

Non-steroidal progesterone receptor modulators

5 The present invention relates to non-steroidal progesterone receptor modulators, to a process for their preparation, to the use of the progesterone receptor modulators for producing medicaments, and to pharmaceutical compositions which comprise these compounds.

10 The steroid hormone progesterone controls in a decisive manner the reproductive process in the female body. Progesterone is secreted in large quantities during the cycle and pregnancy respectively by the ovary and the placenta. Progesterone in cooperation with oestrogens brings about cyclic changes in the uterine mucosa (endometrium) during the menstrual cycle. Elevated progesterone levels after ovulation influence the uterine mucosa to convert it into a state permitting nidation of an embryo
15 (blastocyst). During pregnancy, progesterone controls the relaxation of the myometrium and maintains the function of the decidual tissue.

It is further known that progesterone inhibits endometrial proliferation by suppressing oestrogen-mediated mitosis in uterine tissue (K. Chwalisz, R.M. Brenner, U. Fuhrmann,
20 H. Hess-Stumpp, W. Elger, Steroids 65, 2000, 741-751).

Progesterone and progesterone receptors are also known to play a significant part in pathophysiological processes. Progesterone receptors have been detected in the foci of endometriosis, but also in tumours of the uterus, of the breast and of the CNS. It is
25 further known that uterine leiomyomas grow progesterone-dependently.

The effects of progesterone in the tissues of the genital organs and in other tissues occur through interactions with progesterone receptors which are responsible for the cellular effects.

30

Progesterone receptor modulators are either pure agonists or inhibit the effect of progesterone partly or completely. Accordingly, substances are defined as pure agonists, partial agonists (SPRMs) and pure antagonists.

35 In accordance with ability of progesterone receptor modulators to influence the effect of the progesterone receptor, these compounds have a considerable potential as

therapeutic agents for gynaecological and oncological indications and for obstetrics and fertility control.

Pure progesterone receptor antagonists completely inhibit the effect of progesterone on the progesterone receptor. They have anti-ovulatory properties and the ability to inhibit oestrogen effects in the endometrium, as far as complete atrophy. They are therefore particularly suitable for intervening in the female reproductive process, e.g. post-ovulation, in order to prevent nidation, during pregnancy in order to increase the reactivity of the uterus to prostaglandins or oxytocin, or in order to achieve opening and softening ("ripening") of the cervix, and to induce a great readiness of myometrium to contract.

A beneficial effect on the pathological event is expected in foci of endometriosis and in tumour tissues which are equipped with progesterone receptors after administration of pure progesterone receptor antagonists. There might be particular advantages for influencing pathological states such as endometriosis or uterine leiomyomas if ovulation inhibition can additionally be achieved by the progesterone receptor antagonists. Ovulation inhibition also dispenses with some of the ovarian hormone production and thus the stimulating effect, deriving from this proportion, on the pathologically altered tissue.

The first progesterone receptor antagonist described, RU 486 (also mifepristone), was followed by a large number of analogues with progesterone receptor-antagonistic activity of varying strength. Whereas RU 486 shows an antiglucocorticoid effect in addition to the progesterone receptor-antagonistic effect, compounds synthesized later are notable in particular for a more selective effect as progesterone receptor antagonists.

Besides steroidal compounds such as onapristone or lilopristone, which are notable by comparison with RU 486 for a better dissociation of the progesterone receptor-antagonistic effect and the antiglucocorticoid effect, also known from the literature are various non-steroidal structures whose antagonistic effect on the progesterone receptor is being investigated [see, for example, S. A. Leonhardt and D. P. Edwards, *Exp. Biol. Med.* 227: 969-980 (2002) and R. Winneker, A. Fensome, J. E. Wrobel, Z. Zhang, P. Zhang, *Seminars in Reproductive Medicine*, Volume 23: 46-57 (2005)]. However, compounds disclosed to date have only moderate antagonistic activity compared with the known steroidal structures. The most effective non-steroidal compounds are

reported to have *in vitro* activities which are 10% of the activity of RU 486.

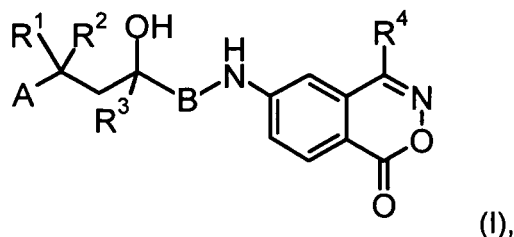
The antiglucocorticoid activity is disadvantageous for therapeutic use, where the inhibition of progesterone receptors is at the forefront of the therapy. An antiglucocorticoid activity causes unwanted side effects at the dosages necessary for therapy. This may prevent administration of a therapeutically worthwhile dose or lead to discontinuation of the treatment.

Partial or complete reduction of the antiglucocorticoid properties is therefore an important precondition for therapy with progesterone receptor antagonists, especially for those indications requiring treatment lasting weeks or months.

In contrast to the pure antagonists, partial progesterone receptor agonists (SPRMs) show a residual agonistic property which may vary in strength. This leads to these substances showing potentially agonistic effects on the progesterone receptor in certain organ systems (D. DeManno, W. Elger, R. Garg, R. Lee, B. Schneider, H. Hess-Stumpp, G. Schuber, K. Chwalisz, Steroids 68, 2003, 1019-1032). Such an organ-specific and dissociated effect may be of therapeutic benefit for the described indications.

It is therefore an object of the present invention to provide further non-steroidal progesterone receptor modulators. These compounds are intended to have a reduced antiglucocorticoid effect and therefore be suitable for the therapy and prophylaxis of gynaecological disorders such as endometriosis, leiomyomas of the uterus, dysfunctional bleeding and dysmenorrhoea. The compounds according to the invention are additionally intended to be suitable for the therapy and prophylaxis of hormone-dependent tumours, for example of breast, endometrial, ovarian and prostate carcinomas. The compounds are intended furthermore to be suitable for use in female fertility control and for female hormone replacement therapy.

The object is achieved according to the present invention by the provision of non-steroidal compounds of the general formula I



in which

R^1 and R^2 are independently of one another a hydrogen atom, a linear or nonlinear, branched or unbranched C_1 - C_5 -alkyl group, further forming together with the C atom of the chain a ring having a total of 3-7 members,

R^3 is a radical $C\equiv C-R^a$, where

R^a is a hydrogen or a C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl, C_2 - C_8 -alkynyl, C_3 - C_{10} -cycloalkyl, heterocycloalkyl optionally substituted one or more times, identically or differently, by K, or an aryl or heteroaryl optionally substituted one or more times, identically or differently by L,

K is a cyano, halogen, hydroxy, nitro, $-C(O)R^b$, CO_2R^b , $-O-R^b$, $-S-R^b$, $SO_2NR^cR^d$, $-C(O)-NR^cR^d$, $-OC(O)-NR^cR^d$, $-C=NOR^b$, $-NR^cR^d$ or C_3 - C_{10} -cycloalkyl, heterocycloalkyl optionally substituted one or more times, identically or differently, by M, or aryl or heteroaryl optionally substituted one or more times by L,

L is C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl, C_2 - C_8 -alkynyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -perfluoroalkoxy, C_1 - C_6 -alkoxy, C_1 - C_6 -alkoxy, $(CH_2)_p$ - C_3 - C_{10} -cycloalkyl, $(CH_2)_p$ -heterocycloalkyl, $(CH_2)_p$ CN, $(CH_2)_p$ Hal, $(CH_2)_p$ NO₂, $(CH_2)_p$ - C_6 - C_{12} -aryl, $(CH_2)_p$ -heteroaryl, $-(CH_2)_pPO_3(R^b)_2$,

$-(CH_2)_pNR^cR^d$, $-(CH_2)_pNR^eCOR^b$,
 $-(CH_2)_pNR^eCSR^b$, $-(CH_2)_pNR^eS(O)R^b$,
 $-(CH_2)_pNR^eS(O)_2R^b$, $-(CH_2)_pNR^eCONR^cR^d$,
 $-(CH_2)_pNR^eCOOR^b$, $-(CH_2)_pNR^eC(NH)NR^cR^d$,
 $-(CH_2)_pNR^eCSNR^cR^d$, $-(CH_2)_pNR^eS(O)NR^cR^d$,
 $-(CH_2)_pNR^eS(O)_2NR^cR^d$, $-(CH_2)_pCOR^b$,
 $-(CH_2)_pCSR^b$, $-(CH_2)_pS(O)R^b$,
 $-(CH_2)_pS(O)(NH)R^b$, $-(CH_2)_pS(O)_2R^b$,
 $-(CH_2)_pS(O)_2NR^cR^d$, $-(CH_2)_pSO_2OR^b$,
 $-(CH_2)_pCO_2R^b$, $-(CH_2)_pCONR^cR^d$,
 $-(CH_2)_pCSNR^cR^d$, $-(CH_2)_pOR^b$, $-(CH_2)_pSR^b$,

- 5
- M
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- $-(CH_2)_pCR^b(OH)-R^e$, $-(CH_2)_p-C=NOR^b$,
 $-O-(CH_2)_n-O-$, $-O-(CH_2)_n-CH_2-$, $-O-CH=CH-$ or
 $-(CH_2)_{n+2}-$, where n is 1 or 2, and the terminal
oxygen atoms and/or carbon atoms are linked
to directly adjacent ring carbon atoms,
is C_1-C_6 -alkyl or a group $-COR^b$, CO_2R^b , $-O-R^b$,
or $-NR^cR^d$, where

 R^b is a hydrogen or a C_1-C_6 -alkyl, C_2-C_8 -
alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -
cycloalkyl, C_6-C_{12} -aryl or C_1-C_3 -
perfluoroalkyl and
 R^c and R^d are independently of one another a
hydrogen, C_1-C_6 -alkyl, C_2-C_8 -alkenyl,
 C_2-C_8 -alkynyl, C_3-C_{10} -cycloalkyl,
 C_6-C_{12} -aryl, $C(O)R^b$ or a hydroxy
group, where if
 R^c is a hydroxy group, then R^d can only
be a hydrogen, a C_1-C_6 -alkyl, C_2-C_8 -
alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -
cycloalkyl or C_6-C_{12} -aryl and vice
versa, and
 R^e is a hydrogen, C_1-C_6 -alkyl, C_2-C_8 -
alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -cyclo-
alkyl or C_6-C_{12} -aryl, and
p can be a number from 0-6,

or
 R^3 is a radical $C=C-R^gR^h$, where
 R^g and R^h are independently of one another a hydrogen or a
 C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkynyl
optionally substituted one or more times, identically
or differently, by X, in which
X is a cyano, halogen, hydroxy, nitro,
 $-C(O)R^b$, CO_2R^b , $-O-R^b$, $-C(O)-NR^cR^d$,
 $-NR^cR^d$ with the meanings already

mentioned before for R^b , R^c and R^d , and

- R^4 is a hydrogen atom, a methyl or an ethyl group or a partly or completely fluorinated C_1 - C_3 -alkyl group,
- 5 A is a mono- or bicyclic carbocyclic or heterocyclic aromatic ring which may optionally be substituted one or more times by C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl, C_2 - C_8 -alkynyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -perfluoroalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, $(CH_2)_p$ - C_3 - C_{10} -cycloalkyl, $(CH_2)_p$ -heterocycloalkyl, $(CH_2)_p$ CN, $(CH_2)_p$ Hal, $(CH_2)_p$ NO₂,
 10 $(CH_2)_p$ - C_6 - C_{12} -aryl, $(CH_2)_p$ -heteroaryl,
 $-(CH_2)_p$ PO₃(R^b)₂, $-(CH_2)_p$ NR^c R^d , $-(CH_2)_p$ NR^eCOR^b, $-(CH_2)_p$ NR^eCSR^b,
 $-(CH_2)_p$ NR^eS(O) R^b , $-(CH_2)_p$ NR^eS(O)₂ R^b , $-(CH_2)_p$ NR^eCONR^c R^d ,
 $-(CH_2)_p$ NR^eCOOR^b, $-(CH_2)_p$ NR^eC(NH)NR^c R^d , $-(CH_2)_p$ NR^eCSNR^c R^d ,
 $-(CH_2)_p$ NR^eS(O)NR^c R^d , $-(CH_2)_p$ NR^eS(O)₂NR^c R^d , $-(CH_2)_p$ COR^b,
 15 $-(CH_2)_p$ CSR^b, $-(CH_2)_p$ S(O) R^b , $-(CH_2)_p$ S(O)(NH) R^b , $-(CH_2)_p$ S(O)₂ R^b ,
 $-(CH_2)_p$ S(O)₂NR^c R^d , $-(CH_2)_p$ SO₂OR^b, $-(CH_2)_p$ CO₂ R^b , $-(CH_2)_p$ CONR^c R^d ,
 $-(CH_2)_p$ CSNR^c R^d , $-(CH_2)_p$ OR^b, $-(CH_2)_p$ SR^b, $-(CH_2)_p$ CR^b(OH)- R^d ,
 $-(CH_2)_p$ -C=NOR^b, -O-(CH₂)_n-O-, -O-(CH₂)_n-CH₂-, -O-CH=CH- or
 $-(CH_2)_{n+2}$ -, where n is 1 or 2, and the terminal oxygen atoms and/or
 20 carbon atoms are linked to directly adjacent ring carbon atoms, or
- A is a radical -CO₂ R^b , C(O)NR^c R^d , COR^b,
- or
- 25 A is an alkenyl group -CR⁵=CR⁶ R^7 , where
 R^5 , R^6 and R^7 are identical or different and are independently of
 one another hydrogen atoms, halogen atoms, aryl
 radicals or an unsubstituted or partly or completely
 30 fluorinated C_1 - C_5 -alkyl group, or
- A is an alkynyl group -C≡CR⁵, with the meaning stated above for R^5 , and
- B is a carbonyl or a CH₂ group,
- 35 and their pharmaceutically acceptable salts.

The compounds according to the invention of the general formula I may, owing to the presence of centres of asymmetry, exist as different stereoisomers. Both the racemates and the separate stereoisomers belong to the subject matter of the present invention.

