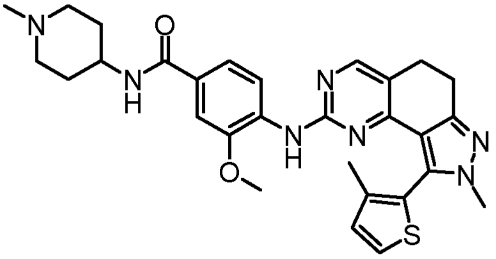
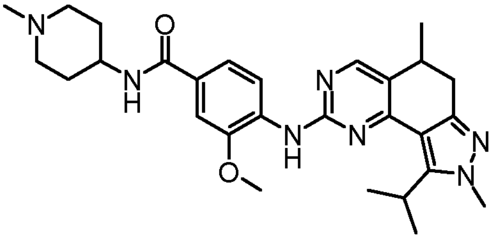
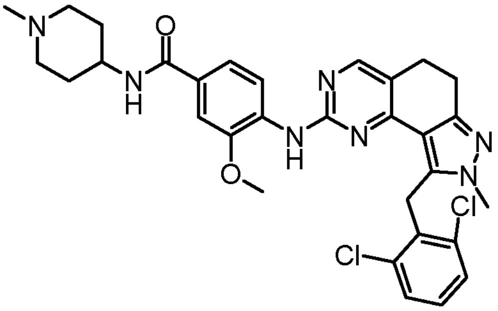
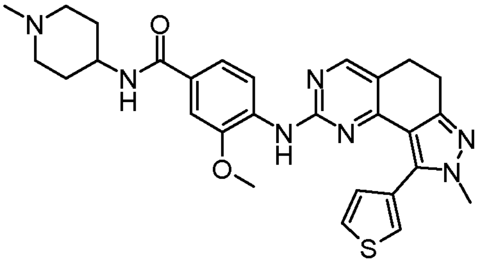
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-86		1.76	530.5	G
III-87		1.90	542.3	G
III-88		1.96	530.2	G
III-89		1.92	516.3	G
III-90		2.06	568.2	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-91		1.90	612.3	G
III-92		1.91	586.2	G
III-93		1.76	572.3	G
III-94		1.97	514.2	G
III-95		1.81	594.2	G

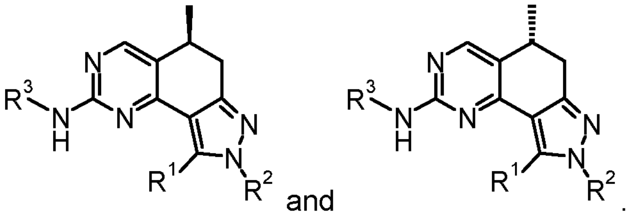
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-96		1.83	536.2	G
III-97		1.61	506.3	G
III-98		1.57	492.3	G
III-99		1.71	532.3	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
III-100		1.77	502.3	G
III-101		1.95	476.3	G
III-102		1.92	518.2	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
III-103		1.48	564	G

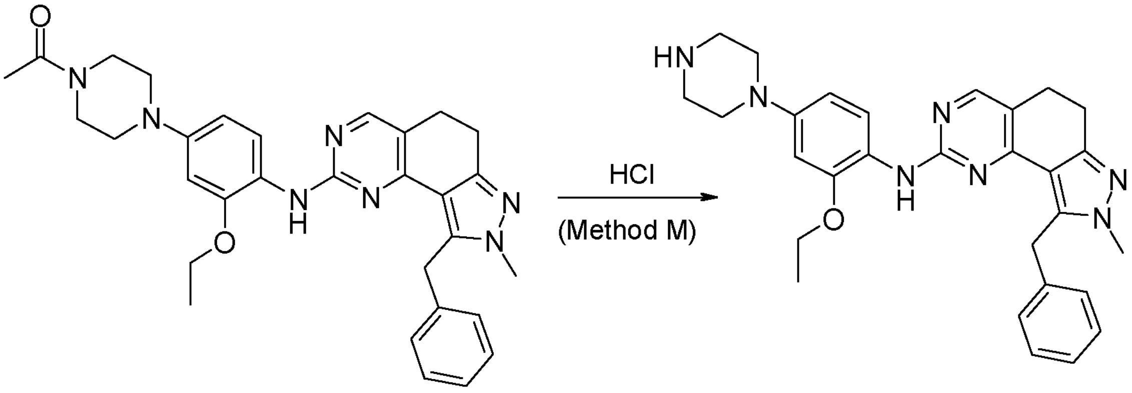
No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
III-104		1.37	572	G
III-105		1.47	544	G
III-106*		1.78	504	G
III-107		1.51	606	G
III-108		1.7	530	G

* Structure includes both enantiomers in each case, i.e.



4.3. Preparation of other novel compounds (I) by derivatisation of amines (method M/method N/method O/method P)

Preparation of compound IV-1 by amide cleaving

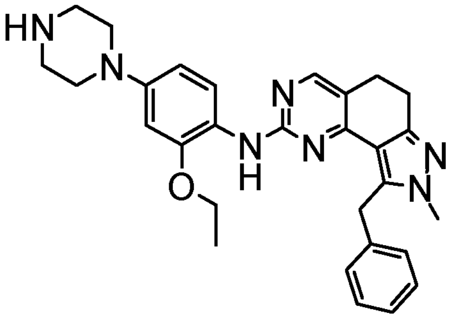
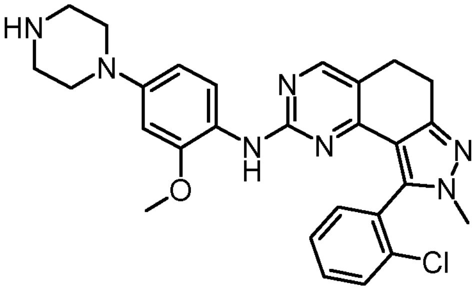


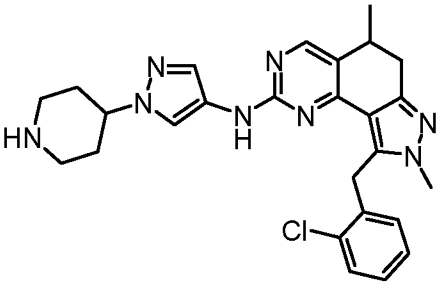
I-14 **IV-1**

Amide cleaving (method M). The starting compound **I-14** (1.2 g, 2.23 mmol) is stirred in conc. HCl (3 mL)/EtOH (3 mL) for 10 min. at 120°C in a microwave reactor. The reaction mixture is made basic with potassium carbonate solution and exhaustively extracted with DCM. The organic phase is washed with water, dried on sodium sulphate, filtered and evaporated down. The crude product is purified by column chromatography .

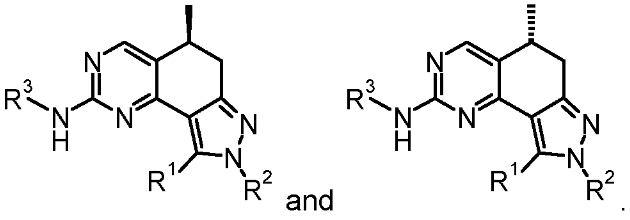
Analogously to **IV-1** further free amines are obtained by amide cleaving (Table 13).

Table 13

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-1		1.85	496.3	G
IV-2		0.71	502.2	A

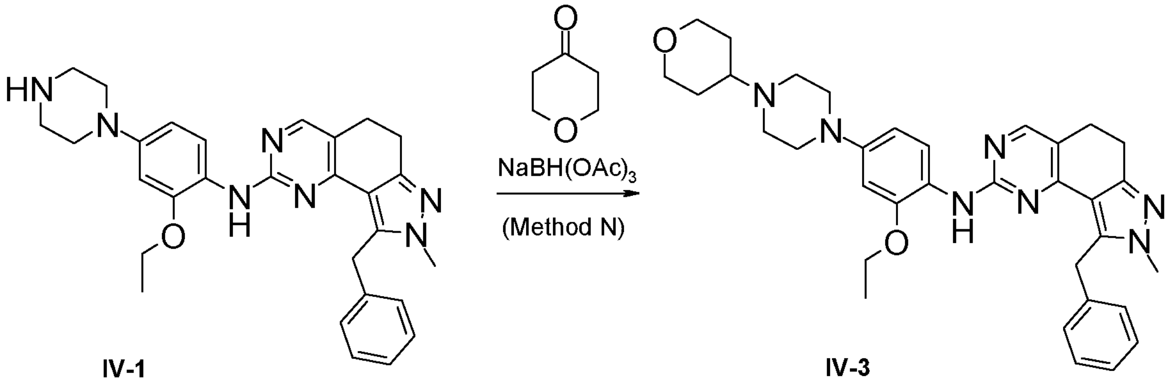
No.	Structure	t_{ret} [min]	$[M+H]^+$	analysis
IV-2a*		1.29	489	G

* Structure includes both enantiomers in each case, i.e.



5

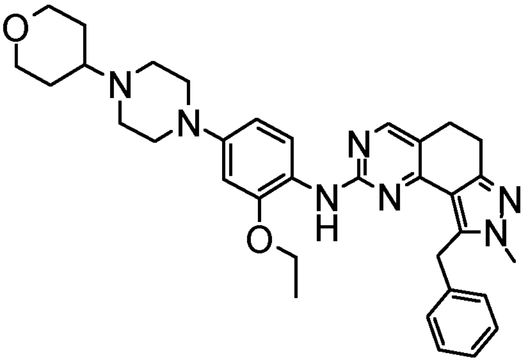
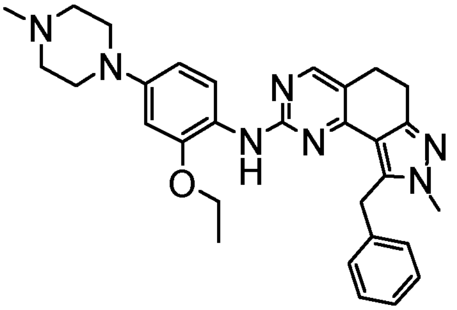
Preparation of compound IV-3 by reductive amination (method N)

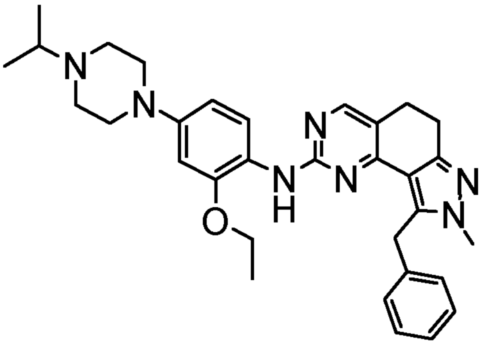
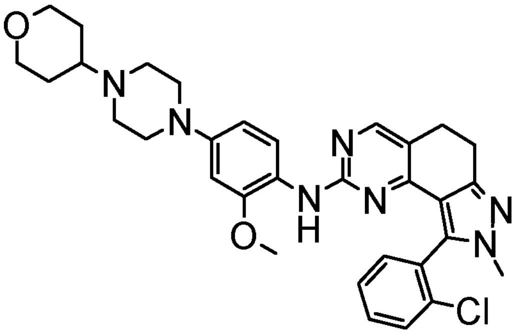
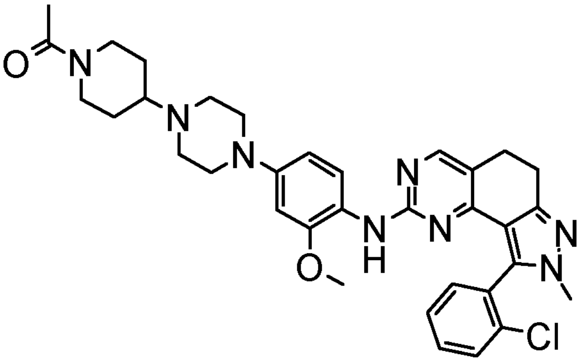
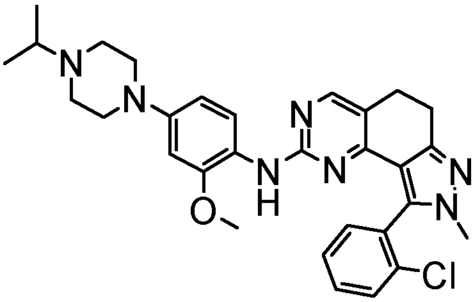


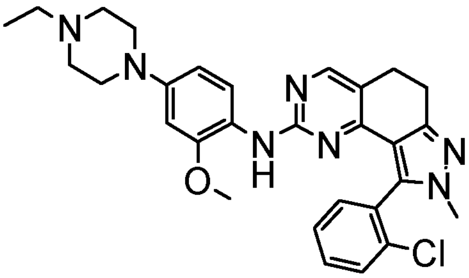
Reductive amination (method N). The starting compound **IV-1** (80 mg, 0.16 mmol) in anhydrous NMP (500 µL) is combined with tetrahydro-4*H*-pyran-4-one (45 µL, 0.48 mmol) and sodium triacetoxyborohydride (107 mg, 0.48 mmol) and stirred for 1.5 h at RT. The reaction mixture is purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried.