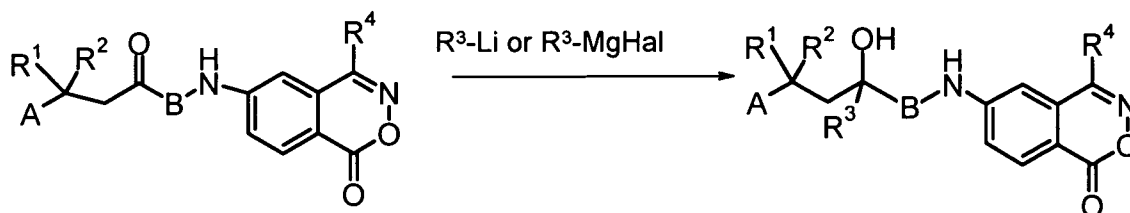
- 5 The present invention further includes the novel compounds as active pharmaceutical ingredients, the preparation thereof, their therapeutic use and pharmaceutical dosage forms which comprise the novel substances.

10 The compounds according to the invention of the general formula (I) or their pharmaceutically acceptable salts can be used to produce a medicament, in particular for the treatment and prophylaxis of gynaecological disorders such as endometriosis, leiomyomas of the uterus, dysfunctional bleeding and dysmenorrhoea. The compounds according to the invention may further be used for the treatment and prophylaxis of hormone-dependent tumours such as, for example, for breast, prostate and endometrial carcinoma.

15 The compounds according to the invention of the general formula (I) or their pharmaceutically acceptable salts are suitable for use for female fertility control or for female hormone replacement therapy.

20 The present invention additionally relates to a process for preparing the compounds of the general formula (I). The substituent R^3 is introduced by selective addition reaction of organometallic compounds such as lithium alkynyls or magnesium haloalkynyls onto a keto group. This leads either directly or after carrying out further modifications to the compounds according to the invention of the general formula (I).

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30 The compounds according to the invention are prepared by selective addition of organometallic compounds onto keto amides which have been described for example in the published specifications US 2002/0077356, US 6,323,199B1, WO 200375915 and WO 9854159. The organometallic compounds may be for example lithium alkynyl or magnesium haloalkynyl compounds. These are generated for example by reacting the appropriate alkynes with butyllithium or Grignard compounds. The corresponding

- organometallic alkenyl compounds can also be prepared in analogy thereto. The reactivity of the keto groups is in this case distinctly higher by comparison with the amide carbonyl and with the benzoxazinone, so that a selective addition is achieved on suitable choice of the reaction conditions. Alternatively, the alkynyl or alkenyl radicals introduced as R^3 can also be further modified later. Reactions suitable for these modifications are those known to the skilled person, such as oxidation, reduction, substitution, alkylation, palladium-catalysed reaction. Any protective groups present are eliminated at a suitable time.
- 10 The non-steroidal compounds according to the invention of the general formula I have strong antagonistic or strong partial agonistic effects on the progesterone receptor. They show a strong dissociation of effects in relation to their strength of binding to the progesterone receptor and to the glucocorticoid receptor. Whereas known progesterone receptor antagonists such as mifepristone (RU 486) show, besides the desired high
- 15 binding affinity for the progesterone receptor, likewise a high affinity for the glucocorticoid receptor, the compounds according to the invention are notable for a very low glucocorticoid receptor binding with simultaneously a high progesterone receptor affinity.
- 20 The substituents, defined as groups, of the compounds according to the invention of the general formula I may in each case have the following meanings:
- C_1-C_5 -, C_1-C_6 - and C_1-C_8 -alkyl group means linear or nonlinear, branched or unbranched alkyl radicals. Examples thereof are a methyl, ethyl, n-propyl, isopropyl, n-,
- 25 iso-, tert-butyl, an n-pentyl, 2,2-dimethylpropyl, 3-methylbutyl, hexyl, heptyl or octyl group.
- Preferred in the meaning of R^a in this connection are the methyl, ethyl, n-propyl or n-butyl group and an n-pentyl group.
- Preferred in the meaning of R^1 and R^2 are methyl or ethyl.
- 30 Alkenyl means linear or nonlinear, branched or unbranched alkenyl radicals. Examples of the meaning of a C_2-C_8 -alkenyl group in the context of the invention are the following: vinyl, allyl, 3-buten-1-yl or 2,3-dimethyl-2-propenyl. If the aromatic system A is substituted by a C_2-C_8 -alkenyl radical, it is preferably a vinyl group.
- 35 Alkynyl means linear or nonlinear, branched or unbranched alkynyl radicals. A C_2-C_8 -

alkynyl radical is intended to be for example an ethynyl, propynyl, butynyl, pentynyl, hexynyl and octynyl group, preferably an ethynyl or propynyl group.

5 Examples which may be mentioned of C₃-C₁₀-cycloalkyl are cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. Cyclopropyl, cyclopentyl and cyclohexyl are preferred.

10 Heterocycloalkyl in the meaning of R^a, K and L means 3-8-membered heterocycloalkyl radicals. Examples of heterocycloalkyl are morpholiny, tetrahydrofuranyl, pyranly, piperaziny, piperidiny, pyrrolidiny, oxirany, oxetany, aziridiny, dioxolany and dioxany. In this connection, the position of the heteroatom in relation to the point of linkage can be any chemically possible position.

15 Possible examples of C₁-C₆-alkoxyl-C₁-C₆-alkoxy group are methoxymethoxy, ethoxymethoxy or 2-methoxyethoxy.

A radical OR^b in the context of the invention is a hydroxy, methoxy, ethoxy, n-propoxy, isopropoxy, n-, iso-, tert-butoxy or n-pentoxy, 2,2-dimethylpropoxy or 3-methylbutoxy group. Hydroxy, methoxy and ethoxy are preferred.

20 Suitable for a partly or completely fluorinated C₁-C₅-alkyl group are the perfluorinated alkyl groups above. Of these, preference is given in particular to the trifluoromethyl or pentafluoroethyl group and, partly fluorinated alkyl groups, for example the 5,5,5,4,4-pentafluoropentyl or 5,5,5,4,4,3,3-heptafluoropentyl group.

25 A halogen atom may be a fluorine, chlorine, bromine or iodine atom. Fluorine, chlorine or bromine is preferred here.

30 If R¹ and R² form together with the C atom of the chain a 3-7 membered ring, this is for example a cyclopropyl, -butyl, -pentyl or -hexyl ring. The cyclopropyl and the cyclopentyl ring are preferred.

The mono- or bicyclic carbocyclic aromatic ring A, which may be substituted more than once, is a carbocyclic or heterocyclic aryl radical.
In the former case it is for example a phenyl or naphthyl radical, preferably a phenyl radical.

35 It is possible to use as heterocyclic radical for example a monocyclic heterocyclic

radical, for example the thienyl, furyl, pyranlyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, thiazolyl, oxazolyl, furazanyl, pyrrolinyl, imidazolinyl, pyrazolinyl, thiazolinyl, triazolyl, tetrazolyl radical, in particular all the possible isomers in relation to the positions of the heteroatoms.

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R³ means in the case of an aryl radical an optionally substituted phenyl, 1- or 2-naphthyl radical, with preference for the phenyl radical. Examples of a heteroaryl radical are the 2-, 3- or 4-pyridinyl, the 2- or 3-furyl, the 2- or 3-thienyl, the 2- or 3-pyrrolyl, the 2-, 4- or 5-imidazolyl, the pyrazinyl, the 2-, 4- or 5-pyrimidinyl or 3- or 4-pyridazinyl radical.

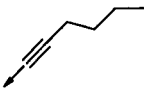
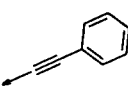
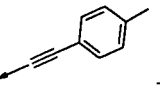
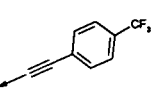
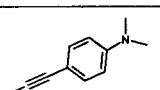
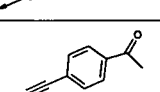
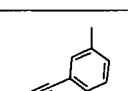
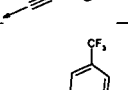
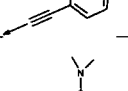
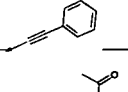
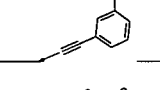
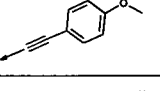
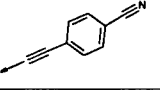
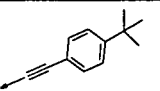
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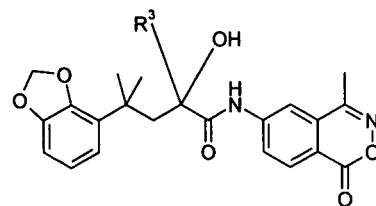
The number p for a (CH₂)_p radical may be a number from 0 to 6, preferably 0 to 2. "Radical" means according to the invention all functional groups stated in connection with (CH₂)_p.

15 In the case where the compounds of the general formula I (B = -CH₂-) are in the form of salts, this is possible for example in the form of the hydrochloride, sulphate, nitrate, tartrate, citrate, fumarate, succinate or benzoate.

20 If the compounds according to the invention are in the form of racemic mixtures, they can be fractionated by methods of racemate resolution familiar to the skilled person into the pure optically active forms. For example, the racemic mixtures can be separated into the pure isomers by chromatography on a support material which is itself optically active (CHIRALPAK AD[®]). It is also possible to esterify the free hydroxy group in a racemic compound of the general formula I with an optically active acid, and to separate
25 the resulting diastereoisomeric esters by fractional crystallization or chromatography and to hydrolyse the separated esters in each case to the optically pure isomers. It is possible to use as optically active acid for example mandelic acid, camphorsulphonic acid or tartaric acid.

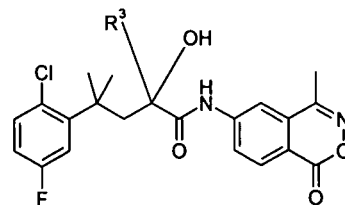
30 The compounds specified below, and the use thereof, are preferred according to the invention:

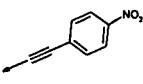
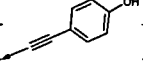
No.	Racemic or enantiomer	R3
1	rac	
2	-	
3	+	
4	rac	
5	+	
6	-	
7	rac	
8	+	
9	-	
10	rac	
11	+	
12	-	
13	rac	
14	+	
15	-	
16	rac	
17	+	
18	-	
19	rac	
20	+	
21	-	
22	rac	
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36	-	
37	rac	
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44	+	
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47	+	
48	-	

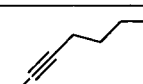
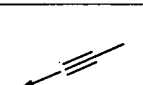
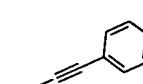
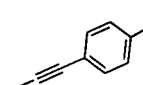
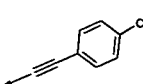
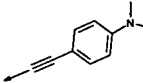
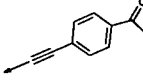
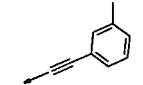
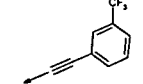
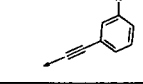
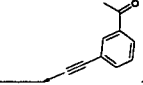
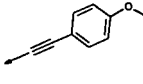


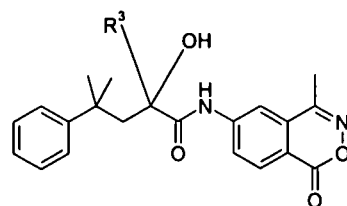
49	rac	
50	+	
51	-	

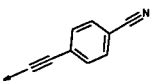
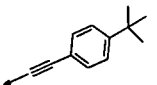
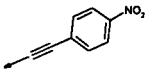
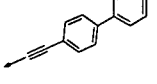
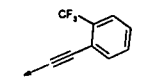
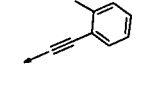
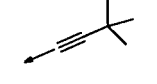
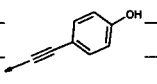
No.	Racemic or enantiomer	R3
52	rac	
53	-	
54	+	
55	rac	
56	+	
57	-	
58	rac	
59	+	
60	-	
61	rac	
62	+	
63	-	
64	rac	
65	+	
66	-	
67	rac	
68	+	
69	-	
70	rac	
71	+	
72	-	
73	rac	
74	+	
75	-	
76	rac	
77	+	
78	-	
79	rac	
80	+	
81	-	
82	rac	
83	+	
84	-	
85	rac	
86	+	
87	-	
88	rac	
89	+	
90	-	
91	rac	
92	+	
93	-	
94	rac	
95	+	
96	-	

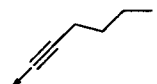
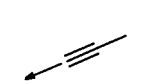
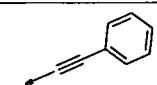
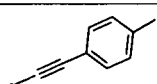
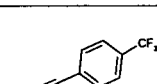
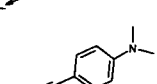
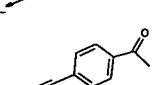


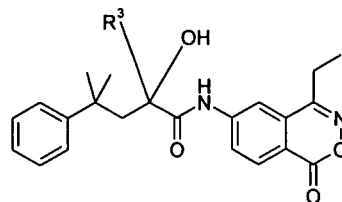
97	rac	
98	+	
99	-	
100	rac	
101	+	
102	-	
103	rac	
104	+	
105	-	

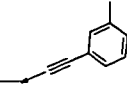
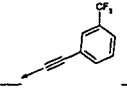
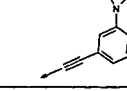
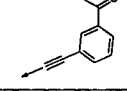
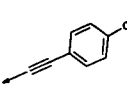
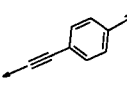
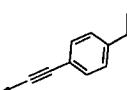
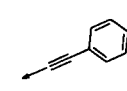
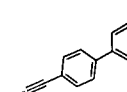
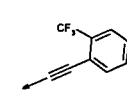
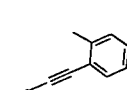
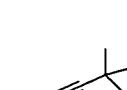
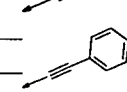
No.	Racemic or enantiomer	R3
106	rac	
107	-	
108	+	
109	rac	
110	+	
111	-	
112	rac	
113	+	
114	-	
115	rac	
116	+	
117	-	
118	rac	
119	+	
120	-	
121	rac	
122	+	
123	-	
124	rac	
125	+	
126	-	
127	rac	
128	+	
129	-	
130	rac	
131	+	
132	-	
133	rac	
134	+	
135	-	
136	rac	
137	+	
138	-	
139	rac	
140	+	
141	-	
142	rac	
143	+	
144	-	

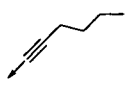
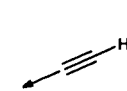


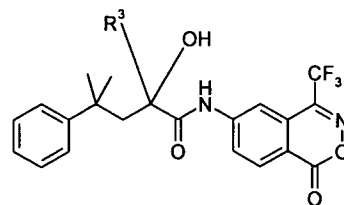
145	rac	
146	+	
147	-	
148	rac	
149	+	
150	-	
151	rac	
152	+	
153	-	
154	rac	
155	+	
156	-	
157	rac	
158	+	
159	-	
160	rac	
161	+	
162	-	
163	rac	
164	+	
165	-	
166	rac	
167	+	
168	-	

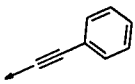
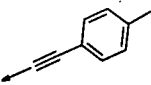
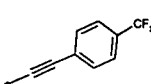
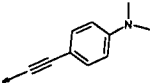
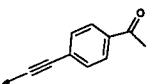
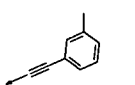
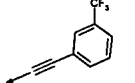
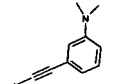
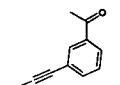
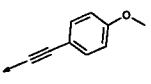
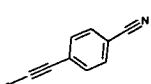
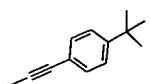
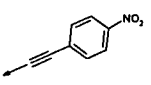
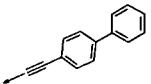
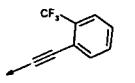
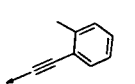
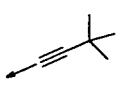
No.	Racemic or enantiomer	R3
169	rac	
170	-	
171	+	
172	rac	
173	+	
174	-	
175	rac	
176	+	
177	-	
178	rac	
179	+	
180	-	
181	rac	
182	+	
183	-	
184	rac	
185	+	
186	-	
187	rac	
188	+	
189	-	
190	rac	
191	+	
192	-	



193	rac	
194	+	
195	-	
196	rac	
197	+	
198	-	
199	rac	
200	+	
201	-	
202	rac	
203	+	
204	-	
205	rac	
206	+	
207	-	
208	rac	
209	+	
210	-	
211	rac	
212	+	
213	-	
214	rac	
215	+	
216	-	
217	rac	
218	+	
219	-	
220	rac	
221	+	
222	-	
223	rac	
224	+	
225	-	
226	rac	
227	+	
228	-	
229	rac	
230	+	
231	-	

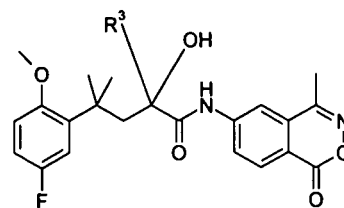
No.	Racemic or enantiomer	R3
232	rac	
233	-	
234	+	
235	rac	
236	+	
237	-	
238	rac	
239	+	
240	-	

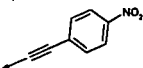
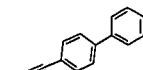
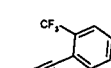
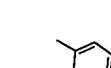


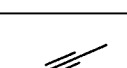
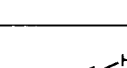
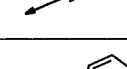
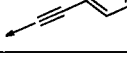
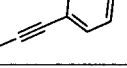
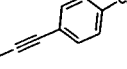
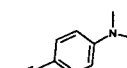
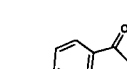
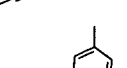
241	rac	
242	+	
243	-	
244	rac	
245	+	
246	-	
247	rac	
248	+	
249	-	
250	rac	
251	+	
252	-	
253	rac	
254	+	
255	-	
256	rac	
257	+	
258	-	
259	rac	
260	+	
261	-	
262	rac	
263	+	
264	-	
265	rac	
266	+	
267	-	
268	rac	
269	+	
270	-	
271	rac	
272	+	
273	-	
274	rac	
275	+	
276	-	
277	rac	
278	+	
279	-	
280	rac	
281	+	
282	-	
283	rac	
284	+	
285	-	
286	rac	
287	+	
288	-	
289	rac	
290	+	
291	-	

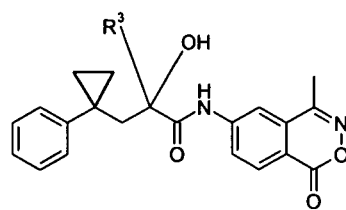
292	rac	
293	+	
294	-	

No.	Racemic or enantiomer	R3
295	rac	
296	-	
297	+	
298	rac	
299	+	
300	-	
301	rac	
302	+	
303	-	
304	rac	
305	+	
306	-	
307	rac	
308	+	
309	-	
310	rac	
311	+	
312	-	
313	rac	
314	+	
315	-	
316	rac	
317	+	
317	-	
319	rac	
320	+	
321	-	
322	rac	
323	+	
324	-	
325	rac	
326	+	
327	-	
328	rac	
329	+	
330	-	
331	rac	
332	+	
333	-	
334	rac	
335	+	
336	-	
337	rac	
338	+	
339	-	



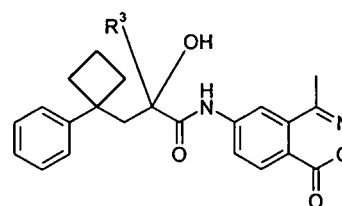
340	rac	
341	+	
342	-	
343	rac	
344	+	
345	-	
346	rac	
347	+	
348	-	
349	rac	
350	+	
351	-	
352	rac	
353	+	
354	-	
355	rac	
356	+	
357	-	

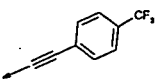
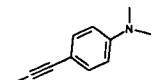
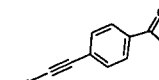
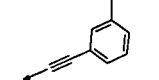
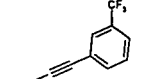
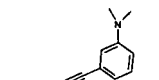
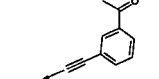
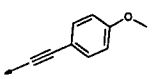
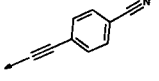
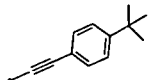
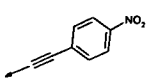
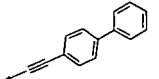
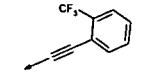
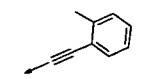
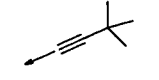
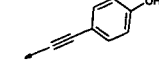
No.	Racemic or enantiomer	R3
358	rac	
359	-	
360	+	
361	rac	
362	+	
363	-	
364	rac	
365	+	
366	-	
367	rac	
368	+	
369	-	
370	rac	
371	+	
372	-	
373	rac	
374	+	
375	-	
376	rac	
377	+	
378	-	
379	rac	
380	+	
381	-	
382	rac	
383	+	
384	-	
385	rac	
386	+	
387	-	

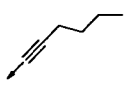
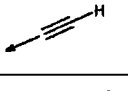
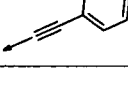
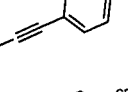
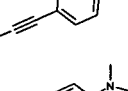
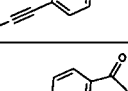
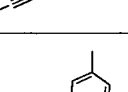
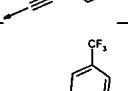
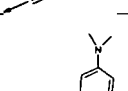
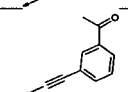
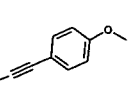
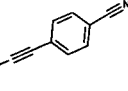


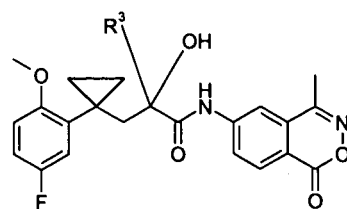
388	rac	
389	+	
390	-	
391	rac	
392	+	
393	-	
394	rac	
395	+	
396	-	
397	rac	
398	+	
399	-	
400	rac	
401	+	
402	-	
403	rac	
404	+	
405	-	
406	rac	
407	+	
408	-	
409	rac	
410	+	
411	-	
412	rac	
413	+	
414	-	
415	rac	
416	+	
417	-	
418	rac	
419	+	
420	-	

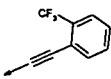
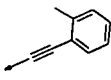
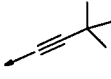
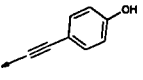
No.	Racemic or enantiomer	R3
421	rac	
422	-	
423	+	
424	rac	
425	+	
426	-	
427	rac	
428	+	
429	-	
430	rac	
431	+	
432	-	
433	rac	
434	+	
435	-	

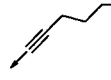
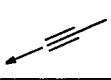
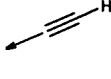
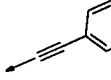
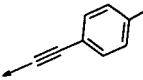
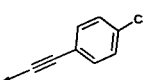
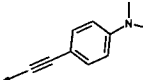
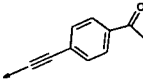
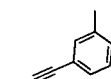
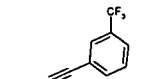
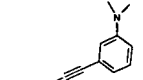
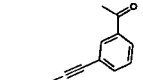


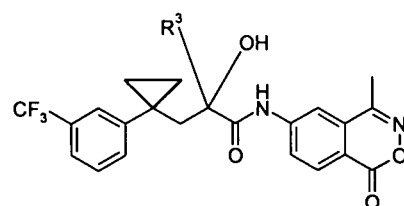
436	rac	
437	+	
438	-	
439	rac	
440	+	
441	-	
442	rac	
443	+	
444	-	
445	rac	
446	+	
447	-	
448	rac	
449	+	
450	-	
451	rac	
452	+	
453	-	
454	rac	
455	+	
456	-	
457	rac	
458	+	
459	-	
460	rac	
461	+	
462	-	
463	rac	
464	+	
465	-	
466	rac	
467	+	
468	-	
469	rac	
470	+	
471	-	
472	rac	
473	+	
474	-	
475	rac	
476	+	
477	-	
478	rac	
479	+	
480	-	
481	rac	
482	+	
483	-	

No.	Racemic or enantiomer	R3
484	rac	
485	-	
486	+	
487	rac	
488	+	
489	-	
490	rac	
491	+	
492	-	
493	rac	
494	+	
495	-	
496	rac	
497	+	
498	-	
499	rac	
500	+	
501	-	
502	rac	
503	+	
504	-	
505	rac	
506	+	
507	-	
508	rac	
509	+	
510	-	
511	rac	
512	+	
513	-	
514	rac	
515	+	
516	-	
517	rac	
518	+	
519	-	
520	rac	
521	+	
522	-	
523	rac	
524	+	
525	-	
526	rac	
527	+	
528	-	
529	rac	
530	+	
531	-	
532	rac	
533	+	
534	-	



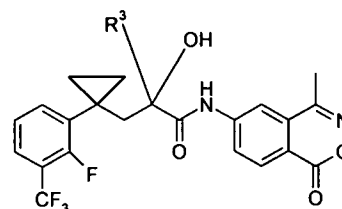
535	rac	
536	+	
537	-	
538	rac	
539	+	
540	-	
541	rac	
542	+	
543	-	
544	rac	
545	+	
546	-	

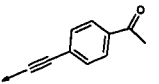
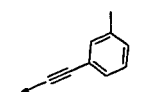
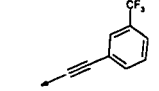
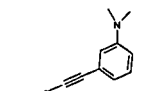
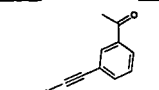
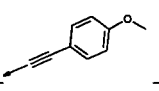
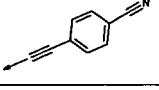
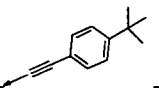
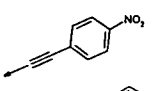
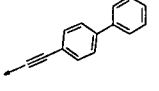
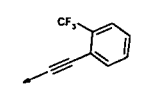
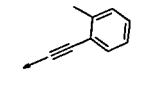
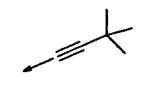
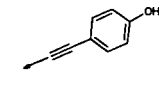
No.	Racemic or enantiomer	R3
547	rac	
548	-	
549	+	
550	rac	
551	+	
552	-	
553	rac	
554	+	
555	-	
556	rac	
557	+	
558	-	
559	rac	
560	+	
561	-	
562	rac	
563	+	
564	-	
565	rac	
566	+	
567	-	
568	rac	
569	+	
570	-	
571	rac	
572	+	
573	-	
574	rac	
575	+	
576	-	
577	rac	
578	+	
579	-	
580	rac	
581	+	
582	-	

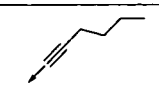


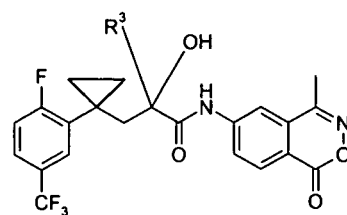
583	rac	
584	+	
585	-	
586	rac	
587	+	
588	-	
589	rac	
590	+	
591	-	
592	rac	
593	+	
594	-	
595	rac	
596	+	
597	-	
598	rac	
599	+	
600	-	
601	rac	
602	+	
603	-	
604	rac	
605	+	
606	-	
607	rac	
608	+	
609	-	

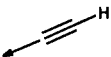
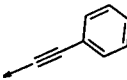
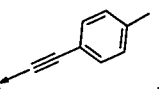
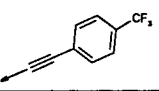
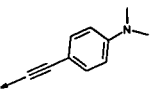
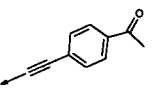
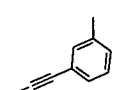
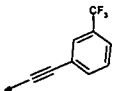
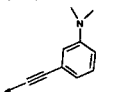
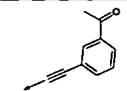
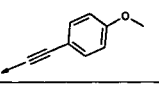
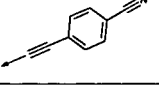
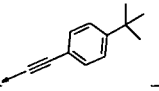
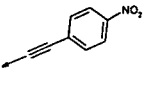
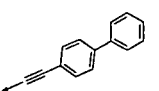
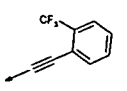
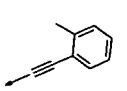
No.	Racemic or enantiomer	R3
610	rac	
611	-	
612	+	
613	rac	
614	+	
615	-	
616	rac	
617	+	
618	-	
619	rac	
620	+	
621	-	
622	rac	
623	+	
624	-	
625	rac	
626	+	
627	-	
628	rac	
629	+	
630	-	