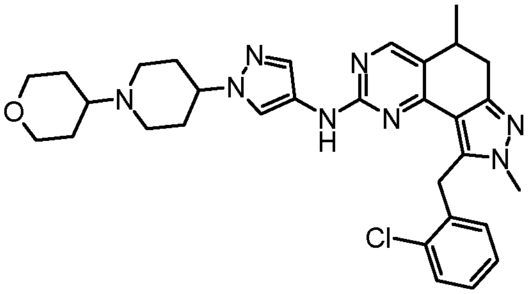
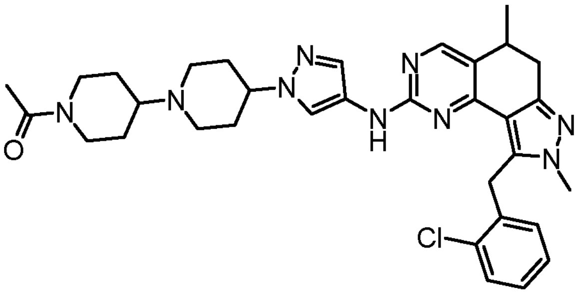
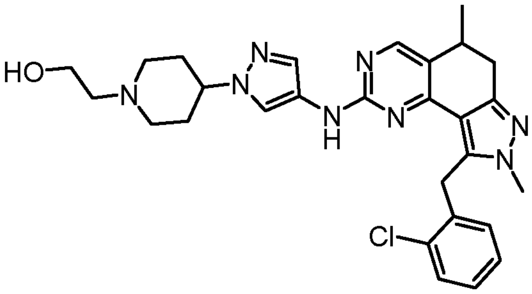
Analogously to **IV-3** further novel compounds are obtained by reductive amination (Table 14).

Table 14

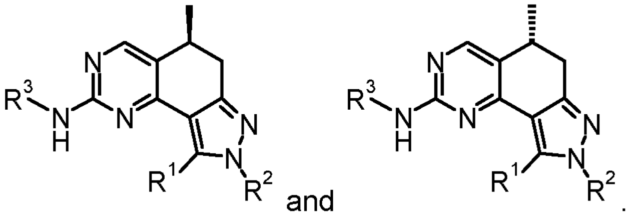
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-3		1.99	580.3	G
IV-4		1.97	510.3	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-5		2.19	538.3	G
IV-6		1.58	586.2	G
IV-7		1.48	627.5	G
IV-8		1.92	544.5	G

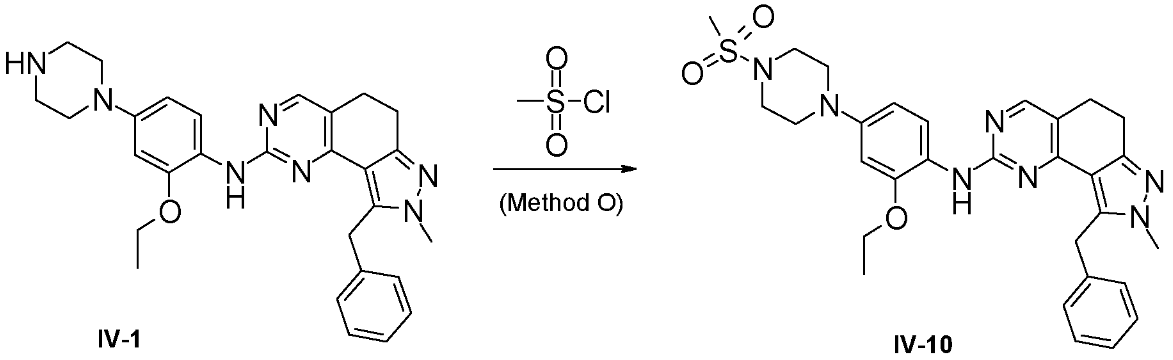
No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-9		1.81	530.2	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Analysis
IV-9a		1.46	573	G
IV-9b		1.33	614	G
IV-9c		1.37	533	G

* Structure includes both enantiomers in each case, i.e.



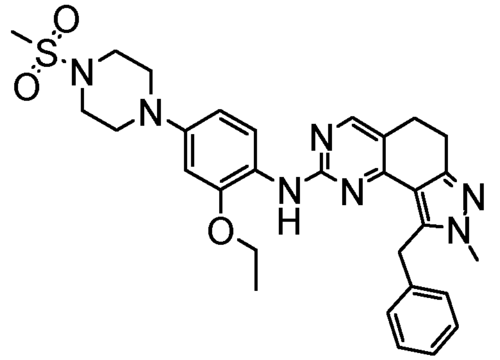
Preparation of compound IV-10 by sulphonamidation (method O)



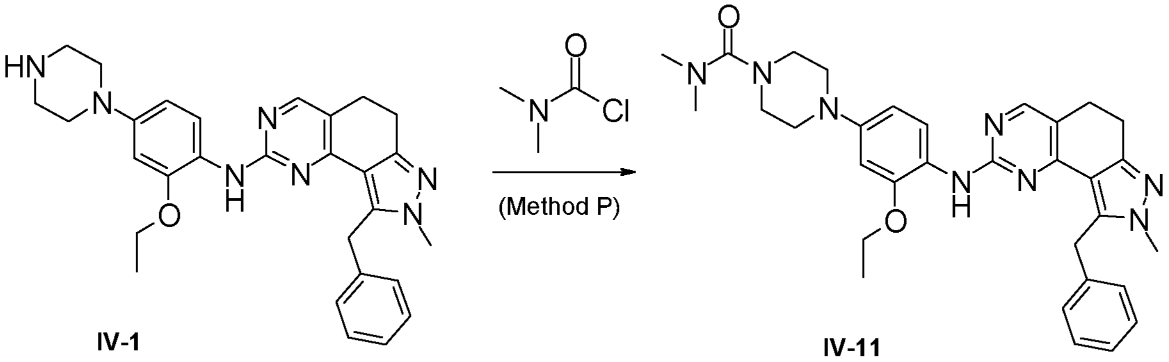
Sulphonamide formation (method O). The starting compound **IV-1** (100 mg, 0.20 mmol) in anhydrous DCM (0.5 mL) is combined with methanesulphonic acid chloride (22 µL, 0.28 mmol) and triethylamine (90 µL, 0.62 mmol) and stirred for 3 h at RT. The reaction mixture is evaporated down, the residue is taken up in DMSO (500 µL) and purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried.

Analogously to **IV-10** further novel compounds are obtained by reaction with sulphonic acid chlorides.

Table 15

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-10		1.94	574.0	G

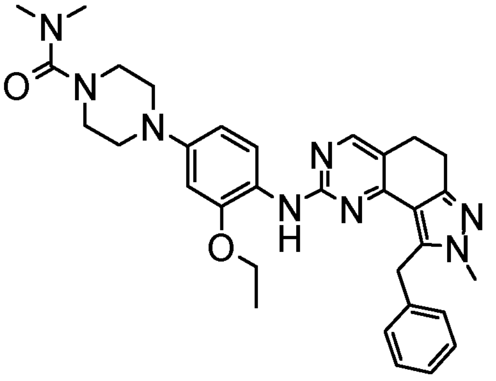
Preparation of compound IV-11 by amidation (method P)



Amide formation (method P). The starting compound **IV-1** (100 mg, 0.20 mmol) in anhydrous DCM (0.5 mL) is combined with dimethylcarbamyl chloride (30 mg, 0.28 mmol) and triethylamine (90 µL, 0.62 mmol) and stirred for 3 h at RT. The reaction mixture is evaporated down, the residue is taken up in DMSO (0.5 mL) and purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried. Alternatively **method L** may be used for the amide linking.

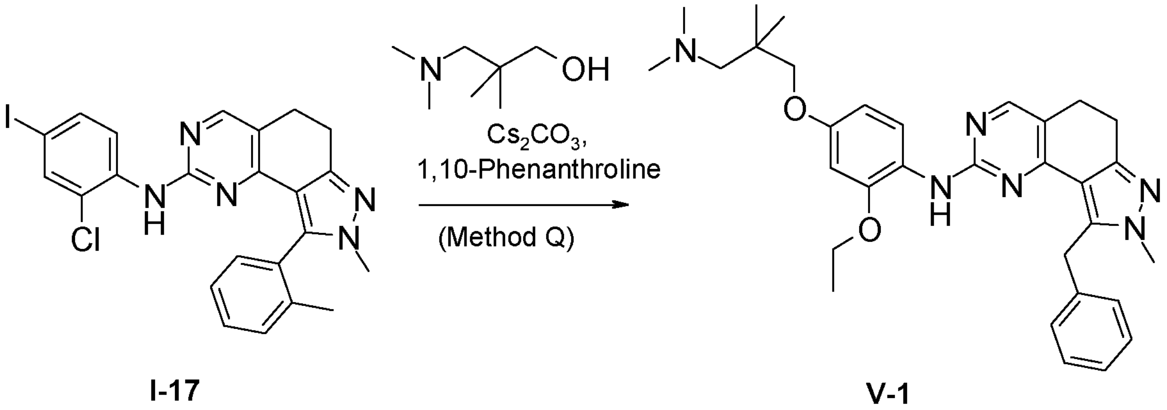
Analogously to **IV-11** further novel compounds may be obtained by reaction with acid chlorides or amide coupling of acids.

Table 16

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
IV-11		1.96	567.3	G

4.4. Preparation of other novel compounds (I) by alkoxylation catalysed by transition metals (method Q)

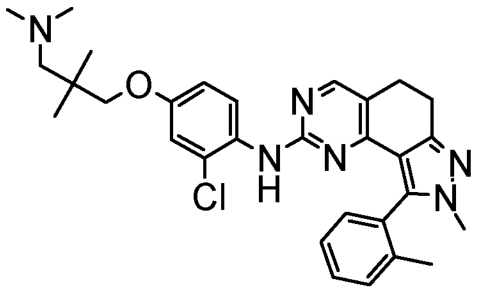
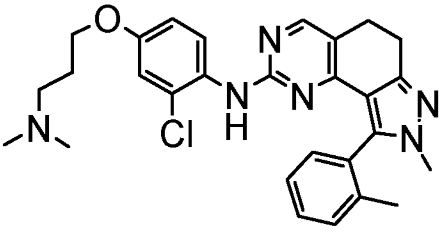
Preparation of compound V-1

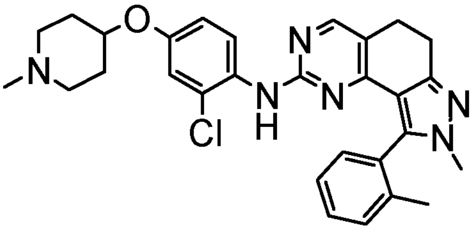
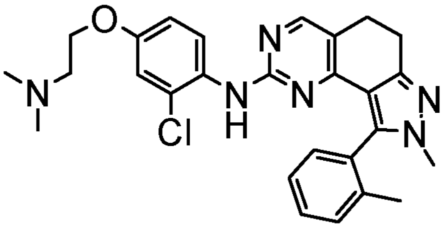
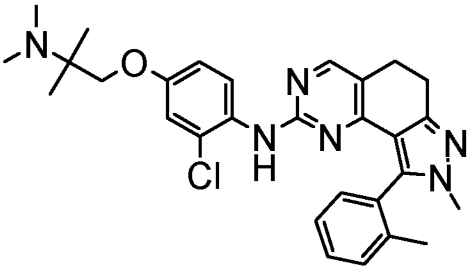
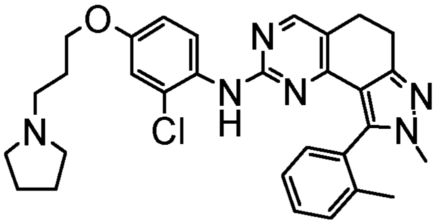
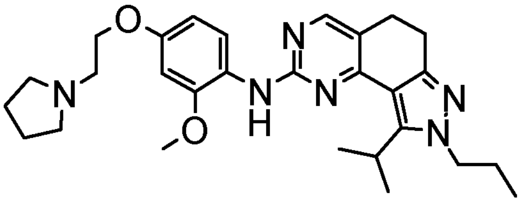
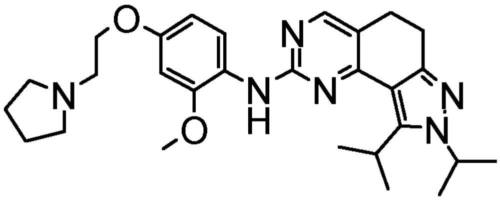


Educt **I-17** (75 mg, 0.14 mmol), caesium carbonate (92 mg, 0.28 mmol), 1,10-phenanthroline (5 mg, 0.03 mmol) and copper-I-iodide (3 mg, 0.015 mmol) are stirred in 3-dimethylamino-2,2-dimethyl-1-propanol (95 mg, 0.71 mmol) for 60 h at 100°C under argon. The reaction mixture is taken up in DMSO, filtered and purified by preparative HPLC-MS. The fractions containing the reaction product are freeze-dried.

Analogously to **V-1** further novel compounds **(I)** are obtained (Table 17).

Table 17

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
V-1		2.63	531.2	G
V-2		2.21	503.3	G

No.	Structure	t_{ret} [min]	$[M+H]^+$	Method of analysis
V-3		2.16	515.2	G
V-4		2.11	489.3	G
V-5		2.26	517.3	G
V-6		2.38	529.3	G
V-7		2.17	491.3	G
V-8		2.18	491.3	G

The following Examples describe the biological activity of the compounds according to the invention, without restricting the invention to these Examples.

Compounds of general formula **(1)** are characterised by their many possible applications in the therapeutic field. Particular mention should be made of those applications in which the inhibiting effect on the proliferation of cultivated human tumour cells but also on the proliferation of other cells such as endothelial cells, for example, are involved.

Insulin-like Growth Factor-1 Receptor (IGF-1R)-Kinase Assay

The kinase activity is measured by DELFIA® assay (dissociation-enhanced lanthanide fluorescence immunoassay, Perkin Elmer). The cytoplasmic kinase domain of human IGF-1R (amino acids 964 – 1370) is expressed as a fusion protein with a glutathione-S-transferase tag (IGF-1R-GST) in High Five™ Cells (Invitrogen). Enzyme activity is measured in the presence of substances and a control substance. Poly-glutamate-tyrosine peptide (pEY, Sigma Aldrich) and biotinylated pEY (bio-pEY) are used as reaction substrates.

10 µL of substance in 25 % DMSO are mixed with 30 µL of IGF-1R-GST solution (67 mM HEPES pH 7.4, 15 µg/mL pEY, 1.7 µg/mL bio-pEY, 13.3 mM $MgCl_2$, 3.3 mM dithiothreitol, 0.0033 % Brij 35, 2 ng IGF-1R-GST) in 96-well plates. The reactions are started with 10 µL of a 750 µM ATP solution. After 40 min at RT the reactions are stopped with 50 µL of stop solution (250 mM EDTA, 20 mM HEPES pH 7.4). 90 µL from each reaction are transferred onto streptavidin-coated 96-well plates. After 120 min incubation at RT the plates are washed three times with 200 µL phosphate-buffered saline (PBS) per well. The plates are incubated for 60 min with 100 µL of europium-coupled antibody against phospho-tyrosine (diluted 1/2000 in Perkin Elmer DELFIA assay buffer) per well. The plates are washed three times with 200 µL per well of DELFIA washing buffer. 100 µL DELFIA Enhancement Solution (Perkin Elmer) is added to each well, and the plates are incubated for 10 min. The fluorescence signal is measured with a Wallac Victor TRF Reader. IC_{50} values for the inhibition of the IGF-1R-kinase activity are calculated using the programmes Fifty (Version 2) and GraphPad (Version 3.0).

Table 18 shows the IC_{50} values of the example compounds determined using the above assay.

Table 18

No.	IGF1R IC$_{50}$ [nM]
I-2	73
I-3	25
I-9	73
I-10	25
I-12	14
I-13	13
I-14	4
I-15	3
I-16	4
I-18	15
I-19	50
I-20	62
I-21	2
I-22	12
I-23	2
I-24	5
I-25	48
I-26	2
I-27	0.18
I-28	179
I-29	5
I-30	2
I-31	34
I-32	433
I-33	398
I-34	226
I-35	242
I-36	409
I-37	264
I-38	299
I-39	63
I-40	3
I-41	4
I-42	1
I-43	3
I-44	196
I-45	11
I-46	9
I-47	89
I-48	0.69
I-49	2
I-50	1
I-51	4
I-52	475
I-53	11
I-54	91
I-55	22
I-56	120
I-57	91
I-58	11
I-59	36
I-60	226
I-61	207
I-62	155
I-63	1
I-64	37
I-65	1
I-66	2
I-67	30
I-68	219
I-69	9
I-70	231
I-71	5
I-72	11
I-73	208
I-74	169
I-75	219
I-76	1
I-77	7
I-78	0.92
I-79	2
I-80	43
I-81	20
I-82	56
I-83	21
I-84	38
I-85	437
I-86	15
I-87	60
I-88	11
I-89	20
I-90	700
I-91	2
I-92	23
I-93	1
I-94	2
I-95	106
I-96	0.8
I-97	0.19
I-98	13

No.	IGF1R IC_{50} [nM]
I-99	13
I-100	50
I-101	11
I-102	17
I-103	169
I-104	11
I-105	500
I-106	1000
I-107	17
I-108	1000
I-109	6
I-110	0.19
I-111	12
I-112	0.87
I-113	29
I-114	140
I-115	471
I-116	785
I-117	922
I-118	1939
I-119	2035
I-120	2354
I-121	2612
I-122	2613
I-123	2976
I-124	135
I-125	27
I-126	77
I-127	7
I-128	96
I-129	11

No.	IGF1R IC_{50} [nM]
I-130	54
I-131	22
I-132	1132
I-133	1000
I-134	46
I-135	264
I-136	23
I-137	108
I-138	131
I-139	63
I-140	0.5
I-141	4
I-142	0.3
I-143	0.4
I-144	15
I-145	277
I-146	1
I-147	13
I-148	1
I-149	39
I-150	2
I-151	2
I-152	13
I-153	1
I-154	71
I-155	2
I-156	16
I-157	1
I-158	4
I-159	42
I-160	25

No.	IGF1R IC_{50} [nM]
I-161	148
I-162	8
I-163	13
I-164	71
I-165	105
II-2	73
II-3	21
II-7	246
II-8	29
II-10	282
II-11	29
II-12	244
II-13	246
II-14	94
II-15	61
II-16	500
II-17	73
II-18	21
III-1	10
III-2	17
III-3	92
III-4	17
III-5	44
III-6	13
III-7	21
III-8	7
III-9	4
III-10	8
III-11	4
III-12	11
III-13	3

No.	IGF1R IC$_{50}$ [nM]
III-14	3
III-15	5
III-16	5
III-17	5
III-18	9
III-19	0.75
III-20	1
III-21	0.54
III-22	0.27
III-23	2
III-24	2
III-25	1
III-26	2
III-27	2
III-28	1
III-29	1
III-30	2
III-31	1
III-32	1
III-33	2
III-34	4
III-35	3
III-36	3
III-37	3
III-38	1
III-39	2
III-40	1
III-41	2
III-42	1
III-43	1
III-44	2

No.	IGF1R IC$_{50}$ [nM]
III-45	1
III-46	3
III-47	1
III-48	1
III-49	2
III-50	26
III-51	183
III-52	6
III-53	8
III-54	11
III-55	7
III-56	8
III-57	36
III-58	5
III-59	2
III-60	0.57
III-61	5
III-62	76
III-63	22
III-64	21
III-65	4
III-66	6
III-67	117
III-68	3
III-69	2
III-70	6
III-71	15
III-72	2
III-73	6
III-74	3
III-75	4

No.	IGF1R IC$_{50}$ [nM]
III-76	10
III-77	5
III-78	4
III-79	12
III-80	3
III-81	4
III-82	8
III-83	1
III-84	2
III-85	3
III-86	0.87
III-87	7
III-88	6
III-89	6
III-90	13
III-91	11
III-92	10
III-93	10
III-94	7
III-95	9
III-96	4
III-97	387
III-98	34
III-99	193
III-100	21
III-101	64
III-102	54
IV-1	0.63
IV-3	0.43
IV-4	0.31
IV-5	0.26

No.	IGF1R IC_{50} [nM]
IV-6	1
IV-7	1
IV-8	0.5
IV-9	1
IV-10	14

No.	IGF1R IC_{50} [nM]
IV-11	2
V-1	12
V-2	13
V-3	5
V-4	7

No.	IGF1R IC_{50} [nM]
V-5	8
V-6	7
V-7	180
V-8	109

No.	IGF1R IC_{50} [nM]
I-166	0.6
I-167	0.6
I-168	1
I-169	0.2
I-170	3
I-171	0.2
I-172	0.3
I-173	0.3
I-174	0.4
I-175	0.4
I-176	0.4
I-177	0.5
I-178	0.5
I-179	0.6
I-180	0.6
I-181	0.6
I-182	0.6
I-183	0.7
I-184	1
I-185	1
I-186*	1
I-187	1
I-188	2

No.	IGF1R IC_{50} [nM]
I-189	2
I-190	2
I-191	2
I-192	2
I-193	2
I-194*	2
I-195	2
I-196	3
I-197	3
I-198	3
I-199	3
I-200	3
I-201	3
I-202	3
I-203	3
I-204*	3
I-205	3
I-206	3
I-207	3
I-208	4
I-209	4
I-210	4
I-211	4

No.	IGF1R IC_{50} [nM]
I-212	4
I-213	4
I-214	4
I-215	5
I-216*	5
I-217	5
I-218	5
I-219	5
I-220	5
I-221*	5
I-222	5
I-223	5
I-224	5
I-225	5
I-226	5
I-227	6
I-228	6
I-229	6
I-230	6
I-231	6
I-232	6
I-233	6
I-234	6

No.	IGF1R IC$_{50}$ [nM]
I-235	6
I-236	6
I-237	6
I-238	6
I-239	7
I-240	8
I-241	8
I-242	8
I-243	8
I-244	8
I-245	8
I-246	8
I-247	9
I-248	9
I-249	10
I-250	10
I-251	10
I-252	10
I-253	10
I-254	10
I-255	12
I-256	12
I-257	12
I-258	12
I-259	13
I-260	13
I-261*	13
I-262	14
I-263	14
I-264*	15
I-265	15
I-266	15
I-267	16
I-268	16
I-269	17
I-270	17
I-271	18
I-272	18
I-273	18
I-274	18
I-275	18
I-276	19
I-277	19
I-278	21
I-279	22
I-280	23
I-281	23
I-282	23
I-283	23
I-284	25
I-285*	28
I-286	31
I-287	36
I-288	48
I-289	51
I-290	57
I-291	58
I-292	59
I-293	70
I-294	70
I-295	89
III-103	0.3
III-104	0.4
III-105	1
III-106*	5
III-107	5
III-108	8
IV-2a*	2
IV-9a	1
IV-9b	1
IV-9c	1

Cellular IGF-1R-phosphorylation assay

The activity of substances against the phosphorylation of IGF-1R in activated cells is measured as follows: mouse fibroblast cells (transfected with human IGF-1R, Fibro-hIGF-1R) are cultivated in standard medium (DMEM, 10 % foetal calf serum (FCS, Gibco), 1x MEM Non-Essential Amino Acids (NEAA, Gibco), 7.5 % sodium hydrogen carbonate (Gibco) and 0.3 mg/mL Puromycin (Sigma)) in a humid incubator at 37°C with 5 %

CO_2/95 % air.