631	rac	
632	+	
633	-	
634	rac	
635	+	
636	-	
637	rac	
638	+	
639	-	
640	rac	
641	+	
642	-	
643	rac	
644	+	
645	-	
646	rac	
647	+	
648	-	
649	rac	
650	+	
651	-	
652	rac	
653	+	
654	-	
655	rac	
656	+	
657	-	
658	rac	
659	+	
660	-	
661	rac	
662	+	
663	-	
664	rac	
665	+	
666	-	
667	rac	
668	+	
669	-	
670	rac	
671	+	
672	-	

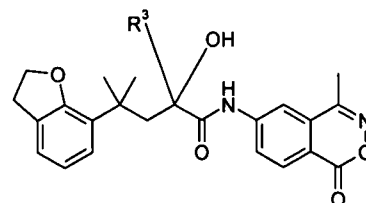
No.	Racemic or enantiomer	R3
673	rac	
674	-	
675	+	
676	rac	
677	+	
678	-	



679	rac	
680	+	
681	-	
682	rac	
683	+	
684	-	
685	rac	
686	+	
687	-	
688	rac	
689	+	
690	-	
691	rac	
692	+	
693	-	
694	rac	
695	+	
696	-	
697	rac	
698	+	
699	-	
700	rac	
701	+	
702	-	
703	rac	
704	+	
705	-	
706	rac	
707	+	
708	-	
709	rac	
710	+	
711	-	
712	rac	
713	+	
714	-	
715	rac	
716	+	
717	-	
718	rac	
719	+	
720	-	
721	rac	
722	+	
723	-	
724	rac	
725	+	
726	-	
727	rac	
728	+	
729	-	

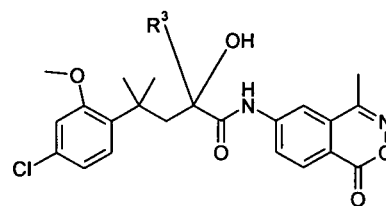
730	rac	
731	+	
732	-	
733	rac	
734	+	
735	-	

No.	Racemic or enantiomer	R3
736	rac	
737	-	
738	+	
739	rac	
740	+	
741	-	
742	rac	
743	+	
744	-	
745	rac	
746	+	
747	-	
748	rac	
749	+	
750	-	
751	rac	
752	+	
753	-	
754	rac	
755	+	
756	-	
757	rac	
758	+	
759	-	
760	rac	
761	+	
762	-	
763	rac	
764	+	
765	-	
766	rac	
767	+	
768	-	
769	rac	
770	+	
771	-	
772	rac	
773	+	
774	-	
775	rac	
776	+	
777	-	



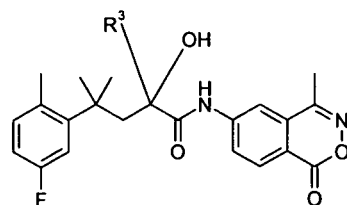
778	rac	
779	+	
780	-	
781	rac	
782	+	
783	-	
784	rac	
785	+	
786	-	
787	rac	
788	+	
789	-	
790	rac	
791	+	
792	-	
793	rac	
794	+	
795	-	
796	rac	
797	+	
798	-	

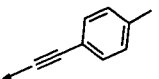
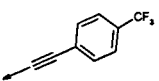
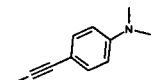
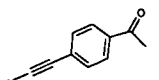
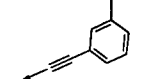
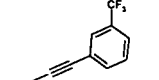
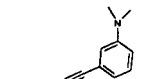
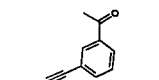
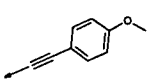
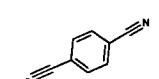
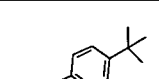
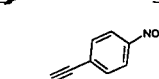
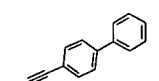
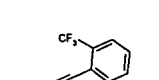
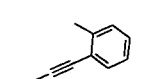
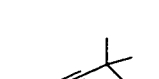
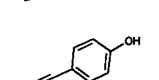
No.	Racemic or enantiomer	R3
799	rac	
800	-	
801	+	
802	rac	
803	+	
804	-	
805	rac	
806	+	
807	-	
808	rac	
809	+	
810	-	
811	rac	
812	+	
813	-	
814	rac	
815	+	
816	-	
817	rac	
818	+	
819	-	
820	rac	
821	+	
822	-	
823	rac	
824	+	
825	-	

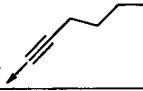
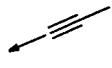
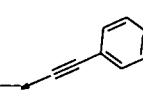
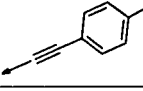
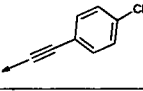
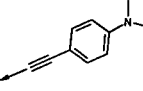
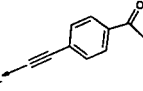
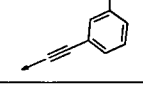
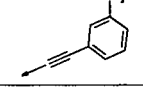
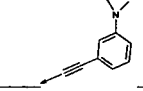
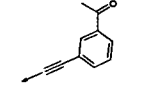
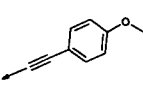
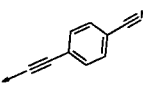
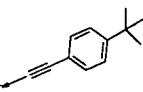
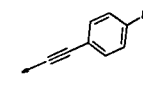


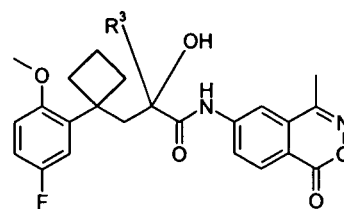
826	rac	
827	+	
828	-	
829	rac	
830	+	
831	-	
832	rac	
833	+	
834	-	
835	rac	
836	+	
837	-	
838	rac	
839	+	
840	-	
841	rac	
842	+	
843	-	
844	rac	
845	+	
846	-	
847	rac	
848	+	
849	-	
850	rac	
851	+	
852	-	
853	rac	
854	+	
855	-	
856	rac	
857	+	
858	-	
859	rac	
860	+	
861	-	

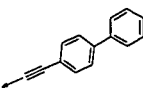
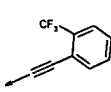
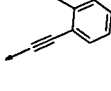
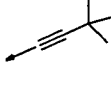
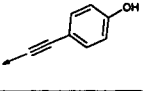
No.	Racemic or enantiomer	R3
862	rac	
863	-	
864	+	
865	rac	
866	+	
867	-	
868	rac	
869	+	
870	-	
871	rac	
872	+	
873	-	

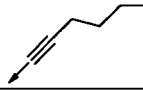
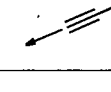
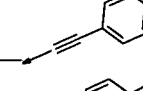
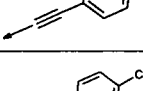
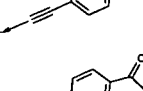
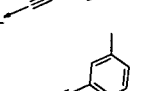
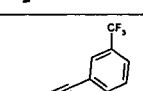
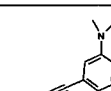


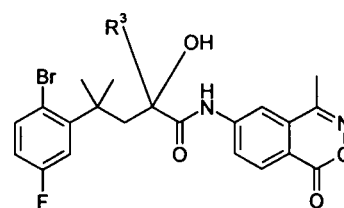
874	rac	
875	+	
876	-	
877	rac	
878	+	
879	-	
880	rac	
881	+	
882	-	
883	rac	
884	+	
885	-	
886	rac	
887	+	
888	-	
889	rac	
890	+	
891	-	
892	rac	
893	+	
894	-	
895	rac	
896	+	
897	-	
898	rac	
899	+	
900	-	
901	rac	
902	+	
903	-	
904	rac	
905	+	
906	-	
907	rac	
908	+	
909	-	
910	rac	
911	+	
912	-	
913	rac	
914	+	
915	-	
916	rac	
917	+	
918	-	
919	rac	
920	+	
921	-	
922	rac	
923	+	
924	-	

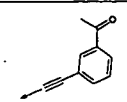
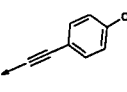
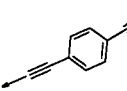
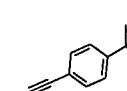
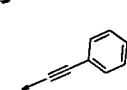
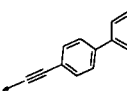
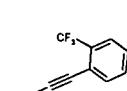
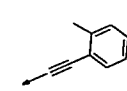
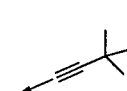
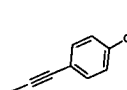
No.	Racemic or enantiomer	R3
925	rac	
926	-	
927	+	
928	rac	
929	+	
930	-	
931	rac	
932	+	
933	-	
934	rac	
935	+	
936	-	
937	rac	
938	+	
939	-	
940	rac	
941	+	
942	-	
943	rac	
944	+	
945	-	
946	rac	
947	+	
948	-	
949	rac	
950	+	
951	-	
952	rac	
953	+	
954	-	
955	rac	
956	+	
957	-	
958	rac	
959	+	
960	-	
961	rac	
962	+	
963	-	
964	rac	
965	+	
966	-	
967	rac	
968	+	
969	-	
970	rac	
971	+	
972	-	

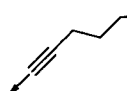
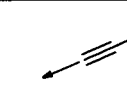
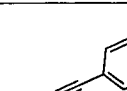
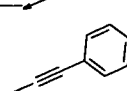
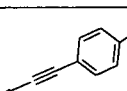


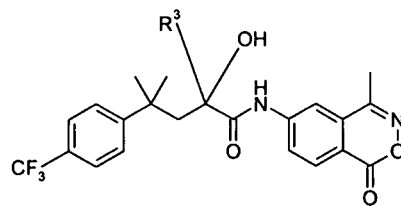
973	rac	
974	+	
975	-	
976	rac	
977	+	
978	-	
979	rac	
980	+	
981	-	
982	rac	
983	+	
984	-	
985	rac	
986	+	
987	-	

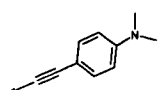
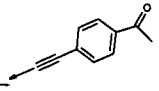
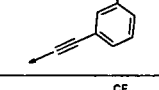
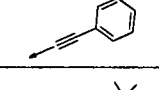
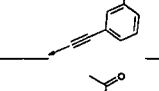
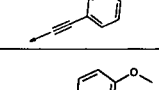
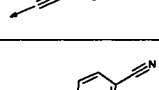
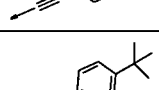
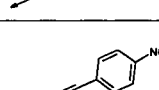
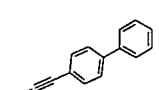
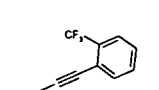
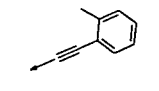
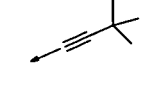
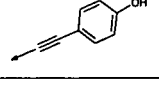
No.	Racemic or enantiomer	R3
988	rac	
989	-	
990	+	
991	rac	
992	+	
993	-	
994	rac	
995	+	
996	-	
997	rac	
998	+	
999	-	
1000	rac	
1001	+	
1002	-	
1003	rac	
1004	+	
1005	-	
1006	rac	
1007	+	
1008	-	
1009	rac	
1010	+	
1011	-	
1012	rac	
1013	+	
1014	-	
1015	rac	
1016	+	
1017	-	
1018	rac	
1019	+	
1020	-	

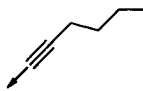
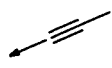
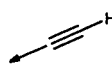
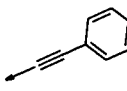
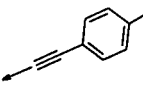
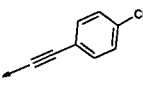
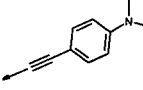
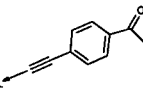
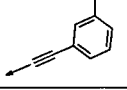
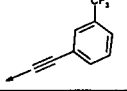
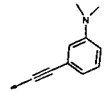
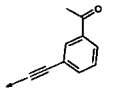
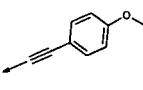
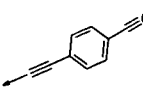
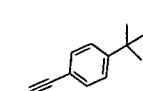
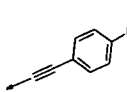
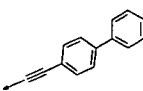


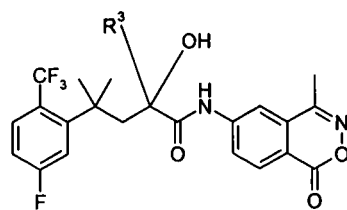
1021	rac	
1022	+	
1023	-	
1024	rac	
1025	+	
1026	-	
1027	rac	
1028	+	
1029	-	
1030	rac	
1031	+	
1032	-	
1033	rac	
1034	+	
1035	-	
1036	rac	
1037	+	
1038	-	
1039	rac	
1040	+	
1041	-	
1042	rac	
1043	+	
1044	-	
1045	rac	
1046	+	
1047	-	
1048	rac	
1049	+	
1050	-	

No.	Racemic or enantiomer	R3
1051	rac	
1052	-	
1053	+	
1054	rac	
1055	+	
1056	-	
1057	rac	
1058	+	
1059	-	
1060	rac	
1061	+	
1062	-	
1063	rac	
1064	+	
1065	-	
1066	rac	
1067	+	
1068	-	