10000 Fibro-hIGF-1R cells per well in 200 µL of standard medium are seeded into 96-well plates and cultivated overnight. The next day, the medium is suction filtered and the cells are cultivated in 90 µL serum-reduced medium (DMEM, 0.5 % FCS, 1x MEM NEAA, 7.5 % sodium hydrogen carbonate) for a further 24 h. 10 µL of substance solution (diluted in serum-reduced medium) is added thereto, and the cells are incubated for a further 120 min in the incubator. The phosphorylation of IGF-1R is activated for 30 min by the addition of IGF-1 (20 ng/mL in serum-reduced medium). All further incubations are carried out at RT. The supernatant is suction filtered from the wells, and the cells are fixed in 100 µL per well of 4 % paraformaldehyde (diluted in PBS). The supernatant in the well is suction filtered and the cells are permeabilised for 5 min in 300 µL per well of 0.1 % TritonX-100 (diluted in PBS). The supernatants are suction filtered once again and the cells are incubated for 20 min in quenching buffer (PBS with 0.1 % TritonX-100 and 1.2 % hydrogen peroxide), to inhibit the endogenous peroxidase of the cells. The cells are washed for 5 min with 300 µL per well of PBS with 0.1 % TritonX-100 and then incubated for 60 min with 100 µL per well of blocking buffer (PBS with 0.1 % TritonX-100 and 5 % Bovine Serum Albumin (BSA)). The blocking buffer is exchanged for 50 µL of the first antibody buffer (1/1000 dilute anti-phospho-IGF-1 receptor β (Tyr1135/1136) / insulin receptor β (Tyr1150/1151) (19H7) rabbit monoclonal antibody from Cell Signaling Technology in blocking buffer) and the plates are incubated overnight at 4°C. The next day the plates are washed for 5 min with 300 µL PBS/0.1 % TritonX-100 at RT and then incubated for 60 min with 50 µL per well of the second antibody buffer (1/500 diluted Goat Anti-Rabbit Immunoglobulin-Horseradish Peroxidase (HRP) (Dako) in blocking buffer) at RT. The plates are washed first for 5 min with 300 µL PBS/0.1 % TritonX-100 and then for a further 5 min with 300 µL PBS at RT . The plates are developed for 10 min with 100 µL per well of a peroxidase solution (1:1 mixture of TMB Peroxidase Substrate and Peroxidase Solution B from Kirkegaard & Perry Laboratories, Inc.). The reactions are stopped with 100 µL per well of stop solution (1M phosphoric acid). The absorbance in each well is measured at 450 nm with a SpectraMax Absorbance Reader. EC_{50} values for inhibiting the phosphorylation of the IGF-1R in activated cells are calculated using the programmes Fifty (Version 2) and GraphPad (Version 3.0).

Compounds **(I)** according to the invention generally display a good inhibitory effect in the cellular assay described above, i.e. for example an EC_{50} value of less than 5 µmol/L, often less than 3 µmol/L.

Cell Proliferation Assays

Compounds were tested for their anti-proliferative effects in the TC-71 (Ewing's sarcoma) and HCT 116 (colorectal carcinoma) cancer cell lines in vitro. Published scientific data has described that interference with the Insulin-like Growth Factor-1 Receptor (IGF-1R) signaling pathway reduces the proliferation of TC-71 cells [1]. Therefore TC-71 cells served as a positive control cell line for monitoring the activity of compounds against IGF-1R-mediated cell proliferation. In contrast, published data has demonstrated that the proliferation of HCT 116 cells is independent of IGF-1R signaling [2]. Therefore the HCT 116 cell line served as a negative control.

2000 TC-71 cells or 1000 HCT 116 cells were seeded per well in 180 µL IMDM + 10 % foetal calf serum (FCS) + penicillin/streptomycin into 96-well microtitre plates. The plates were placed in a cell culture incubator (37°C in a humidified atmosphere of 95 % O_2/5 % CO_2) overnight. The following day, serial dilutions of compounds, prepared in duplicates, were transferred onto the cell layers (controls without compound). The cells were cultivated for a further 72 h in the cell culture incubator. 20 µL of Alamar Bluet™ (Serotec Ltd, Düsseldorf, Germany) was added to each well and the plates incubated for 7 h in the cell culture incubator. Fluorescence (extinction wavelength of 544 nm and emission at 590 nm) was then measured and the normalized data fitted by iterative calculation with a sigmoidal curve analysis program (Graph Pad Prism) with a variable Hill slope to determine the IC_{50} values.

The EC_{50} values of the following compounds were determined on TC-71 cells: **I-23**, **I-30**, **I-40**, **I-42**, **I-97**, **I-109**, **I-112**, **I-147**, **I-157**, **I-166** – **I-168**, **I-171**, **I-172**, **I-175** – **I-178**, **I-180** – **I-182**, **I-185** – **I-187**, **I-189**, **I-191** – **I-214**, **I-217** – **I-263**, **I-265** – **I-284**, **I-286** – **I-289**, **I-293**, **I-294**, **II-3**, **II-18**, **III-38**, **III-105**, **III-107**, **IV-2a**, **IV-9a**, **IV-9b** and **IV-9c**.

The EC_{50} values for all these compounds are less than 3 µM, very often less than 500 nM.

In addition to TC-71, several other cancer cell lines from diverse tissue origins, which have previously been demonstrated to be sensitive to IGF-1R inhibition, were shown to be sensitive to compounds **(I)**. Examples include COLO 205 (colorectal cancer) [3], LP-1 (multiple myeloma) [4] and HL-60 (acute myeloid leukemia) [5].

Reference List

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On the basis of their biological properties the compounds of general formula **(I)** according to the invention, their tautomers, racemates, enantiomers, diastereomers, mixtures thereof and the salts of all the above-mentioned forms are suitable for treating diseases characterised by excessive or abnormal cell proliferation.

Such diseases include for example: viral infections (e.g. HIV and Kaposi's sarcoma); inflammatory and autoimmune diseases (e.g. colitis, arthritis, Alzheimer's disease, glomerulonephritis and wound healing); bacterial, fungal and/or parasitic infections; leukaemias, lymphomas and solid tumours (e.g. carcinomas and sarcomas), skin diseases (e.g. psoriasis); diseases based on hyperplasia which are characterised by an increase in the number of cells (e.g. fibroblasts, hepatocytes, bones and bone marrow cells, cartilage or smooth muscle cells or epithelial cells (e.g. endometrial hyperplasia)); bone diseases and cardiovascular diseases (e.g. restenosis and hypertrophy). They are also suitable for protecting proliferating cells (e.g. hair, intestinal, blood and progenitor cells) from DNA damage caused by radiation, UV treatment and/or cytostatic treatment.

For example, the following cancers may be treated with compounds according to the invention, without being restricted thereto: brain tumours such as for example acoustic neurinoma, astrocytomas such as pilocytic astrocytomas, fibrillary astrocytoma, protoplasmic astrocytoma, gemistocytary astrocytoma, anaplastic astrocytoma and glioblastoma, brain lymphomas, brain metastases, hypophyseal tumour such as prolactinoma, HGH (human growth hormone) producing tumour and ACTH producing tumour (adrenocorticotropic hormone), craniopharyngiomas, medulloblastomas, meningeomas and oligodendrogliomas; nerve tumours (neoplasms) such as e.g. tumours of the vegetative nervous system such as neuroblastoma sympathicum, ganglioneuroma, paraganglioma (pheochromocytoma, chromaffinoma) and glomus-caroticum tumour, tumours on the peripheral nervous system such as amputation neuroma, neurofibroma, neurinoma (neurilemmoma, Schwannoma) and malignant Schwannoma, as well as tumours of the central nervous system such as brain and bone marrow tumours; intestinal cancer such as for example carcinoma of the rectum, colon carcinoma, colorectal carcinoma, anal carcinoma, carcinoma of the large bowel, tumours of the small intestine and duodenum; eyelid tumours such as basalioma or basal cell carcinoma; pancreatic cancer or carcinoma of the pancreas; bladder cancer or carcinoma of the bladder; lung cancer (bronchial carcinoma) such as for example small-cell bronchial carcinomas (oat cell carcinomas) and non-small cell bronchial carcinomas (NSCLC) such as plate epithelial carcinomas, adenocarcinomas and large-cell bronchial carcinomas; breast cancer such as for example mammary carcinoma such as infiltrating ductal carcinoma, colloid carcinoma, lobular invasive carcinoma, tubular carcinoma, adenocystic carcinoma and papillary carcinoma; non-Hodgkin's lymphomas (NHL) such as for example Burkitt's lymphoma, low-malignancy non-Hodgkin's lymphomas (NHL) and mucosis fungoides; uterine cancer or endometrial carcinoma or corpus carcinoma; CUP syndrome (Cancer of Unknown Primary); ovarian cancer or ovarian carcinoma such as mucinous, endometrial or serous cancer; gall bladder cancer; bile duct cancer such as for example Klatskin tumour; testicular cancer such as for example seminomas and non-seminomas; lymphoma (lymphosarcoma) such as for example malignant lymphoma, Hodgkin's disease, non-Hodgkin's lymphomas (NHL) such as chronic lymphatic leukaemia, leukaemic reticuloendotheliosis, immunocytoma, plasmocytoma (multiple myeloma), immunoblastoma, Burkitt's lymphoma, T-zone mycosis fungoides, large-cell anaplastic lymphoblastoma and lymphoblastoma; laryngeal cancer such as for example tumours of the vocal cords, supraglottal, glottal and subglottal laryngeal tumours; bone cancer such as for example osteochondroma, chondroma, chondroblastoma, chondromyxoid fibroma, osteoma, osteoid osteoma, osteoblastoma, eosinophilic granuloma, giant cell tumour, chondrosarcoma, osteosarcoma, Ewing's sarcoma, reticulo-sarcoma, plasmocytoma, fibrous dysplasia, juvenile bone cysts and aneurysmatic bone cysts; head and neck tumours such as for example tumours of the lips, tongue, floor of the mouth, oral cavity, gums, palate, salivary glands, throat, nasal cavity, paranasal sinuses, larynx and middle ear; liver cancer such as for example liver cell carcinoma or hepatocellular carcinoma (HCC); leukaemias, such as for example acute leukaemias such as acute lymphatic/lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML); chronic leukaemias such as chronic lymphatic leukaemia (CLL), chronic myeloid leukaemia (CML); stomach cancer or gastric carcinoma such as for example papillary, tubular and mucinous adenocarcinoma, signet ring cell carcinoma, adenosquamous carcinoma, small-cell carcinoma and undifferentiated carcinoma; melanomas such as for example superficially spreading, nodular, lentigo-maligna and acral-lentiginous melanoma; renal cancer such as e.g. kidney cell carcinoma or hypernephroma or Grawitz's tumour; oesophageal cancer or carcinoma of the oesophagus; penile cancer; prostate cancer; throat cancer or carcinomas of the pharynx such as for example nasopharynx carcinomas, oropharynx carcinomas and hypopharynx carcinomas; retinoblastoma; vaginal cancer or vaginal carcinoma; plate epithelial carcinomas, adenocarcinomas, in situ carcinomas, malignant melanomas and sarcomas; thyroid carcinomas such as for example papillary, follicular and medullary thyroid carcinoma, as well as anaplastic carcinomas; spinalioma, epidormoid carcinoma and plate epithelial carcinoma of the skin; thymomas, cancer of the urethra and cancer of the vulva.

The new compounds may be used for the prevention, short-term or long-term treatment of the above-mentioned diseases, optionally also in combination with radiotherapy or other "state-of-the-art" compounds, such as e.g. cytostatic or cytotoxic substances, cell proliferation inhibitors, anti-angiogenic substances, steroids or antibodies.

The compounds of general formula **(I)** may be used on their own or in combination with other active substances according to the invention, optionally also in combination with other pharmacologically active substances.

Chemotherapeutic agents which may be administered in combination with the compounds according to the invention, include, without being restricted thereto, hormones, hormone analogues and antihormones (e.g. tamoxifen, toremifene, raloxifene, fulvestrant, megestrol acetate, flutamide, nilutamide, bicalutamide, aminoglutethimide, cyproterone acetate, finasteride, buserelin acetate, fludrocortisone, fluoxymesterone, medroxyprogesterone, octreotide), aromatase inhibitors (e.g. anastrozole, letrozole, liarozole, vorozole, exemestane, atamestane), LHRH agonists and antagonists (e.g. goserelin acetate, luprolide), inhibitors of growth factors (growth factors such as for example "platelet derived growth factor (PDGF)", “fibroblast growth factor (FGF)”, “vascular endothelial growth factor (VEGF)”, “epidermal growth factor (EGF)”, “insuline-like growth factors (IGF)”, “human epidermal growth factor (HER, e.g. HER2, HER3, HER4)” and "hepatocyte growth factor (HGF)"), inhibitors are for example "growth factor" antibodies, "growth factor receptor" antibodies and tyrosine kinase inhibitors, such as for example cetuximab, gefitinib, imatinib, lapatinib and trastuzumab); antimetabolites (e.g. antifolates such as methotrexate, raltitrexed, pyrimidine analogues such as 5-fluorouracil, capecitabin and gemcitabin, purine and adenosine analogues such as mercaptopurine, thioguanine, cladribine and pentostatin, cytarabine, fludarabine); antitumour antibiotics (e.g. anthracyclins such as doxorubicin, daunorubicin, epirubicin and idarubicin, mitomycin-C, bleomycin, dactinomycin, plicamycin, streptozocin); platinum derivatives (e.g. cisplatin, oxaliplatin, carboplatin); alkylation agents (e.g. estramustin, meclorethamine, melphalan, chlorambucil, busulphan, dacarbazin, cyclophosphamide, ifosfamide, temozolomide, nitrosoureas such as for example carmustin and lomustin, thiotepa); antimitotic agents (e.g. Vinca alkaloids such as for example vinblastine, vindesin, vinorelbin and vincristine; and taxanes such as paclitaxel, docetaxel); topoisomerase inhibitors (e.g. epipodophyllotoxins such as for example etoposide and etopophos, teniposide, amsacrin, topotecan, irinotecan, mitoxantron), serine/threonine kinase inhibitors (e.g. PDK 1 inhibitors, B-Raf inhibitors, mTOR inhibitors, PI3K inhibitors, STK 33 inhibitors, AKT inhibitors, PLK 1 inhibitors, inhibitors of CDKs, Aurora kinase inhibitors), tyrosine kinase inhibitors (e.g. PTK2/FAK inhibitors), protein protein interaction inhibitors (e.g. IAP, Mcl-1, MDM2/MDMX), MEK inhibitors, rapamycin analogs (e.g. everolimus, temsirolimus) and various chemotherapeutic agents such as amifostin, anagrelid, clodronat, filgrastin, interferon alpha, leucovorin, rituximab, procarbazine, levamisole, mesna, mitotane, pamidronate and porfimer.