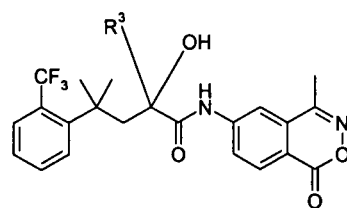
1069	rac	
1070	+	
1071	-	
1072	rac	
1073	+	
1074	-	
1075	rac	
1076	+	
1077	-	
1078	rac	
1079	+	
1080	-	
1081	rac	
1082	+	
1083	-	
1084	rac	
1085	+	
1086	-	
1087	rac	
1088	+	
1089	-	
1090	rac	
1091	+	
1092	-	
1093	rac	
1094	+	
1095	-	
1096	rac	
1097	+	
1098	-	
1099	rac	
1100	+	
1101	-	
1102	rac	
1103	+	
1104	-	
1105	rac	
1106	+	
1107	-	
1108	rac	
1109	+	
1110	-	
1111	rac	
1112	+	
1113	-	

No.	Racemic or enantiomer	R3
1114	rac	
1115	-	
1116	+	
1117	rac	
1118	+	
1119	-	
1120	rac	
1121	+	
1122	-	
1123	rac	
1124	+	
1125	-	
1126	rac	
1127	+	
1128	-	
1129	rac	
1130	+	
1131	-	
1132	rac	
1133	+	
1134	-	
1135	rac	
1136	+	
1137	-	
1138	rac	
1139	+	
1140	-	
1141	rac	
1142	+	
1143	-	
1144	rac	
1145	+	
1146	-	
1147	rac	
1148	+	
1149	-	
1150	rac	
1151	+	
1152	-	
1153	rac	
1154	+	
1155	-	
1156	rac	
1157	+	
1158	-	
1159	rac	
1160	+	
1161	-	
1162	rac	
1163	+	
1164	-	



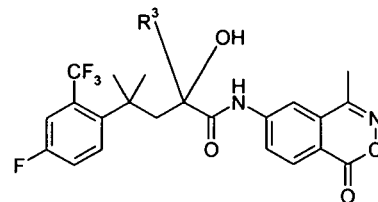
1165	rac	
1166	+	
1167	-	
1168	rac	
1169	+	
1170	-	
1171	rac	
1172	+	
1173	-	
1174	rac	
1175	+	
1176	-	

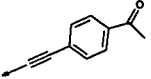
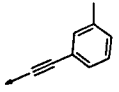
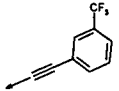
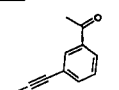
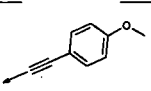
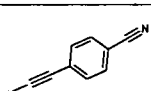
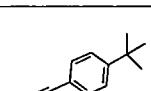
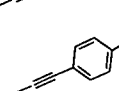
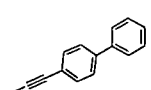
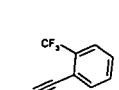
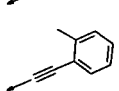
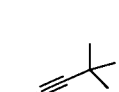
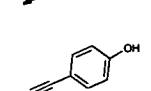
No.	Racemic or enantiomer	R3
1177	rac	
1178	-	
1179	+	
1180	rac	
1181	+	
1182	-	
1183	rac	
1184	+	
1185	-	
1186	rac	
1187	+	
1188	-	
1189	rac	
1190	+	
1191	-	
1192	rac	
1193	+	
1194	-	
1195	rac	
1196	+	
1197	-	
1198	rac	
1199	+	
1200	-	
1202	rac	
1202	+	
1203	-	
1204	rac	
1205	+	
1206	-	
1207	rac	
1208	+	
1209	-	
1210	rac	
1211	+	
1212	-	

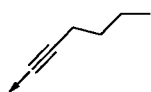
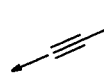


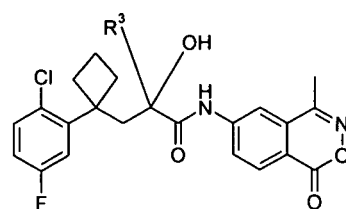
1213	rac	
1214	+	
1215	-	
1216	rac	
1217	+	
1218	-	
1219	rac	
1220	+	
1221	-	
1222	rac	
1223	+	
1224	-	
1225	rac	
1226	+	
1227	-	
1228	rac	
1229	+	
1230	-	
1231	rac	
1232	+	
1233	-	
1234	rac	
1235	+	
1236	-	
1237	rac	
1238	+	
1239	-	

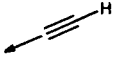
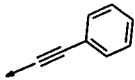
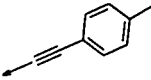
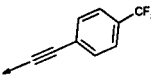
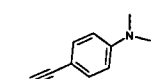
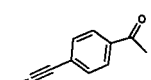
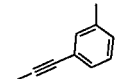
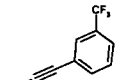
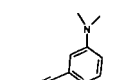
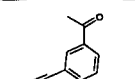
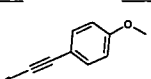
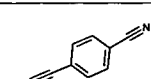
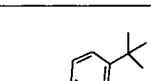
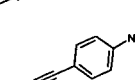
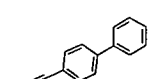
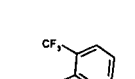
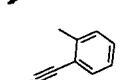
No.	Racemic or enantiomer	R3
1240	rac	
1241	-	
1242	+	
1243	rac	
1244	+	
1245	-	
1246	rac	
1247	+	
1248	-	
1249	rac	
1250	+	
1251	-	
1252	rac	
1253	+	
1254	-	
1255	rac	
1256	+	
1257	-	
1258	rac	
1259	+	
1260	-	



1261	rac	
1262	+	
1263	-	
1264	rac	
1265	+	
1266	-	
1267	rac	
1268	+	
1269	-	
1270	rac	
1271	+	
1272	-	
1273	rac	
1274	+	
1275	-	
1276	rac	
1277	+	
1278	-	
1279	rac	
1280	+	
1281	-	
1282	rac	
1283	+	
1284	-	
1285	rac	
1286	+	
1287	-	
1288	rac	
1289	+	
1290	-	
1291	rac	
1292	+	
1293	-	
1294	rac	
1295	+	
1296	-	
1297	rac	
1298	+	
1299	-	
1300	rac	
1301	+	
1302	-	

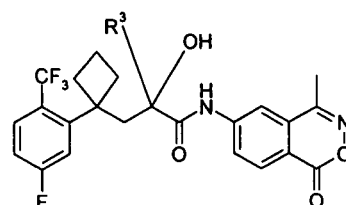
No.	Racemic or enantiomer	R3
1303	rac	
1304	-	
1305	+	
1306	rac	
1307	+	
1308	-	



1309	rac	
1310	+	
1311	-	
1312	rac	
1313	+	
1314	-	
1315	rac	
1316	+	
1317	-	
1318	rac	
1319	+	
1320	-	
1321	rac	
1322	+	
1323	-	
1324	rac	
1325	+	
1326	-	
1327	rac	
1328	+	
1329	-	
1330	rac	
1331	+	
1332	-	
1333	rac	
1334	+	
1335	-	
1336	rac	
1337	+	
1338	-	
1339	rac	
1340	+	
1341	-	
1342	rac	
1343	+	
1344	-	
1345	rac	
1346	+	
1347	-	
1348	rac	
1349	+	
1350	-	
1351	rac	
1352	+	
1353	-	
1354	rac	
1355	+	
1356	-	
1357	rac	
1358	+	
1359	-	

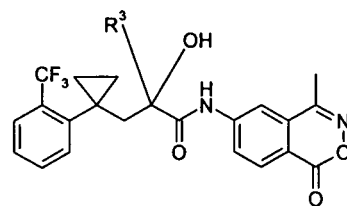
1360	rac	
1361	+	
1362	-	
1362	rac	
1364	+	
1365	-	

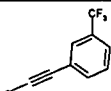
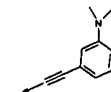
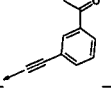
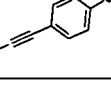
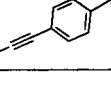
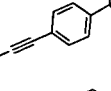
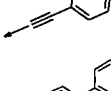
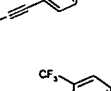
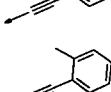
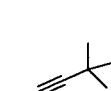
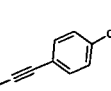
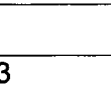
No.	Racemic or enantiomer	R3
1366	rac	
1367	-	
1368	+	
1369	rac	
1370	+	
1371	-	
1372	rac	
1373	+	
1374	-	
1375	rac	
1376	+	
1377	-	
1378	rac	
1379	+	
1380	-	
1381	rac	
1382	+	
1383	-	
1384	rac	
1385	+	
1386	-	
1387	rac	
1388	+	
1389	-	
1390	rac	
1391	+	
1392	-	
1393	rac	
1394	+	
1395	-	
1396	rac	
1397	+	
1398	-	
1399	rac	
1400	+	
1401	-	
1402	rac	
1403	+	
1404	-	
1405	rac	
1406	+	
1407	-	

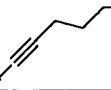
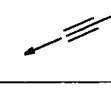
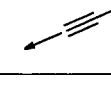
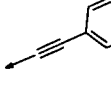


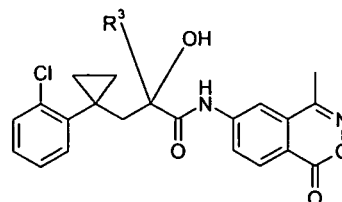
1408	rac	
1409	+	
1410	-	
1411	rac	
1412	+	
1413	-	
1414	rac	
1415	+	
1416	-	
1417	rac	
1418	+	
1419	-	
1420	rac	
1421	+	
1422	-	
1423	rac	
1424	+	
1425	-	
1426	rac	
1427	+	
1428	-	

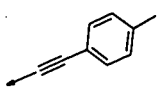
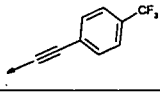
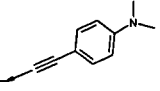
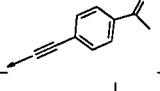
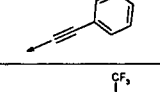
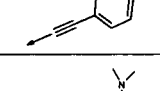
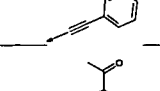
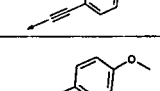
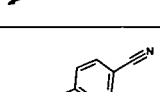
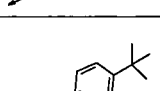
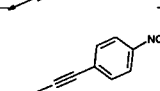
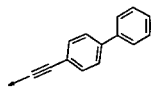
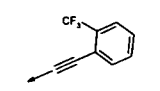
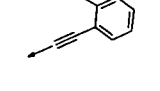
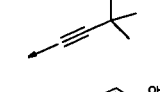
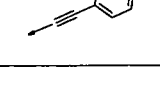
No.	Racemic or enantiomer	R3
1429	rac	
1430	-	
1431	+	
1432	rac	
1433	+	
1434	-	
1435	rac	
1436	+	
1437	-	
1438	rac	
1439	+	
1440	-	
1441	rac	
1442	+	
1443	-	
1444	rac	
1445	+	
1446	-	
1447	rac	
1448	+	
1449	-	
1450	rac	
1451	+	
1452	-	
1453	rac	
1454	+	
1455	-	

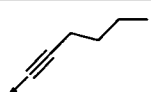
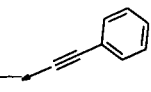
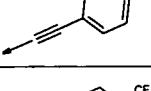
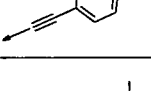
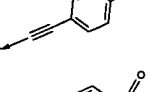
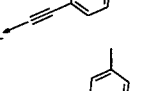
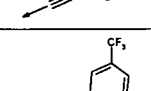
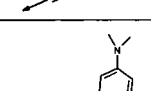
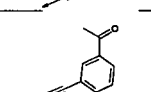
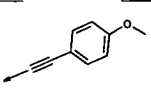
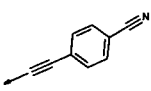
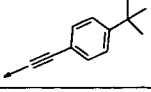
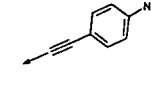
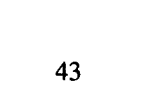


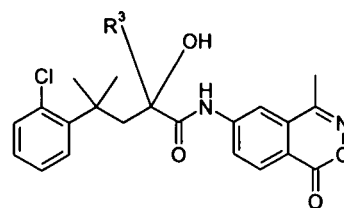
1456	rac	
1457	+	
1458	-	
1459	rac	
1460	+	
1461	-	
1462	rac	
1463	+	
1464	-	
1465	rac	
1466	+	
1467	-	
1468	rac	
1469	+	
1470	-	
1471	rac	
1472	+	
1473	-	
1474	rac	
1475	+	
1476	-	
1477	rac	
1478	+	
1479	-	
1480	rac	
1481	+	
1482	-	
1483	rac	
1484	+	
1485	-	
1486	rac	
1487	+	
1488	-	
1489	rac	
1490	+	
1491	-	

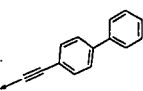
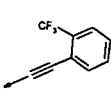
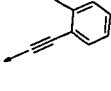
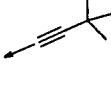
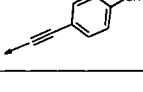
No.	Racemic or enantiomer	R3
1492	rac	
1493	-	
1494	+	
1495	rac	
1496	+	
1497	-	
1498	rac	
1499	+	
1500	-	
1501	rac	
1502	+	
1503	-	

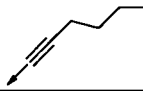
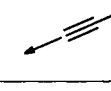
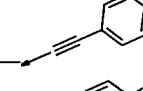
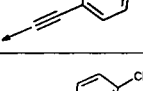
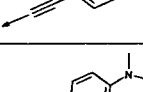
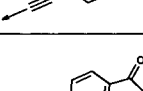
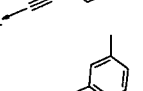
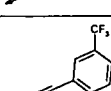
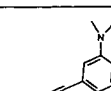


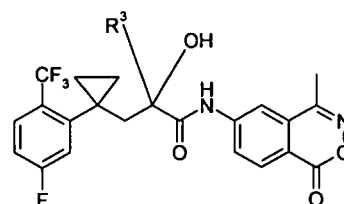
1504	rac	
1505	+	
1506	-	
1507	rac	
1508	+	
1509	-	
1510	rac	
1511	+	
1512	-	
1513	rac	
1514	+	
1515	-	
1516	rac	
1517	+	
1518	-	
1519	rac	
1520	+	
1521	-	
1522	rac	
1523	+	
1524	-	
1525	rac	
1526	+	
1527	-	
1528	rac	
1529	+	
1530	-	
1531	rac	
1532	+	
1533	-	
1534	rac	
1535	+	
1536	-	
1537	rac	
1538	+	
1539	-	
1540	rac	
1541	+	
1542	-	
1543	rac	
1544	+	
1545	-	
1546	rac	
1547	+	
1548	-	
1549	rac	
1550	+	
1551	-	
1552	rac	
1553	+	
1554	-	

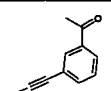
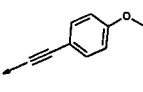
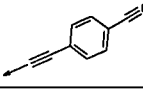
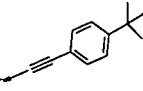
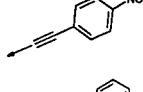
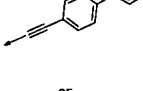
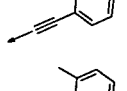
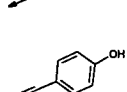
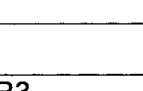
No.	Racemic or enantiomer oder Enantiomer	R3
1555	rac	
1556	-	
1557	+	
1558	rac	
1559	+	
1560	-	
1561	rac	
1562	+	
1563	-	
1564	rac	
1565	+	
1566	-	
1567	rac	
1568	+	
1569	-	
1570	rac	
1571	+	
1572	-	
1573	rac	
1574	+	
1575	-	
1576	rac	
1577	+	
1578	-	
1579	rac	
1580	+	
1581	-	
1582	rac	
1583	+	
1584	-	
1585	rac	
1586	+	
1587	-	
1588	rac	
1589	+	
1590	-	
1591	rac	
1592	+	
1593	-	
1594	rac	
1595	+	
1596	-	
1597	rac	
1598	+	
1599	-	
1600	rac	
1601	+	
1602	-	

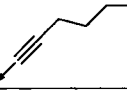
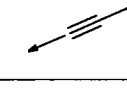
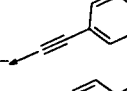
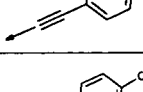
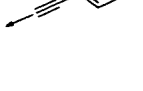


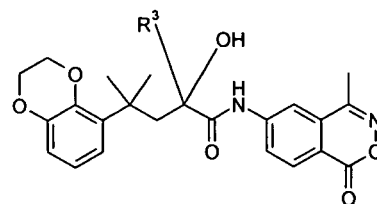
1603	rac	
1604	+	
1605	-	
1606	rac	
1607	+	
1608	-	
1609	rac	
1610	+	
1611	-	
1612	rac	
1613	+	
1614	-	
1615	rac	
1616	+	
1617	-	

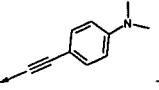
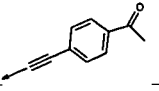
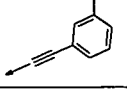
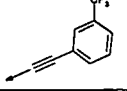
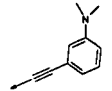
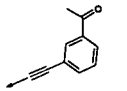
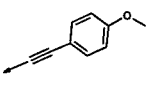
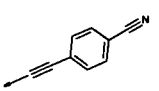
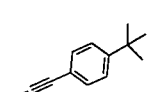
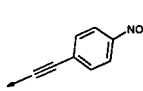
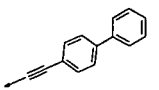
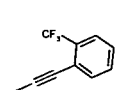
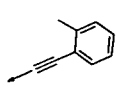
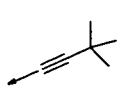
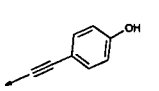
No.	Racemic or enantiomer	R3
1618	rac	
1619	-	
1620	+	
1621	rac	
1622	+	
1623	-	
1624	rac	
1625	+	
1626	-	
1627	rac	
1628	+	
1629	-	
1630	rac	
1631	+	
1632	-	
1633	rac	
1634	+	
1635	-	
1636	rac	
1637	+	
1638	-	
1639	rac	
1640	+	
1641	-	
1642	rac	
1643	+	
1644	-	
1645	rac	
1646	+	
1647	-	
1648	rac	
1649	+	
1650	-	



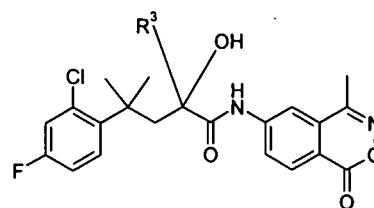
1651	rac	
1652	+	
1653	-	
1654	rac	
1655	+	
1656	-	
1657	rac	
1658	+	
1659	-	
1660	rac	
1661	+	
1662	-	
1663	rac	
1664	+	
1665	-	
1666	rac	
1667	+	
1668	-	
1669	rac	
1670	+	
1671	-	
1672	rac	
1673	+	
1674	-	
1675	rac	
1676	+	
1677	-	
1678	rac	
1679	+	
1680	-	

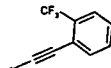
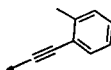
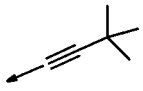
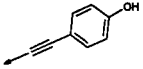
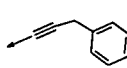
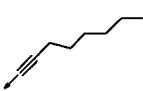
No.	Racemic or enantiomer	R3
1681	rac	
1682	-	
1683	+	
1684	rac	
1685	+	
1686	-	
1687	rac	
1688	+	
1689	-	
1690	rac	
1691	+	
1692	-	
1693	rac	
1694	+	
1695	-	
1696	rac	
1697	+	
1698	-	

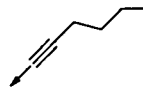
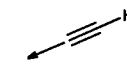
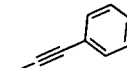
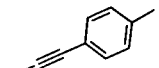
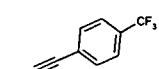
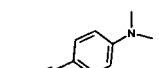
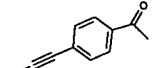
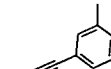
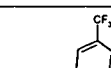


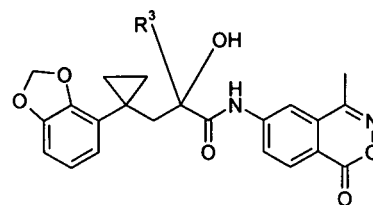
1699	rac	
1700	+	
1701	-	
1702	rac	
1703	+	
1704	-	
1705	rac	
1706	+	
1707	-	
1708	rac	
1709	+	
1710	-	
1711	rac	
1712	+	
1713	-	
1714	rac	
1715	+	
1716	-	
1717	rac	
1718	+	
1719	-	
1720	rac	
1721	+	
1722	-	
1723	rac	
1724	+	
1725	-	
1726	rac	
1727	+	
1728	-	
1729	rac	
1730	+	
1731	-	
1732	rac	
1733	+	
1734	-	
1735	rac	
1736	+	
1737	-	
1738	rac	
1739	+	
1740	-	
1741	rac	
1742	+	
1743	-	

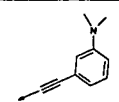
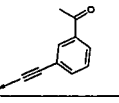
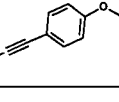
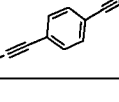
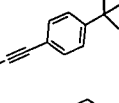
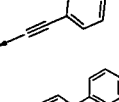
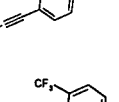
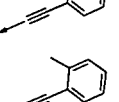
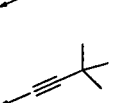
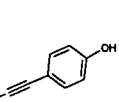
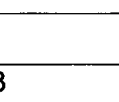
No.	Racemic or enantiomer	R3
1744	rac	
1745	-	
1746	+	
1747	rac	
1748	+	
1749	-	
1750	rac	
1751	+	
1752	-	
1753	rac	
1754	+	
1755	-	
1756	rac	
1757	+	
1758	-	
1759	rac	
1760	+	
1761	-	
1762	rac	
1763	+	
1764	-	
1765	rac	
1766	+	
1767	-	
1768	rac	
1769	+	
1770	-	
1771	rac	
1772	+	
1773	-	
1774	rac	
1775	+	
1776	-	
1777	rac	
1778	+	
1779	-	
1780	rac	
1781	+	
1782	-	
1783	rac	
1784	+	
1785	-	
1786	rac	
1787	+	
1788	-	
1789	rac	
1790	+	
1791	-	
1792	rac	
1793	+	
1794	-	

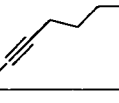
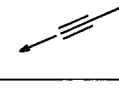
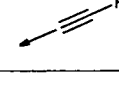
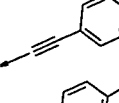
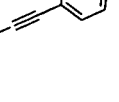


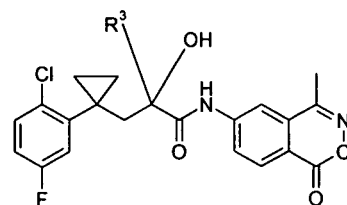
1795	rac	
1796	+	
1797	-	
1798	rac	
1799	+	
1800	-	
1801	rac	
1802	+	
1803	-	
1804	rac	
1805	+	
1806	-	
1807	rac	
1808	+	
1809	-	
1810	rac	
1811	+	
1812	-	

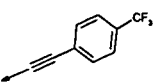
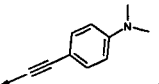
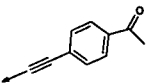
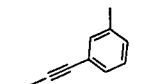
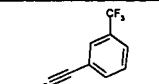
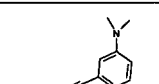
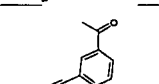
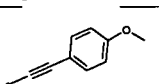
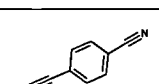
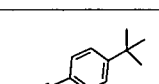
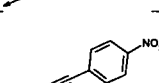
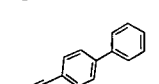
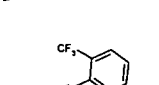
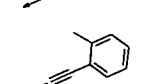
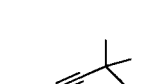
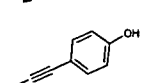
No.	Racemic or enantiomer	R3
1813	rac	
1814	-	
1815	+	
1816	rac	
1817	+	
1818	-	
1819	rac	
1820	+	
1821	-	
1822	rac	
1823	+	
1824	-	
1825	rac	
1826	+	
1827	-	
1828	rac	
1829	+	
1830	-	
1831	rac	
1832	+	
1833	-	
1834	rac	
1835	+	
1836	-	
1837	rac	
1838	+	
1839	-	
1840	rac	
1841	+	
1842	-	

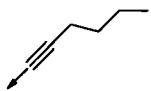
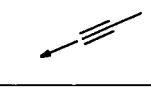
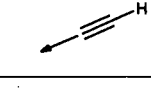
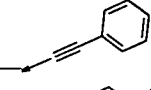
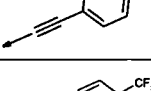
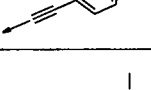
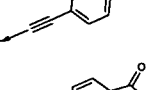
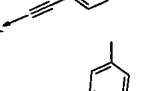
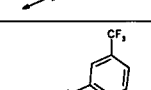
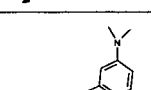
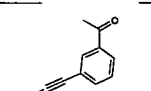
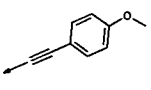
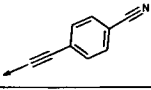


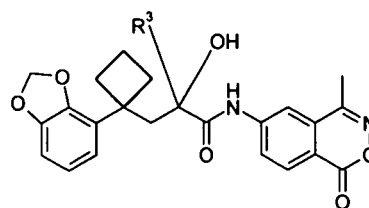
1843	rac	
1844	+	
1845	-	
1846	rac	
1847	+	
1848	-	
1849	rac	
1850	+	
1851	-	
1852	rac	
1853	+	
1854	-	
1855	rac	
1856	+	
1857	-	
1858	rac	
1859	+	
1860	-	
1861	rac	
1862	+	
1863	-	
1864	rac	
1865	+	
1866	-	
1867	rac	
1868	+	
1869	-	
1870	rac	
1871	+	
1872	-	
1873	rac	
1874	+	
1875	-	

No.	Racemic or enantiomer	R3
1876	rac	
1877	-	
1878	+	
1879	rac	
1880	+	
1881	-	
1882	rac	
1883	+	
1884	-	
1885	rac	
1886	+	
1887	-	
1888	rac	
1889	+	
1890	-	

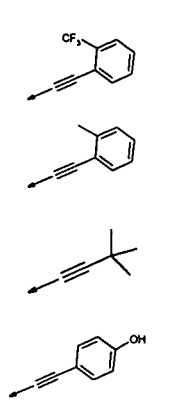


1891	rac	
1892	+	
1893	-	
1894	rac	
1895	+	
1896	-	
1897	rac	
1898	+	
1899	-	
1900	rac	
1901	+	
1902	-	
1903	rac	
1904	+	
1905	-	
1906	rac	
1907	+	
1908	-	
1909	rac	
1910	+	
1911	-	
1912	rac	
1913	+	
1914	-	
1915	rac	
1916	+	
1917	-	
1918	rac	
1919	+	
1920	-	
1921	rac	
1922	+	
1923	-	
1924	rac	
1925	+	
1926	-	
1927	rac	
1928	+	
1929	-	
1930	rac	
1931	+	
1932	-	
1933	rac	
1934	+	
1935	-	
1936	rac	
1937	+	
1938	-	