Other possible combination partners are 2-chlorodesoxyadenosine, 2-fluorodesoxy-cytidine, 2-methoxyoestradiol, 2C4, 3-alethine, 131-I-TM-601, 3CPA, 7-ethyl-10-hydroxycamptothecin, 16-aza-epothilone B, A 105972, A 204197, aldesleukin, alitretinoin, altretamine, alvocidib, amonafide, anthrapyrazole, AG-2037, AP-5280, apaziquone, apomine, aranose, arglabin, arzoxifene, atamestane, atrasentan, auristatin PE, AVLB, AZ10992, ABX-EGF, ARRY-300, ARRY-142886/AZD-6244, ARRY-704/AZD-8330, AS-703026, azacytidine, azaepothilone B, azonafide, BAY-43-9006, BBR-3464, BBR-3576, bevacizumab, biricodar dicitrate, BCX-1777, bleocin, BLP-25, BMS-184476, BMS-247550, BMS-188797, BMS-275291, BNP-1350, BNP-7787, BIBW 2992, BIBF 1120, BI 836845, BI 2536, BI 6727, BI 847325, bleomycinic acid, bleomycin A, bleomycin B, bryostatin-1, bortezomib, brostallicin, busulphan, CA-4 prodrug, CA-4, CapCell, calcitriol, canertinib, canfosfamide, capecitabine, carboxyphthalatoplatin, CCI-779, CEP-701, CEP-751, CBT-1 cefixime, ceflatonin, ceftriaxone, celecoxib, celmoleukin, cemadotin, CH4987655/RO-4987655, chlorotrianisene, cilengitide, ciclosporin, CDA-II, CDC-394, CKD-602, clofarabin, colchicin, combretastatin A4, CHS-828, CLL-Thera, CMT-3 cryptophycin 52, CTP-37, CP-461, CV-247, cyanomorpholinodoxorubicin, cytarabine, D 24851, decitabine, deoxorubicin, deoxyrubicin, deoxycoformycin, depsipeptide, desoxyepothilone B, dexamethasone, dexrazoxanet, diethylstilbestrol, diflomotecan, didox, DMDC, dolastatin 10, doranidazole, E7010, E-6201, edatrexat, edotreotide, efaproxiral, eflornithine, EKB-569, EKB-509, elsamitrucin, epothilone B, epratuzumab, ER-86526, erlotinib, ET-18-OCH3, ethynylcytidine, ethynyloestradiol, exatecan, exatecan mesylate, exemestane, exisulind, fenretinide, floxuridine, folic acid, FOLFOX, FOLFIRI, formestane, galarubicin, gallium maltolate, gefinitib, gemtuzumab, gimatecan, glufosfamide, GCS-IOO, G17DT immunogen, GMK, GPX-100, GSK-5126766, GSK-1120212, GW2016, granisetron, hexamethylmelamine, histamine, homoharringtonine, hyaluronic acid, hydroxyurea, hydroxyprogesterone caproate, ibandronate, ibritumomab, idatrexate, idenestrol, IDN-5109, IMC-1C11, immunol, indisulam, interferon alpha-2a, interferon alpha-2b, interleukin-2, ionafarnib, iproplatin, irofulven, isohomohalichondrin-B, isoflavone, isotretinoin, ixabepilone, JRX-2, JSF-154, J-107088, conjugated oestrogens, kahalid F, ketoconazole, KW-2170, lobaplatin, leflunomide, lenograstim, leuprolide, leuporelin, lexidronam, LGD-1550, linezolid, lutetium texaphyrin, lometrexol, losoxantrone, LU 223651, lurtotecan, mafosfamide, marimastat, mechloroethamine, methyltestosteron, methylprednisolone, MEN-10755, MDX-H210, MDX-447, MGV, midostaurin, minodronic acid, mitomycin, mivobulin, MK-2206, MLN518, motexafin gadolinium, MS-209, MS-275, MX6, neridronate, neovastat, nimesulide, nitroglycerin, nolatrexed, norelin, N-acetylcysteine, 06-benzylguanine, omeprazole, oncophage, ormiplatin, ortataxel, oxantrazole, oestrogen, patupilone, pegfilgrastim, PCK-3145, pegfilgrastim, PBI-1402, PEG-paclitaxel, PEP-005, P-04, PKC412, P54, PI-88, pelitinib, pemetrexed, pentrix, perifosine, perillylalcohol, PG-TXL, PG2, PLX-4032/RO-5185426, PT-100, picoplatin, pivaloyloxymethylbutyrate, pixantrone, phenoxodiol O, PKI166, plevitrexed, plicamycin, polyprenic acid, porfiromycin, prednisone, prednisolone, quinamed, quinupristin, RAF-265, ramosetron, ranpirnase, RDEA-119/BAY 869766, rebeccamycin analogues, revimid, RG-7167, rhizoxin, rhu-MAb, risedronate, rituximab, rofecoxib, Ro-31-7453, RO-5126766, RPR 109881A, rubidazone, rubitecan, R-flurbiprofen, S-9788, sabarubicin, SAHA, sargramostim, satraplatin, SB 408075, SU5416, SU6668, SDX-101, semustin, seocalcitol, SM-11355, SN-38, SN-4071, SR-27897, SR-31747, SRL-172, sorafenib, spiroplatin, squalamine, suberanilohydroxamic acid, sutent, T 900607, T 138067, TAS-103, tacedinaline, talaporfin, tariquitar, taxotere, taxoprexin, tazarotene, tegafur, temozolamide, tesmilifene, testosterone, testosterone propionate, tetraplatin, tetrodotoxin, tezacitabine, thalidomide, theralux, therarubicin, thymectacin, tiazofurin, tipifarnib, tirapazamine, tocladesine, tomudex, toremofin, trabectedin, TransMID-107, transretinic acid, traszutumab, tretinoin, triacetyluridine, triapine, trimetrexate, TLK-286TXD 258, urocidin, valrubicin, vatalanib, vincristine, vinflunine, virulizin, WX-UK1, vectibix, xeloda, XELOX, XL-281, XL-518/R-7420, YM-511, YM-598, ZD-4190, ZD-6474, ZD-4054, ZD-0473, ZD-6126, ZD-9331, ZDI839, zoledronat and zosuquidar.

Suitable preparations include for example tablets, capsules, suppositories, solutions - particularly solutions for injection (s.c., i.v., i.m.) and infusion - elixirs, emulsions or dispersible powders. The content of the pharmaceutically active compound(s) should be in the range from 0.1 to 90 wt.-%, preferably 0.5 to 50 wt.-% of the composition as a whole, *i.e.* in amounts which are sufficient to achieve the dosage range specified below. The doses specified may, if necessary, be given several times a day.

Suitable tablets may be obtained, for example, by mixing the active substance(s) with known excipients, for example inert diluents such as calcium carbonate, calcium phosphate or lactose, disintegrants such as corn starch or alginic acid, binders such as starch or gelatine, lubricants such as magnesium stearate or talc and/or agents for delaying release, such as carboxymethyl cellulose, cellulose acetate phthalate, or polyvinyl acetate. The tablets may also comprise several layers.

Coated tablets may be prepared accordingly by coating cores produced analogously to the tablets with substances normally used for tablet coatings, for example collidone or shellac, gum arabic, talc, titanium dioxide or sugar. To achieve delayed release or prevent incompatibilities the core may also consist of a number of layers. Similarly the tablet coating may consist of a number of layers to achieve delayed release, possibly using the excipients mentioned above for the tablets.

Syrups or elixirs containing the active substances or combinations thereof according to the invention may additionally contain a sweetener such as saccharine, cyclamate, glycerol or sugar and a flavour enhancer, e.g. a flavouring such as vanillin or orange extract. They may also contain suspension adjuvants or thickeners such as sodium carboxymethyl cellulose, wetting agents such as, for example, condensation products of fatty alcohols with ethylene oxide, or preservatives such as p-hydroxybenzoates.

Solutions for injection and infusion are prepared in the usual way, e.g. with the addition of isotonic agents, preservatives such as p-hydroxybenzoates, or stabilisers such as alkali metal salts of ethylenediamine tetraacetic acid, optionally using emulsifiers and/or dispersants, whilst if water is used as the diluent, for example, organic solvents may optionally be used as solvating agents or dissolving aids, and transferred into injection vials or ampoules or infusion bottles.

Capsules containing one or more active substances or combinations of active substances may for example be prepared by mixing the active substances with inert carriers such as lactose or sorbitol and packing them into gelatine capsules.

Suitable suppositories may be made for example by mixing with carriers provided for this purpose, such as neutral fats or polyethyleneglycol or the derivatives thereof.

Excipients which may be used include, for example, water, pharmaceutically acceptable organic solvents such as paraffins (e.g. petroleum fractions), vegetable oils (e.g. groundnut or sesame oil), mono- or polyfunctional alcohols (e.g. ethanol or glycerol), carriers such as e.g. natural mineral powders (e.g. kaolins, clays, talc, chalk), synthetic mineral powders (e.g. highly dispersed silicic acid and silicates), sugars (e.g. cane sugar, lactose and glucose) emulsifiers (e.g. lignin, spent sulphite liquors, methylcellulose, starch and polyvinylpyrrolidone) and lubricants (e.g. magnesium stearate, talc, stearic acid and sodium lauryl sulphate).

The preparations are administered by the usual methods, preferably by oral or transdermal route, most preferably by oral route. For oral administration the tablets may, of course contain, apart from the abovementioned carriers, additives such as sodium citrate, calcium carbonate and dicalcium phosphate together with various additives such as starch, preferably potato starch, gelatine and the like. Moreover, lubricants such as magnesium stearate, sodium lauryl sulphate and talc may be used at the same time for the tabletting process. In the case of aqueous suspensions the active substances may be combined with various flavour enhancers or colourings in addition to the excipients mentioned above.

For parenteral use, solutions of the active substances with suitable liquid carriers may be used.

The dosage for intravenous use is from 1 - 1000 mg per hour, preferably between 5 and 500 mg per hour.

However, it may sometimes be necessary to depart from the amounts specified, depending on the body weight, the route of administration, the individual response to the drug, the nature of its formulation and the time or interval over which the drug is administered. Thus, in some cases it may be sufficient to use less than the minimum dose given above, whereas in other cases the upper limit may have to be exceeded. When administering large amounts it may be advisable to divide them up into a number of smaller doses spread over the day.

The formulation examples which follow illustrate the present invention without restricting its scope:

Examples of pharmaceutical formulations

A)

Tablets	per tablet
active substance according to formula **(I)**	100 mg
lactose	140 mg
corn starch	240 mg

polyvinylpyrrolidone	15 mg
magnesium stearate	5 mg
	500 mg

The finely ground active substance, lactose and some of the corn starch are mixed together. The mixture is screened, then moistened with a solution of polyvinylpyrrolidone in water, kneaded, wet-granulated and dried. The granules, the remaining corn starch and the magnesium stearate are screened and mixed together. The mixture is compressed to produce tablets of suitable shape and size.

B) Tablets

Tablets	per tablet
active substance according to formula **(I)**	80 mg
lactose	55 mg
corn starch	190 mg
microcrystalline cellulose	35 mg
polyvinylpyrrolidone	15 mg
sodium-carboxymethyl starch	23 mg
magnesium stearate	2 mg
	400 mg

The finely ground active substance, some of the corn starch, lactose, microcrystalline cellulose and polyvinylpyrrolidone are mixed together, the mixture is screened and worked with the remaining corn starch and water to form a granulate which is dried and screened. The sodiumcarboxymethyl starch and the magnesium stearate are added and mixed in and the mixture is compressed to form tablets of a suitable size.

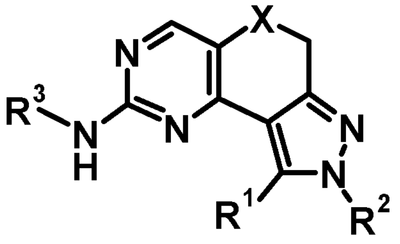
C) Ampoule solution

active substance according to formula **(I)**	50 mg
sodium chloride	50 mg
water for inj.	5 ml

The active substance is dissolved in water at its own pH or optionally at pH 5.5 to 6.5 and sodium chloride is added to make it isotonic. The solution obtained is filtered free from pyrogens and the filtrate is transferred under aseptic conditions into ampoules which are then sterilised and sealed by fusion. The ampoules contain 5 mg, 25 mg and 50 mg of active substance.

Patent Claims

1. Compounds of general formula **(I)**

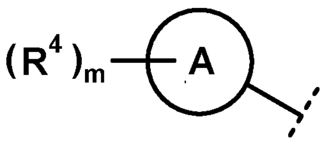


(I) , wherein

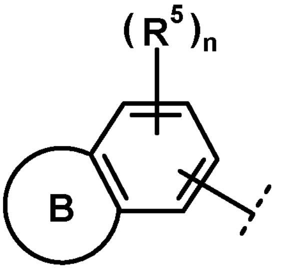
R^1 denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{a} and/or **R**^{b}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

R^2 denotes hydrogen or a group optionally substituted by one or more identical or different **R**^{a} and/or **R**^{b}, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

R^3 denotes a group



or



;

A is selected from among C_{6-10}aryl and 5-12 membered heteroaryl;

B denotes a 5- to 7-membered, non-aromatic hetero ring with at least one heteroatom, selected from among nitrogen, sulphur and oxygen, which optionally carries one or more substituents selected from among C_{1-6}alkyl and =O;

each **R**^{4} is independently selected from among **R**^{a} and **R**^{b};

m denotes 0, 1, 2 or 3;

R^5 is selected from among **R^a** and **R^b**;

n denotes 0 or 1;

X denotes a bond or is selected from among -CH_2- and -CH_2-CH_2- and in the above-mentioned -CH_2- and -CH_2-CH_2- one or two hydrogen atoms are optionally substituted independently of one another by C_{1-4}alkyl, C_{1-4}haloalkyl, -O-C_{1-4}alkyl or halogen;

each **R^a** independently denotes a group optionally substituted by one or more identical or different **R^b** and/or **R^c**, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^b** is independently selected from among -OR^c, -SR^c, -NR^cR^c, halogen, -CN, -NO_2, -C(O)R^c, -C(O)OR^c, -C(O)NR^cR^c, -C(NR^h)NR^cR^c, -OC(O)R^c, -OC(O)OR^c, -S(O)$_2R^c$, -S(O)$_2$NR^cR^c, -NR^hC(O)R^c, -NR^hC(O)OR^c, -NR^hC(O)NR^cR^c, -NR^hC(NR^h)NR^cR^c and -NR^hS(O)$_2R^c$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^c** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^d** and/or **R^e**, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^d** is independently selected from among -OR^e, -SR^e, -NR^eR^e, halogen, -CN, -NO_2, -C(O)R^e, -C(O)OR^e, -C(O)NR^eR^e, -C(NR^h)NR^eR^e, -OC(O)R^e, -OC(O)OR^e, -S(O)$_2R^e$, -S(O)$_2$NR^eR^e, -NR^hC(O)R^e, -NR^hC(O)OR^e, -NR^hC(O)NR^eR^e, -NR^hC(NR^h)NR^eR^e and -NR^hS(O)$_2R^e$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^e** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^f** and/or **R^g**, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^f** is independently selected from among -OR^g, -SR^g, -NR^gR^g, halogen, -CN, -NO_2, -C(O)R^g, -C(O)OR^g, -C(O)NR^gR^g, -C(NR^h)NR^gR^g, -OC(O)R^g, -OC(O)OR^g, -S(O)$_2R^g$, -S(O)$_2$NR^gR^g, -NR^hC(O)R^g, -NR^hC(O)OR^g, -NR^hC(O)NR^gR^g, -NR^hC(NR^h)NR^gR^g and -NR^hS(O)$_2R^g$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^g** is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl, and

each **R^h** is independently selected from among hydrogen and C_{1-6}alkyl,

while the compounds **(I)** may optionally also be present in the form of their tautomers, their racemates, their enantiomers, their diastereomers or their mixtures or as the respective salts of all the above-mentioned forms.

2. Compounds according to claim 1, wherein

R^1 is a group optionally substituted by one or more identical or different **R^{a1}** and/or **R^{b1}**, selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^{a1}** independently denotes a group optionally substituted by one or more identical or different **R^{b1}** and/or C_{1-6}alkyl, selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and C_{6-10}aryl, and

each **R^{b1}** is independently selected from among -OH, -O-C_{1-6}alkyl, halogen and -CN.

3. Compounds according to one of claims 1 or 2, wherein

R^1 is a group optionally substituted by one or more identical or different **R^{a1}** and/or **R^{b1}**, selected from among C_{1-4}alkyl, C_{3-6}cycloalkyl, phenyl, 5- to 6-membered heteroaryl and 3-7 membered heterocyclyl;

each **R^{a1}** independently denotes a group optionally substituted by one or more identical or different **R^{b1}** and/or C_{1-4}alkyl, selected from among C_{1-4}alkyl, C_{3-6}cycloalkyl and phenyl, and

each **R^{b1}** is independently selected from among -O-C_{1-4}alkyl, halogen and –CN.

4. Compounds according to one of claims 1 to 3, wherein

R^1 denotes C_{3-6}alkyl.

5. Compounds according to one of claims 1 to 3, wherein

R^1 denotes phenyl or benzyl, wherein the above-mentioned phenyl and benzyl optionally carry one or more substituents selected from among C_{1-6}alkyl, halogen, -O-C_{1-6}alkyl and -CN.

6. Compounds according to one of claims 1 to 3, wherein

R^1 denotes phenyl or benzyl, wherein the above-mentioned phenyl and benzyl optionally carry one or more substituents selected from among C_{1-4}alkyl, C_{1-4}haloalkyl, halogen, -O-C_{1-4}alkyl, -O-C_{1-4}haloalkyl and -CN.

7. Compounds according to one of claims 1 to 3, wherein

R^1 denotes thienyl, wherein this thienyl optionally carries one or more substituents selected from among C_{1-4}alkyl and halogen.

8. Compounds according to one of claims 1 to 7, wherein

R^2 is hydrogen or a group optionally substituted by one or more identical or different **R^{b2}** and/or C_{6-10}aryl selected from among C_{1-6}alkyl, C_{2-6}alkenyl and 5- to 12-membered heteroaryl;

each **R^{b2}** is independently selected from among -OH, -O-C_{1-6}alkyl, -NH_2, -NH(C_{1-6}alkyl) and -N(C_{1-6}alkyl)$_2$.

9. Compounds according to one of claims 1 to 7, wherein

R^2 is a group optionally substituted by one or more identical or different **R^{b2}** and/or phenyl, selected from among C_{1-4}alkyl, and 5- to 6-membered heteroaryl;

each **R^{b2}** is independently selected from among -O-C_{1-4}alkyl and -N(C_{1-4}alkyl)$_2$.

10. Compounds according to one of claims 1 to 7, wherein

R^2 denotes methyl or ethyl.

11. Compounds according to one of claims 1 to 10, wherein

X denotes a bond or is selected from among -CH_2- and -CH_2-CH_2- and in the above-mentioned $-CH_2-$ and $-CH_2-CH_2-$ one or two hydrogen atoms are optionally substituted by C_{1-4}alkyl.

12. Compounds according to one of claims 1 to 10, wherein

X is selected from among $-CH_2-$ and $-CH_2-CH_2-$ and in the above-mentioned $-CH_2-$ and $-CH_2-CH_2-$ one or two hydrogen atoms are optionally substituted by C_{1-4}alkyl.

13. Compounds according to one of claims 1 to 10, wherein

X is selected from among $-CH_2-$, $-CH(CH_3)-$, $-C(CH_3)_2-$ and $-CH_2-CH_2-$.

14. Compounds according to one of claims 1 to 10, wherein

X denotes $-CH_2-$ or $-CH(CH_3)-$.

15. Compounds according to one of claims 1 to 14, wherein

A is selected from among phenyl, naphthyl, 5- to 6-membered monocyclic heteroaryl and 9- to 10-membered bicyclic heteroaryl.

16. Compounds according to one of claims 1 to 14, wherein

A is selected from among phenyl, benzofuryl, benzothienyl, naphthyl, isoquinolinyl, pyrazolyl, indazolyl, isoxazolyl and imidazo[1,2-*a*]pyridyl.

17. Compounds according to one of claims 1 to 14, wherein

A denotes phenyl.

18. Compounds according to one of claims 1 to 14, wherein

A denotes pyrazolyl.

19. Compounds according to one of claims 1 to 18, wherein

each $\mathbf{R^4}$ is independently selected from among $\mathbf{R^{a3}}$ and $\mathbf{R^{b3}}$;

m denotes 0, 1, 2 or 3;

each $\mathbf{R^{a3}}$ independently denotes a group optionally substituted by one or more identical or different $\mathbf{R^{b3}}$ and/or $\mathbf{R^{c3}}$, selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{b3}}$ is independently selected from among $-OR^{c3}$, $-NR^{c3}R^{c3}$, halogen, $-C(O)R^{c3}$, $-C(O)OR^{c3}$, $-C(O)NR^{c3}R^{c3}$ and $-S(O)_2R^{c3}$;

each $\mathbf{R^{c3}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d3}}$ and/or $\mathbf{R^{e3}}$ selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{d3}}$ is independently selected from among $-OR^{e3}$, $-NR^{e3}R^{e3}$, halogen, $-C(O)R^{e3}$, $-C(O)OR^{e3}$ and $-C(O)NR^{e3}R^{e3}$;

each $\mathbf{R^{e3}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{f3}}$ and/or $\mathbf{R^{g3}}$ selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{f3}}$ is independently selected from among $-OR^{g3}$, $-NR^{g3}R^{g3}$, halogen, $-C(O)R^{g3}$, $-C(O)OR^{g3}$ and $-C(O)NR^{g3}R^{g3}$ and

each $\mathbf{R^{g3}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{6-10}aryl, and 5-12 membered heteroaryl.

20. Compounds according to claim 19, wherein

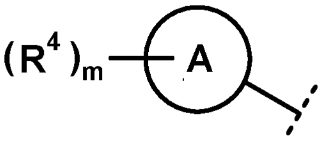
m denotes 1, 2 or 3.

21. Compounds according to claim 19, wherein

m denotes 2.

22. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R^3}$ denotes a group



;

A is selected from among C_{6-10}aryl and 5-12 membered heteroaryl;

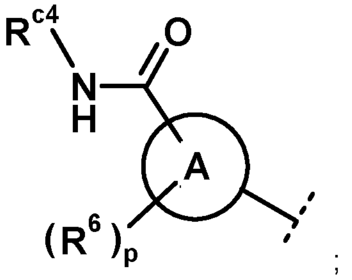
each $\mathbf{R^4}$ is independently selected from among $\mathbf{R^a}$ and $\mathbf{R^b}$;

m denotes 0, 1, 2 or 3 and

$\mathbf{R^a}$ and $\mathbf{R^b}$ are defined as in claim 1.

23. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R^3}$ denotes a group



;

A is selected from among C_{6-10}aryl and 5-12 membered heteroaryl;

each $\mathbf{R^6}$ is independently selected from among C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen;

p denotes 0, 1 or 2;

$\mathbf{R^{c4}}$ denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d4}}$ and/or $\mathbf{R^{e4}}$ selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each $\mathbf{R^{d4}}$ is independently selected from among $-OR^{e4}$, $-SR^{e4}$, $-NR^{e4}R^{e4}$, halogen, -CN, $-NO_2$, $-C(O)R^{e4}$, $-C(O)OR^{e4}$, $-C(O)NR^{e4}R^{e4}$, $-C(NR^{h4})NR^{e4}R^{e4}$, $-OC(O)R^{e4}$, $-OC(O)OR^{e4}$, $-S(O)_2R^{e4}$, $-S(O)_2NR^{e4}R^{e4}$, $-NR^{h4}C(O)R^{e4}$, $-NR^{h4}C(O)OR^{e4}$, $-NR^{h4}C(O)NR^{e4}R^{e4}$, $-NR^{h4}C(NR^{h4})NR^{e4}R^{e4}$ and $-NR^{h4}S(O)_2R^{e4}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each $\mathbf{R^{e4}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{f4}}$ and/or $\mathbf{R^{g4}}$ selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

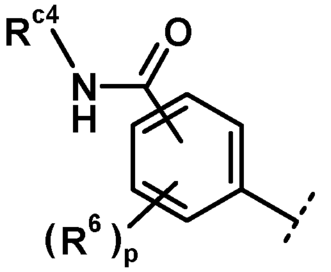
each $\mathbf{R^{f4}}$ is independently selected from among $-OR^{g4}$, $-SR^{g4}$, $-NR^{g4}R^{g4}$, halogen, -CN, $-NO_2$, $-C(O)R^{g4}$, $-C(O)OR^{g4}$, $-C(O)NR^{g4}R^{g4}$, $-C(NR^{h4})NR^{g4}R^{g4}$, $-OC(O)R^{g4}$, $-OC(O)OR^{g4}$, $-S(O)_2R^{g4}$, $-S(O)_2NR^{g4}R^{g4}$, $-NR^{h4}C(O)R^{g4}$, $-NR^{h4}C(O)OR^{g4}$, $-NR^{h4}C(O)NR^{g4}R^{g4}$, $-NR^{h4}C(NR^{g4})NR^{g4}R^{g4}$ and $-NR^{h4}S(O)_2R^{g4}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each $\mathbf{R^{g4}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl and

each $\mathbf{R^{h4}}$ is independently selected from among hydrogen and C_{1-4}alkyl.

24. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R^3}$ denotes a group

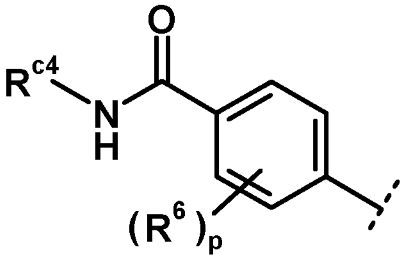


and

$\mathbf{R^{c4}}$, $\mathbf{R^6}$ and **p** are defined as in claim 23.

25. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R^3}$ denotes a group

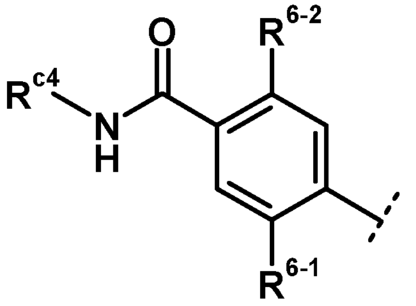


and

$\mathbf{R^{c4}}$, $\mathbf{R^6}$ and **p** are defined as in claim 23.

26. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R^3}$ denotes a group



;

R^{6-1} and R^{6-2} is independently selected from among hydrogen, C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen and

R^{c4} is defined as in claim 23.

27. Compounds according to one of claims 23 to 26, wherein

R^{c4} denotes hydrogen or a group optionally substituted by one or more identical or different R^{d4} and/or R^{e4} selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each R^{d4} is independently selected from among -OR^{e4}, -$NR^{e4}R^{e4}$, halogen, -C(O)R^{e4} and -C(O)$NR^{e4}R^{e4}$;

each R^{e4} independently denotes hydrogen or a group optionally substituted by one or more identical or different R^{f4} and/or R^{g4} selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each R^{f4} is independently selected from among -OR^{g4}, -$NR^{g4}R^{g4}$, halogen, -C(O)R^{g4}, -C(O)$NR^{g4}R^{g4}$ and

each R^{g4} is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{6-10}aryl and 5-12 membered heteroaryl.

28. Compounds according to one of claims 23 to 26, wherein

R^{c4} denotes a group optionally substituted by one or more identical or different R^{d4} and/or R^{e4} selected from among C_{1-6}alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, azetidinyl, pyrrolidinyl, tetrahydropyranyl, 1-aza-bicyclo[2.2.2]octyl, 8-methyl-8-aza-bicyclo[3.2.1]octyl, morpholinyl, piperidinyl and piperazinyl;

each R^{d4} is independently selected from among -OR^{e4}, -$NR^{e4}R^{e4}$, halogen, -C(O)R^{e4} and

$-C(O)NR^{e4}R^{e4}$;

each $\mathbf{R^{e4}}$ independently denotes a group optionally substituted by one or more identical or different $\mathbf{R^{f4}}$ and/or $\mathbf{R^{g4}}$ selected from among C_{1-6}alkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, azetidinyl, pyrrolidinyl, tetrahydropyranyl, 1-aza-bicyclo[2.2.2]octyl, 8-methyl-8-aza-bicyclo[3.2.1]octyl, morpholinyl, piperidinyl and piperazinyl;

each $\mathbf{R^{f4}}$ is independently selected from among $-OR^{g4}$, $-NR^{g4}R^{g4}$, halogen, $-C(O)R^{g4}$, $-C(O)NR^{g4}R^{g4}$ and

each $\mathbf{R^{g4}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, phenyl and 5- to 6-membered heteroaryl.

29. Compounds according to one of claims 23 to 26, wherein

$\mathbf{R^{c4}}$ is selected from among methyl, methoxyethyl, *N,N*-dimethyl-ethyl, *N,N*-dimethyl-propyl,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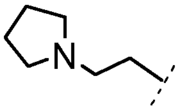
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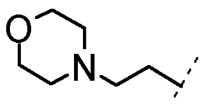
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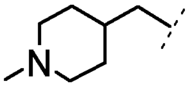
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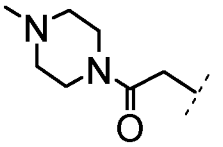
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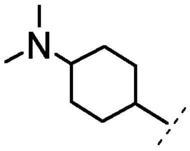
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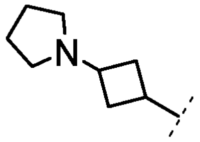
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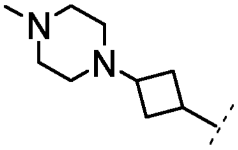
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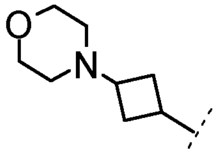
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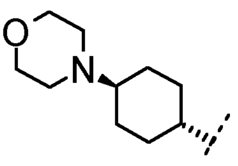
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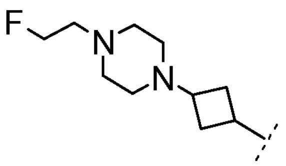
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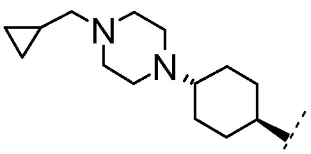
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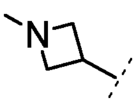
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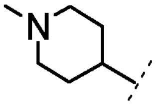
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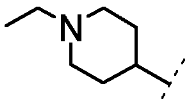
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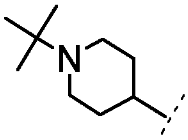
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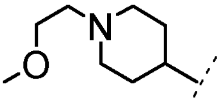
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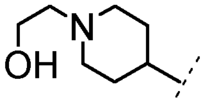
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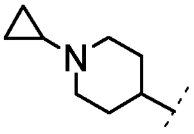
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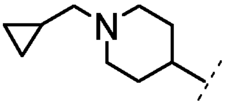
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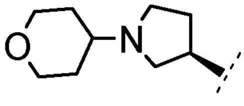
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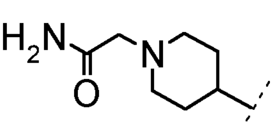
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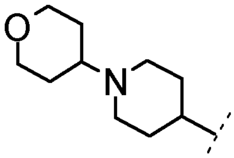
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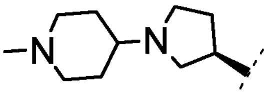
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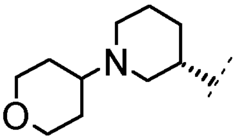
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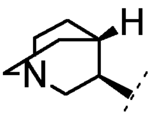
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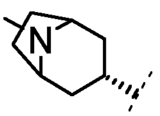
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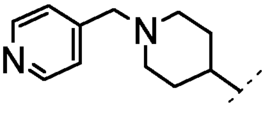
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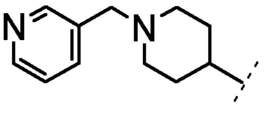
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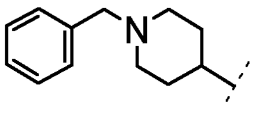
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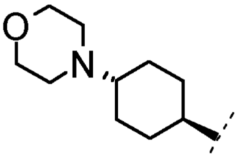
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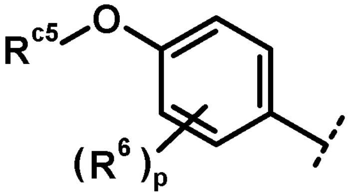
30. Compounds according to one of claims 1 to 14, wherein

$\mathbf{R}^3$ denotes a group



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each $\mathbf{R}^6$ is independently selected from among C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen;

p denotes 0, 1 or 2;

R^{c5} denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}** selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

each **R^{d5}** is independently selected from among $-OR^{e5}$, $-SR^{e5}$, $-NR^{e5}R^{e5}$, halogen, -CN, $-NO_2$, $-C(O)R^{e5}$, $-C(O)OR^{e5}$, $-C(O)NR^{e5}R^{e5}$, $-C(NR^{h5})NR^{e5}R^{e5}$, $-OC(O)R^{e5}$, $-OC(O)OR^{e5}$, $-S(O)_2R^{e5}$, $-S(O)_2NR^{e5}R^{e5}$, $-NR^{h5}C(O)R^{e5}$, $-NR^{h5}C(O)OR^{e5}$, $-NR^{h5}C(O)NR^{e5}R^{e5}$, $-NR^{h5}C(NR^{h5})NR^{e5}R^{e5}$ and $-NR^{h5}S(O)_2R^{e5}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{e5}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f5}** and/or **R^{g5}** selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

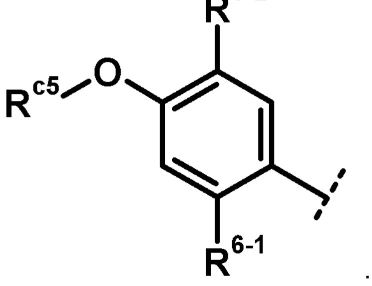
each **R^{f5}** is independently selected from among $-OR^{g5}$, $-SR^{g5}$, $-NR^{g5}R^{g5}$, halogen, -CN, $-NO_2$, $-C(O)R^{g5}$, $-C(O)OR^{g5}$, $-C(O)NR^{g5}R^{g5}$, $-C(NR^{h5})NR^{g5}R^{g5}$, $-OC(O)R^{g5}$, $-OC(O)OR^{g5}$, $-S(O)_2R^{g5}$, $-S(O)_2NR^{g5}R^{g5}$, $-NR^{h5}C(O)R^{g5}$, $-NR^{h5}C(O)OR^{g5}$, $-NR^{h5}C(O)NR^{g5}R^{g5}$, $-NR^{h5}C(NR^{h5})NR^{g5}R^{g5}$ and $-NR^{h5}S(O)_2R^{g5}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each **R^{g5}** is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkylalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl and

each **R^{h5}** is independently selected from among hydrogen and C_{1-4}alkyl.

31. Compounds according to one of claims 1 to 14, wherein

R^3 denotes a group



;

R^{6-1} and **R^{6-2}** are each independently selected from among hydrogen, C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen and

R^{c5} is defined as in claim 30.

32. Compounds according to one of claims 30 or 31, wherein

R^{c5} denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}** selected from among C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl;

each **R^{d5}** is independently selected from among -OR^{e5}, -$NR^{e5}R^{e5}$, halogen, -C(O)R^{e5} and -C(O)$NR^{e5}R^{e5}$ and

each **R^{e5}** is independently selected from among hydrogen, C_{1-6}alkyl, C_{3-10}cycloalkyl and 3- to 14-membered heterocyclyl.

33. Compounds according to one of claims 30 or 31, wherein

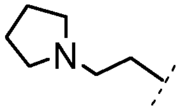
R^{c5} denotes a group optionally substituted by one or more identical or different **R^{d5}** and/or **R^{e5}** selected from among C_{1-6}alkyl and 5- to 6-membered, nitrogen-containing heterocyclyl;

each **R^{d5}** is independently selected from among -OR^{e5}, -$NR^{e5}R^{e5}$, halogen, -C(O)R^{e5} and -C(O)$NR^{e5}R^{e5}$ and

each **R^{e5}** is independently selected from among C_{1-6}alkyl and 5- to 6-membered, nitrogen-containing heterocyclyl.