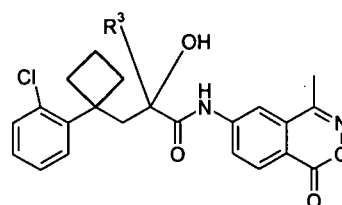
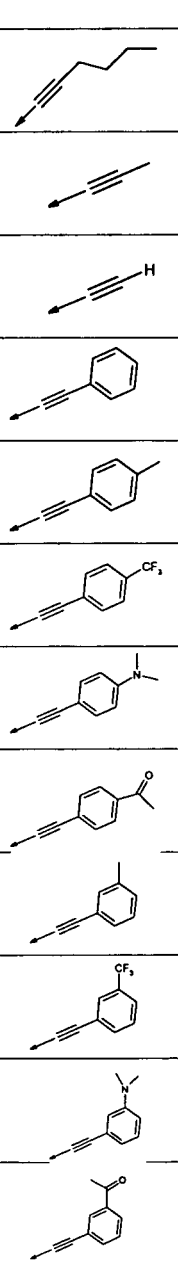
No.	Racemic or enantiomer	R3
1939	rac	
1940	-	
1941	+	
1942	rac	
1943	+	
1944	-	
1945	rac	
1946	+	
1947	-	
1948	rac	
1949	+	
1950	-	
1951	rac	
1952	+	
1953	-	
1954	rac	
1955	+	
1956	-	
1957	rac	
1958	+	
1959	-	
1960	rac	
1961	+	
1962	-	
1963	rac	
1964	+	
1965	-	
1966	rac	
1967	+	
1968	-	
1969	rac	
1970	+	
1971	-	
1972	rac	
1973	+	
1974	-	
1975	rac	
1976	+	
1977	-	
1978	rac	
1979	+	
1980	-	
1981	rac	
1982	+	
1983	-	
1984	rac	
1985	+	
1986	-	
1987	rac	
1988	+	
1989	-	



1990	rac	
1991	+	
1992	-	
1993	rac	
1994	+	
1995	-	
1996	rac	
1997	+	
1998	-	
1999	rac	
2000	+	
2001	-	

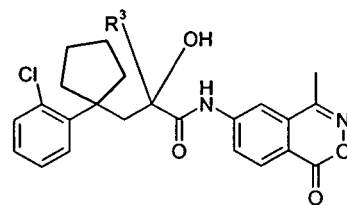


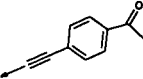
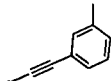
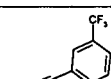
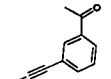
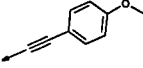
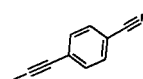
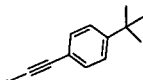
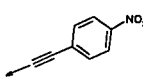
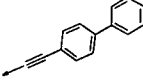
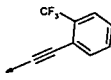
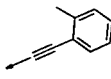
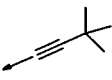
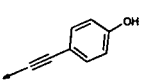
No.	Racemic or enantiomer	R3
2002	rac	
2003	-	
2004	+	
2005	rac	
2006	+	
2007	-	
2008	rac	
2009	+	
2010	-	
2011	rac	
2012	+	
2013	-	
2014	rac	
2015	+	
2016	-	
2017	rac	
2018	+	
2019	-	
2020	rac	
2021	+	
2022	-	
2023	rac	
2024	+	
2025	-	
2026	rac	
2027	+	
2028	-	
2029	rac	
2030	+	
2031	-	
2032	rac	
2033	+	
2034	-	
2035	rac	
2036	+	
2037	-	

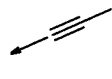


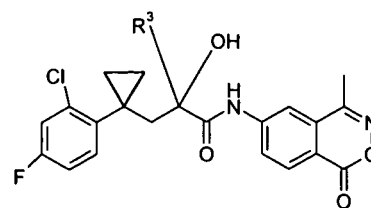
2038	rac	
2039	+	
2040	-	
2041	rac	
2042	+	
2043	-	
2044	rac	
2045	+	
2046	-	
2047	rac	
2048	+	
2049	-	
2050	rac	
2051	+	
2052	-	
2053	rac	
2054	+	
2055	-	
2056	rac	
2057	+	
2058	-	
2059	rac	
2060	+	
2061	-	
2062	rac	
2063	+	
2064	-	

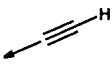
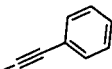
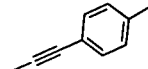
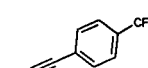
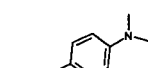
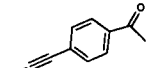
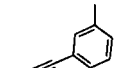
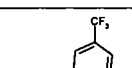
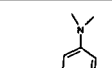
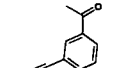
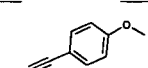
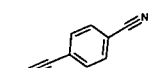
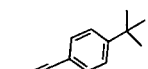
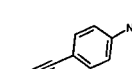
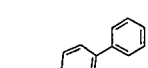
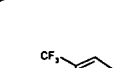
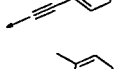
No.	Racemic or enantiomer	R3
2065	rac	
2066	-	
2067	+	
2068	rac	
2069	+	
2070	-	
2071	rac	
2072	+	
2073	-	
2074	rac	
2075	+	
2076	-	
2077	rac	
2078	+	
2079	-	
2080	rac	
2081	+	
2082	-	
2083	rac	
2084	+	
2085	-	

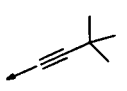
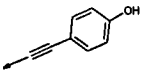


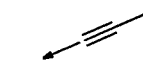
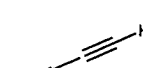
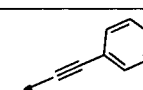
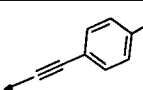
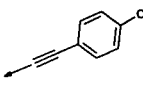
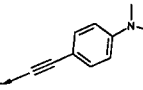
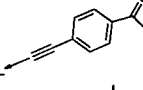
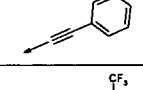
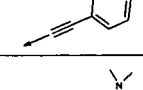
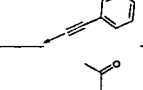
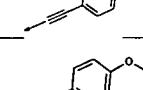
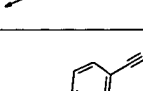
2086	rac	
2087	+	
2088	-	
2089	rac	
2090	+	
2091	-	
2092	rac	
2093	+	
2094	-	
2095	rac	
2096	+	
2097	-	
2098	rac	
2099	+	
2100	-	
2101	rac	
2102	+	
2103	-	
2104	rac	
2105	+	
2106	-	
2107	rac	
2108	+	
2109	-	
2110	rac	
2111	+	
2112	-	
2113	rac	
2114	+	
2115	-	
2116	rac	
2117	+	
2118	-	
2119	rac	
2120	+	
2121	-	
2122	rac	
2123	+	
2124	-	
2125	rac	
2126	+	
2127	-	

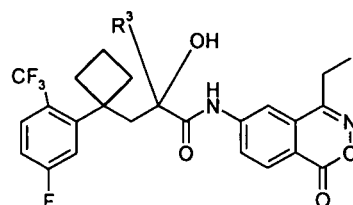
No.	Racemic or enantiomer	R3
2128	rac	
2129	-	
2130	+	
2131	rac	
2132	+	
2133	-	



2134	rac	
2135	+	
2136	-	
2137	rac	
2138	+	
2139	-	
2140	rac	
2141	+	
2142	-	
2143	rac	
2144	+	
2145	-	
2146	rac	
2147	+	
2148	-	
2149	rac	
2150	+	
2151	-	
2152	rac	
2153	+	
2154	-	
2155	rac	
2156	+	
2157	-	
2158	rac	
2159	+	
2160	-	
2161	rac	
2163	+	
2163	-	
2164	rac	
2165	+	
2166	-	
2167	rac	
2168	+	
2169	-	
2170	rac	
2171	+	
2172	-	
2173	rac	
2174	+	
2175	-	
2176	rac	
2177	+	
2178	-	
2179	rac	
2180	+	
2181	-	
2182	rac	
2183	+	
2184	-	

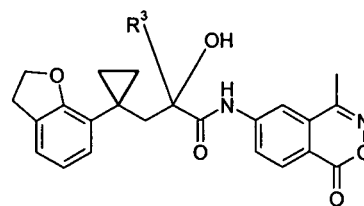
2185	rac	
2186	+	
2187	-	
2188	rac	
2189	+	
2190	-	

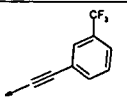
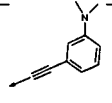
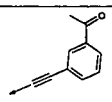
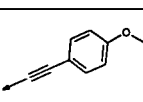
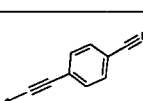
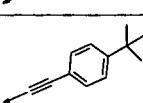
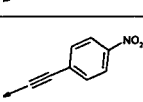
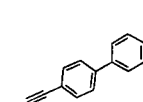
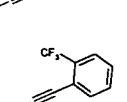
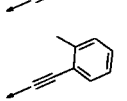
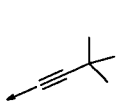
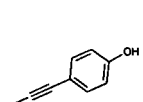
No.	Racemic or enantiomer	R3
2191	rac	
2192	-	
2193	+	
2194	rac	
2195	+	
2196	-	
2197	rac	
2198	+	
2199	-	
2200	rac	
2201	+	
2202	-	
2203	rac	
2204	+	
2205	-	
2206	rac	
2207	+	
2208	-	
2209	rac	
2210	+	
2211	-	
2212	rac	
2213	+	
2214	-	
2215	rac	
2216	+	
2217	-	
2218	rac	
2219	+	
2220	-	
2221	rac	
2222	+	
2223	-	
2224	rac	
2225	+	
2226	-	
2227	rac	
2228	+	
2229	-	
2230	rac	
2231	+	
2232	-	

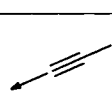
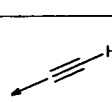
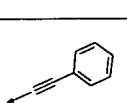


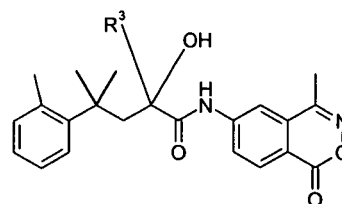
2233	rac	
2234	+	
2235	-	
2236	rac	
2237	+	
2238	-	
2239	rac	
2240	+	
2241	-	
2242	rac	
2243	+	
2244	-	
2245	rac	
2246	+	
2247	-	
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2249	+	
2250	-	
2251	rac	
2252	+	
2253	-	

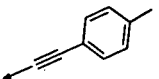
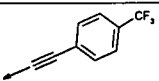
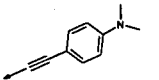
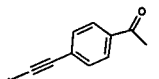
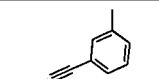
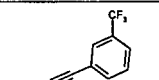
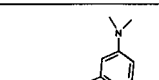
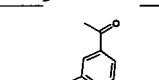
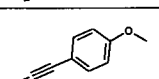
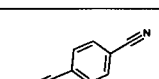
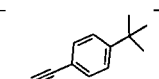
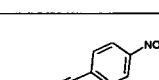
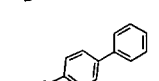
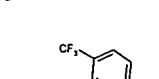
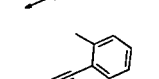
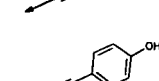
No.	Racemic or enantiomer	R3
2254	rac	
2255	-	
2256	+	
2257	rac	
2258	+	
2259	-	
2260	rac	
2261	+	
2262	-	
2263	rac	
2264	+	
2265	-	
2266	rac	
2267	+	
2268	-	
2269	rac	
2270	+	
2271	-	
2272	rac	
2273	+	
2274	-	
2275	rac	
2276	+	
2277	-	
2278	rac	
2279	+	
2280	-	



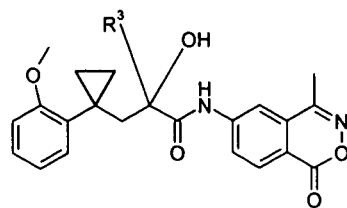
2281	rac	
2282	+	
2283	-	
2284	rac	
2285	+	
2286	-	
2287	rac	
2288	+	
2289	-	
2290	rac	
2291	+	
2292	-	
2293	rac	
2294	+	
2295	-	
2296	rac	
2297	+	
2298	-	
2299	rac	
2300	+	
2301	-	
2302	rac	
2303	+	
2304	-	
2305	rac	
2306	+	
2307	-	
2308	rac	
2309	+	
2310	-	
2311	rac	
2312	+	
2313	-	
2314	rac	
2315	+	
2316	-	

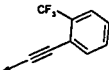
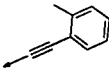
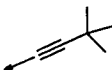
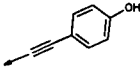
No.	Racemic or enantiomer	R3
2317	rac	
2318	-	
2319	+	
2320	rac	
2321	+	
2322	-	
2323	rac	
2324	+	
2325	-	
2326	rac	
2327	+	
2328	-	

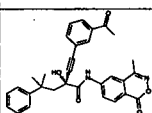
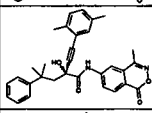
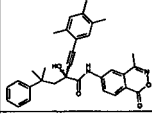
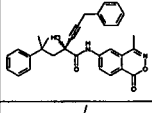
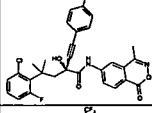
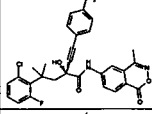
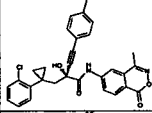
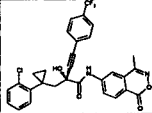
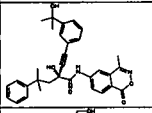
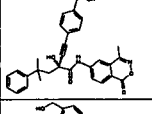
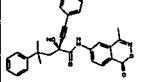


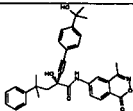
2329	rac	
2330	+	
2331	-	
2332	rac	
2333	+	
2334	-	
2335	rac	
2336	+	
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2338	rac	
2339	+	
2340	-	
2341	rac	
2342	+	
2343	-	
2344	rac	
2345	+	
2346	-	
2347	rac	
2348	+	
2349	-	
2350	rac	
2351	+	
2652	-	
2353	rac	
2354	+	
2355	-	
2356	rac	
2357	+	
2358	-	
2359	rac	
2360	+	
2361	-	
2362	rac	
2363	+	
2364	-	
2365	rac	
2366	+	
2367	-	
2368	rac	
2369	+	
2370	-	
2371	rac	
2372	+	
2373	-	
2374	rac	
2375	+	
2376	-	
2377	rac	
2378	+	
2379	-	

No.	Racemic or enantiomer	R3
2380	rac	
2381	-	
2382	+	
2383	rac	
2384	+	
2385	-	
2386	rac	
2387	+	
2388	-	
2389	rac	
2390	+	
2391	-	
2392	rac	
2393	+	
2394	-	
2395	rac	
2396	+	
2397	-	
2398	rac	
2399	+	
2400	-	
2401	rac	
2402	+	
2403	-	
2404	rac	
2405	+	
2406	-	
2407	rac	
2408	+	
2409	-	
2410	rac	
2411	+	
2412	-	
2413	rac	
2414	+	
2415	-	
2416	rac	
2417	+	
2418	-	
2419	rac	
2420	+	
2421	-	
2422	rac	
2423	+	
2424	-	
2425	rac	
2426	+	
2427	-	
2428	rac	
2429	+	
2430	-	



2431	rac	
2432	+	
2433	-	
2434	rac	
2435	+	
2436	-	
2437	rac	
2438	+	
2439	-	
2440	rac	
2441	+	
2442	-	

No.	Racemic or enantiomer	Structure
2443	rac	
2444	-	
2445	+	
2446	rac	
2447	+	
2448	-	
2449	rac	
2450	+	
2451	-	
2452	rac	
2453	+	
2454	-	
2455	rac	
2456	+	
2457	-	
2458	rac	
2459	+	
2460	-	
2461	rac	
2462	+	
2463	-	
2464	rac	
2465	+	
2466	-	
2467	rac	
2468	+	
2469	-	
2470	rac	
2471	+	
2472	-	
2473	rac	
2474	+	
2475	-	

2476	rac	
2477	+	
2478	-	

Biological characterization of the compounds according to the invention

Progesterone receptor modulators can be identified with the aid of simple methods, test programmes known to the skilled person. It is possible for this purpose for example to incubate a compound to be tested together with a progestogen in a test system for
5 progesterone receptors and to check whether the effect mediated by progesterone is altered in the presence of the modulator in this test system.