34. Compounds according to one of claims 30 or 31, wherein

R^{c5} is selected from among *N*,*N*-dimethylethyl, *N*,*N*-dimethyl-propyl,

,


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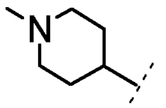

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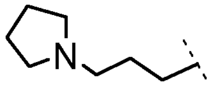
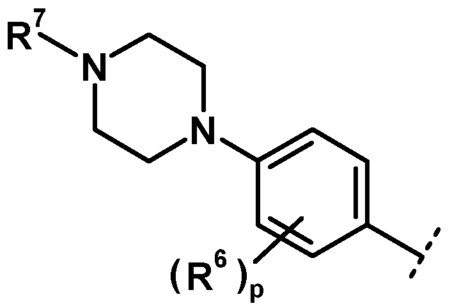


.

35. Compounds according to one of claims 1 to 14, wherein

R^3 denotes a group



;

each $\mathbf{R^6}$ is independently selected from among C_{1-4}alkyl, -O-C_{1-4}alkyl and halogen;

R^7 is selected from among $\mathbf{R^{b6}}$ and $\mathbf{R^{c6}}$;

p denotes 0, 1 or 2;

$\mathbf{R^{b6}}$ is selected from among -C(O)R^{c6}, -C(O)OR^{c6}, -C(O)N$R^{c6}R^{c6}$, -S(O)$_2R^{c6}$ and -S(O)$_2$N$R^{c6}R^{c6}$;

each $\mathbf{R^{c6}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d6}}$ and/or $\mathbf{R^{e6}}$, selected from among C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl;

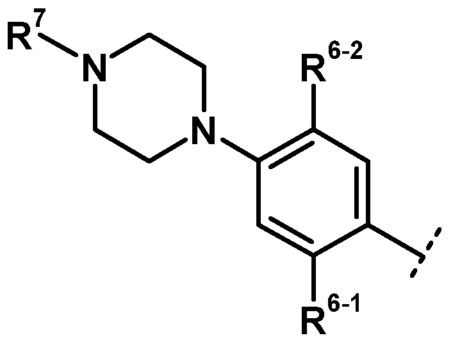
each $\mathbf{R^{d6}}$ is independently selected from among -OR^{e6}, -SR^{e6}, -N$R^{e6}R^{e6}$, halogen, -CN, -NO$_2$, -C(O)R^{e6}, -C(O)OR^{e6}, -C(O)N$R^{e6}R^{e6}$, -C(NR^{h6})N$R^{e6}R^{e6}$, -OC(O)R^{e6}, -OC(O)OR^{e6}, -S(O)$_2R^{e6}$, -S(O)$_2$N$R^{e6}R^{e6}$, -NR^{h6}C(O)R^{e6}, -NR^{h6}C(O)OR^{e6}, -NR^{h6}C(O)N$R^{e6}R^{e6}$, -NR^{h6}C(NR^{h6})N$R^{e6}R^{e6}$ and -NR^{h6}S(O)$_2R^{e6}$, as well as the bivalent substituent =O, while the latter may only be a substituent in non-aromatic ring systems;

each $\mathbf{R^{e6}}$ is independently selected from among hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{4-10}cycloalkenyl, C_{6-10}aryl, 5-12 membered heteroaryl and 3- to 14-membered heterocyclyl, and

each $\mathbf{R^{h6}}$ is independently selected from among hydrogen and C_{1-4}alkyl.

36. Compounds according to one of claims 1 to 14, wherein

R^3 denotes a group



;

$R^{6\text{-}1}$ and $R^{6\text{-}2}$ are independently selected from among hydrogen, $C_{1\text{-}4}$alkyl, -O-$C_{1\text{-}4}$alkyl and halogen and

R^7 is defined as in claim 35.

37. Compounds according to one of claims 35 or 36, wherein

R^7 is selected from among $\mathbf{R^{b6}}$ and $\mathbf{R^{c6}}$;

$\mathbf{R^{b6}}$ is selected from among -C(O)R^{c6}, -C(O)N$R^{c6}R^{c6}$ and -S(O)$_2R^{c6}$;

each $\mathbf{R^{c6}}$ independently denotes hydrogen or a group optionally substituted by one or more identical or different $\mathbf{R^{d6}}$ and/or $\mathbf{R^{e6}}$, selected from among $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl and 5- to 6-membered heterocyclyl;

each $\mathbf{R^{d6}}$ is independently selected from among -OR^{e6}, -N$R^{e6}R^{e6}$, halogen, -C(O)R^{e6} and -C(O)N$R^{e6}R^{e6}$ and

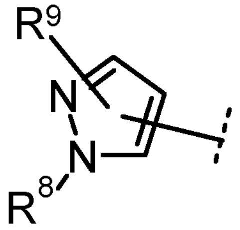
each $\mathbf{R^{e6}}$ is independently selected from among hydrogen, $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl and 5- to 6-membered heterocyclyl.

38. Compounds according to one of claims 1 to 14, wherein

R^3 denotes pyrazolyl, which is optionally mono- or disubstituted by $C_{1\text{-}4}$alkyl or $C_{3\text{-}5}$cycloalkyl.

39. Compounds according to one of claims 1 to 14, wherein

R^3 denotes a group



;

R^8 denotes a group optionally substituted by one or more identical or different **R^{b7}** and/or **R^{c7}**, selected from among $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl and 5- to 7-membered heterocyclyl;

each **R^{b7}** is independently selected from among $-OR^{c7}$, $-NR^{c7}R^{c7}$, halogen, $-C(O)R^{c7}$ and $-C(O)NR^{c7}R^{c7}$;

each **R^{c7}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{d7}** and/or **R^{e7}**, selected from among $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl, 5- to 6-membered heteroaryl and 5- to 7-membered heterocyclyl;

each **R^{d7}** is independently selected from among $-OR^{e7}$, $-NR^{e7}R^{e7}$, halogen, $-C(O)R^{e7}$ and $-C(O)NR^{e7}R^{e7}$;

each **R^{e7}** independently denotes hydrogen or a group optionally substituted by one or more identical or different **R^{f7}** and/or **R^{g7}**, selected from among $C_{1\text{-}6}$alkyl, $C_{3\text{-}6}$cycloalkyl, 5- to 6-membered heteroaryl and 5- to 7-membered heterocyclyl;

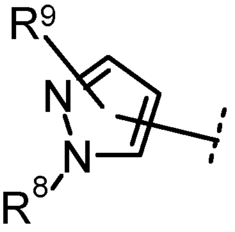
each **R^{f7}** is independently selected from among $-OR^{g7}$, $-NR^{g7}R^{g7}$, halogen, $-C(O)R^{g7}$ and $-C(O)NR^{g7}R^{g7}$;

each **R^{g7}** independently denotes hydrogen or $C_{1\text{-}6}$alkyl;

R^9 is selected from among hydrogen, $C_{1\text{-}4}$alkyl and $C_{3\text{-}5}$cycloalkyl.

40. Compounds according to one of claims 1 to 14, wherein

R^3 denotes a group



;

R^8 is selected from among $C_{1\text{-}4}$alkyl, $C_{3\text{-}5}$cycloalkyl, $C_{1\text{-}4}$alkoxy-$C_{1\text{-}4}$alkyl, ($C_{1\text{-}4}$alkyl)NH-$C_{1\text{-}4}$alkyl and ($C_{1\text{-}4}$alkyl)$_2$N-$C_{1\text{-}4}$alkyl;

R^9 is selected from among hydrogen, $C_{1\text{-}4}$alkyl and $C_{3\text{-}5}$cycloalkyl.

41. Compounds according to claim 1

I-168	(5S)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-194	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-201	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-204	N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-222	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-271	(5S)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-225	N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-9-[(3-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine
I-205	1-[4-[4-[[9-[4-(difluoromethoxy)phenyl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]pyrazol-1-yl]piperidin-1-yl]ethanone;
I-198	N-[1-[2-[2-methoxyethyl(methyl)amino]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-197	8-methyl-9-phenyl-N-[1-(2-pyrrolidin-1-ylethyl)pyrazol-3-yl]-5,6-

	dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-195	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-(naphthalen-1-ylmethyl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-193	9-[(2-chlorophenyl)methyl]-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-189	N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-9-(3-methylthiophen-2-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-187	N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-9-[(2-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-186	1-[4-[4-[(5,8-dimethyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl)amino]pyrazol-1-yl]piperidin-1-yl]ethanone;
I-185	8-methyl-N-[1-[2-(4-methylpiperazin-1-yl)ethyl]pyrazol-3-yl]-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-171	9-(4-chlorophenyl)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-166	2-[4-[2-[3-[(8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl)amino]pyrazol-1-yl]ethyl]piperazin-1-yl]ethanol;
I-167	N-[1-[2-[4-(2-methoxyethyl)piperazin-1-yl]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-217	9-[(3-methoxyphenyl)methyl]-8-methyl-N-(1-methylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-210	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-208	9-benzyl-N-[1-(2-dimethylaminoethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-192	9-[(2-chlorophenyl)methyl]-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-182	8-methyl-9-phenyl-N-[1-(2-piperazin-1-ylethyl)pyrazol-3-yl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-180	9-(3-chlorothiophen-2-yl)-N-[1-(2-methoxyethyl)pyrazol-3-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-176	1-[4-[4-[[9-(4-methoxyphenyl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]pyrazol-1-yl]piperidin-1-yl]ethanone;

I-175	N-[1-[2-[4-(dimethylamino)piperidin-1-yl]ethyl]pyrazol-3-yl]-8-methyl-9-phenyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-181	9-(3-chlorothiophen-2-yl)-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-202	9-[(2-chlorophenyl)methyl]-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-224	N-(1-ethylpyrazol-3-yl)-8-methyl-9-[(3-methylphenyl)methyl]-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-237	9-[4-(difluoromethoxy)phenyl]-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-236	9-[4-(difluoromethoxy)phenyl]-N-[1-(2-dimethylaminoethyl)pyrazol-4-yl]-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-30	9-(2-chlorophenyl)-N-(1-ethylpyrazol-3-yl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-112	4-[[9-(2-chlorophenyl)-8-methyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]-3-methoxy-N-(1-methylpiperidin-4-yl)benzamide;
I-40	9-(2-chlorophenyl)-5,8-dimethyl-N-(1-propane-2-ylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-42	9-(2-chlorophenyl)-5,8-dimethyl-N-(1-methylpyrazol-3-yl)-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-97	9-(2-chlorophenyl)-N-[2-methoxy-4-(4-methylpiperazin-1-yl)phenyl]-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-amine;
I-157	4-[[9-(2-chlorophenyl)-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]-3-methoxy-N-(1-methylpiperidin-4-yl)benzamide;
II-8	4-[[9-(2-chlorophenyl)-5,8-dimethyl-5,6-dihydropyrazolo[3,4-h]quinazolin-2-yl]amino]-3-methoxybenzoic acid;

42. Compounds of general formula **(I)** according to one of claims 1 to 41 – or the pharmaceutically acceptable salts thereof – as medicaments.

43. Compounds of general formula **(I)** according to one of claims 1 to 41 – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer, infections, inflammations and autoimmune diseases.

44. Compounds of general formula **(I)** according to one of claims 1 to 41 – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer.

45. Compounds of general formula **(I)** according to one of claims 1 to 41 – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of non-small cell lung cancers (NSCLC) and hepatocellular carcinomas (HCC).

46. Method for the treatment and/or prevention of cancer comprising administering a therapeutically effective amount of a compound of general formula **(I)** according to one of claims 1 to 41 – or one of the pharmaceutically acceptable salts thereof – to a human.

47. Pharmaceutical preparation containing as active substance one or more compounds of general formula **(I)** according to one of claims 1 to 41 – or the pharmaceutically acceptable salts thereof – optionally in combination with conventional excipients and/or carriers.

48. Pharmaceutical preparation comprising a compound of general formula **(I)** according to one of claims 1 to 41 – or one of the pharmaceutically acceptable salts thereof – and at least one other cytostatic or cytotoxic active substance different from formula **(I)**.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2011/062683

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D487/04 C07D493/14 C07D495/14 C07D498/14 A61K31/517
A61P35/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/037843 A1 (VERTEX PHARMA [US]; JIMENEZ JUAN-MIGUEL [GB]; GREEN JEREMY [US]; GAO H) 28 April 2005 (2005-04-28) cited in the application claims 1,4, 24, 41, 63, 77, 81, 82 -----	1-48
A	WO 2004/104007 A1 (PHARMACIA ITALIA SPA [IT]; TRAQUANDI GABRIELLA [IT]; BRASCA MARIA GABR) 2 December 2004 (2004-12-02) claim 1 -----	1-48

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search 14 September 2011	Date of mailing of the international search report 21/09/2011
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Guazzelli, Giuditta

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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