The substances according to the invention of the general formula I were tested in the following models:

10

Progesterone receptor-binding assay

Measurement of the receptor binding affinity:

The receptor binding affinity was determined by competitive binding of a specifically binding ^3H -labelled hormone (tracer) and of the compound to be tested on receptors in
15 the cytosol from animal target organs. The aim in this case was receptor saturation and reaction equilibrium.

The tracer and increasing concentrations of the compound to be tested (competitor) were coincubated at 0-4°C for 18 h with the receptor-containing cytosol fraction. After removal of unbound tracer with carbon-dextran suspension, the receptor-bound tracer
20 content was measured for each concentration, and the IC_{50} was determined from the concentration series. The relative molar binding affinity (RBA) was calculated as ratio of the IC_{50} values for reference substance and compound to be tested ($\times 100\%$) (RBA of the reference substance = 100%).

25 The following incubation conditions were chosen for the receptor types:

Progesterone receptor:

Uterus cytosol of the estradiol-primed rabbit, homogenized in TED buffer (20 mM Tris/HCl, pH 7.4; 1 mM ethylenediaminetetraacetate, 2 mM dithiothreitol) with
30 250 mM sucrose; stored at -30°C. Tracer: ^3H -ORG 2058, 5 nM; reference substance: progesterone.

Glucocorticoid receptor:

Thymus cytosol from the adrenalectomized rat, thymi stored at -30°C; buffer: TED.
35 Tracer: ^3H -dexamethasone, 20 nM; reference substance: dexamethasone.

The relative receptor binding affinities (RBA values) for the compounds according to the invention of the general formula (I) on the progesterone receptor are between 3 and 100% relative to progesterone. The RBA values at the glucocorticoid receptor are in the range from 3 to 30% relative to dexamethasone.

5

The compounds according to the invention accordingly have a high affinity for the progesterone receptor, but only a low affinity for the glucocorticoid receptor.

Antagonism at the PR-B progesterone receptor

10 The transactivation assay is carried out as described in WO 02/054064.

Agonism on the PR-B progesterone receptor

The transactivation assay is carried out as described in Fuhrmann et al. (Fuhrmann U., Hess-Stump H., Cleve A., Neef G., Schwede W., Hoffmann J., Fritzemeier K.-H., Chwalisz K., Journal of Medicinal Chem, 43, 26, 2000, 5010-5016).

15

No.	Antagonistic Activity		Agonistic Activity	
	IC ₅₀ [nM]	Efficacy [%]	EC ₅₀ [nM]	Efficacy [%]
5	0,2	86	0,2	10
14	6	53	7	35
16	0,7	82	0,5	13
17b	0,03	88	n.b.	7
18	0,2	89	n.b.	8
24	2	100		0
35	2	100		0

Dosage

20 The progesterone receptor modulators can be administered orally, enterally, parenterally or transdermally for the use according to the invention.

Satisfactory results are generally to be expected in the treatment of the indications mentioned hereinbefore when the daily doses cover a range from 1 µg to 500 mg of the compound according to the invention.

25 Suitable dosages of the compounds according to the invention in humans for the treatment of endometriosis, of leiomyomas of the uterus and dysfunctional bleeding and for use in fertility control and for hormone replacement therapy are from 50 µg to

500 mg per day, depending on the age and constitution of the patient, it being possible to administer the necessary daily dose by single or multiple administration.

5 The dosage range for the compounds according to the invention for the treatment of breast carcinomas is 10 mg to 1000 mg per day.

10 The pharmaceutical products based on the novel compounds are formulated in a manner known per se by processing the active ingredient with the carrier substances, fillers, substances influencing disintegration, binders, humectants, lubricants, absorbents, diluents, masking flavours, colorants, etc. which are used in pharmaceutical technology, and converting into the desired administration form. Reference should be made in this connection to Remington's Pharmaceutical Sciences, 15th ed. Mack Publishing Company, Easton, Pennsylvania (1980).

15 Suitable for oral administration are in particular tablets, film-coated tablets, sugar-coated tablets, capsules, pills, powders, granules, pastilles, suspensions, emulsions or solutions.

20 Preparations for injection and infusion are possible for parenteral administration.

Appropriately prepared crystal suspensions can be used for intraarticular injection.

25 Aqueous and oily solutions for injection or suspensions and corresponding depot preparations can be used for intramuscular injection.

For rectal administration, the novel compounds can be used in the form of suppositories, capsules, solutions (e.g. in the form of enemas) and ointments, both for systemic and for local therapy.

30 Furthermore, compositions for vaginal use may also be mentioned as preparation.

For pulmonary administration of the novel compounds, they can be used in the form of aerosols and inhalants.

35 Patches are possible for transdermal administration, and formulations in gels, ointments, fatty ointments, creams, pastes, dusting powders, milk and tinctures are possible for topical application. The dosage of the compounds of the general formula I

in these preparations should be 0.01% - 20% in order to achieve an adequate pharmacological effect.

Corresponding tablets can be obtained for example by mixing active ingredient with
5 known excipients, for example inert diluents such as dextrose, sugar, sorbitol, mannitol, polyvinylpyrrolidone, disintegrants such as maize starch or alginic acid, binders such as starch or gelatin, lubricants such as magnesium stearate or talc and/or means to achieve a depot effect such as carboxypolymethylene, carboxymethylcellulose, cellulose acetate phthalate or polyvinyl acetate. The tablets may also consist of a
10 plurality of layers.

Correspondingly, coated tablets can be produced by coating cores produced in analogy to the tablets with compositions normally used in tablet coatings, for example polyvinylpyrrolidone or shellac, gum arabic, talc, titanium oxide or sugar. The tablet
15 covering may in this case also consist of a plurality of layers, it being possible to use the excipients mentioned above for tablets.

Solutions or suspensions of the compounds according to the invention of the general formula I may additionally comprise taste-improving agents such as saccharin, cyclamate or sugar, and, for example, flavourings such as vanillin or orange extract.
20 They may additionally comprise suspending excipients such as sodium carboxymethylcellulose or preservatives such as p-hydroxybenzoates.

Capsules comprising the compounds of the general formula I can be produced for
25 example by mixing the compound(s) of the general formula I with an inert carrier such as lactose or sorbitol and encapsulating it in gelatin capsules.

Suitable suppositories can be produced for example by mixing with carriers intended for this purpose, such as neutral fats or polyethylene glycol or derivatives.

30 The compounds according to the invention of the general formula (I) or their pharmaceutically acceptable salts can be used, because of their antagonistic or partial agonistic activity, for producing a medicament, in particular for the treatment and prophylaxis of gynaecological disorders such as endometriosis, leiomyomas of the
35 uterus, dysfunctional bleeding and dysmenorrhoea. They can furthermore be employed to counteract hormonal irregularities, for inducing menstruation and alone or in

combination with prostaglandins and/or oxytocin to induce labour.

5 The compounds according to the invention of the general formula (I) or their pharmaceutically acceptable salts are furthermore suitable for producing products for female contraception (see also WO 93/23020, WO 93/21927).

The compounds according to the invention or their pharmaceutically acceptable salts can additionally be employed alone or in combination with a selective estrogen receptor modulator (SERM) for female hormone replacement therapy.

10 In addition, the said compounds have an antiproliferative effect in hormone-dependent tumours. They are therefore suitable for the therapy of hormone-dependent carcinomas such as, for example, for breast, prostate and endometrial carcinomas.

15 The compounds according to the invention or their pharmaceutically acceptable salts can be employed for the treatment of hormone-dependent carcinomas both in first-line therapy and in second-line therapy, especially after tamoxifen failure.

20 The compounds according to the invention, having antagonistic or partially agonistic activity, of the general formula (I) or their pharmaceutically acceptable salts can also be used in combination with compounds having antiestrogenic activity (estrogen receptor antagonists or aromatase inhibitors) or selective estrogen receptor modulators (SERM) for producing pharmaceutical products for the treatment of hormone-dependent tumours. The compounds according to the invention can likewise be used in combination with SERMs or an antiestrogen (estrogen receptor antagonist or
25 aromatase inhibitor) for the treatment of endometriosis or of leiomyomas of the uterus. In the treatment of hormone-dependent tumours the progesterone receptor modulator and the antiestrogen (estrogen receptor antagonists or aromatase inhibitors) or the SERM can be provided for simultaneous or else for sequential administration. In the sequential administration, preferably the antiestrogen (estrogen receptor antagonists or
30 aromatase inhibitors) or SERM is administered first and subsequently the progesterone receptor modulator is administered.

Suitable for combination with the non-steroidal progesterone receptor modulators according to the invention in this connection are for example the following antiestrogens
35 (estrogen receptor antagonists or aromatase inhibitors) or SERMs:
tamoxifen, 5-(4-{5-[(RS)-(4,4,5,5,5-pentafluoropentyl)sulphonyl]pentyloxy}phenyl)-6-

phenyl-8,9-dihydro-7H-benzocyclohepten-2-ol (WO 00/03979), ICI 182 780 (7alpha-[9-(4,4,5,5-pentafluoropentylsulphonyl)nonyl]estra-1,3,5(10)-triene-3,17beta-diol), 11beta-fluoro-7alpha-[5-(methyl{3-[(4,4,5,5-pentafluoropentyl)sulphonyl]propyl}amino)pentyl]estra-1,3,5(10)-triene-3,17beta-diol (WO98/07740), 11beta-fluoro-7alpha-{5-[methyl(7,7,8,8,9,9,10,10,10-nonafluorodecyl)amino]pentyl}estra-1,3,5(10)-triene-3,17beta-diol (WO 99/33855), 11beta-fluoro-17alpha-methyl-7alpha-{5-[methyl(8,8,9,9,9-pentafluorononyl)amino]pentyl}estra-1,3,5(10)-triene-3,17beta-diol (WO 03/045972), clomifen, raloxifen, and further compounds having antiestrogenic activity, and aromatase inhibitors such as, for example, fadrozole, formestane, letrozole, anastrozole or atamestane.

Finally, the present invention also relates to the use of the compounds of the general formula I, where appropriate together with an antiestrogen or SERM, for producing a medicament.

The present invention further relates to pharmaceutical compositions which comprise at least one compound according to the invention, where appropriate in the form of a pharmaceutically/pharmacologically acceptable salt, without or together with pharmaceutically acceptable excipients and/or carriers.

These pharmaceutical compositions and medicaments may be intended for oral, rectal, vaginal, subcutaneous, percutaneous, intravenous or intramuscular administration. Besides conventional carriers and/or diluents, they comprise at least one compound according to the invention.

The medicaments of the invention are produced with the conventional solid or liquid carriers or diluents and the excipients normally used in pharmaceutical technology appropriate for the desired mode of administration with a suitable dosage in a known manner. The preferred preparations consist of a dosage suitable for oral administration. Examples of such dosage forms are tablets, film-coated tablets, sugar-coated tablets, capsules, pills, powders, solutions or suspensions or else depot forms.

The pharmaceutical compositions comprising at least one of the compounds according to the invention are preferably administered orally.

Also suitable are parenteral preparations such as solutions for injection. Further

preparations which may also be mentioned are for example suppositories and compositions for vaginal use.

The following examples serve to illustrate the subject-matter of the invention in more detail without wishing to restrict it thereto.

Preparation of the starting compounds 6-[4-(2-chloro-5-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one, 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one and 6-[3-[1-(2-chlorophenyl)cyclopentyl]-2-oxopropionylamino]-4-methyl-2,3-benzoxazin-1-one has been described in the patent US 2002/0077356, the compound 6-[4-(2,3-dihydro-7-benzofuranyl)-4-methyl-2-oxopentanoylamino]-4-methyl-2,3-benzoxazinone in US patent 6,323,199B1 (example 87 therein), the compound 6-(4-methyl-4-phenyl-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one in the patent WO 199854159 and the compound 6-[3-[1-(2-fluoro-5-trifluoromethylphenyl)cyclopropyl]-2-oxopropionylamino]-4-methyl-2,3-benzoxazin-1-one in the patent WO 200375915.

15 General methods

1-(Benzo[1,3]dioxol-4-yl)-1-methylethanol

57.2 ml of methyl magnesium chloride solution (3M in THF) were added to 25.5 g of 4-acetylbenzo[1,3]dioxole in 375 ml of THF at RT under argon. The mixture was stirred at RT for 16 h and added to ice/2N hydrochloric acid. It was then extracted with ethyl acetate, and the organic phase was washed with water and brine and dried (Na₂SO₄). 27.89 g of 1-[benzo(1,3)dioxol-4-yl]-1-methylethanol were obtained as a brown oil.
¹H-NMR (CDCl₃, ppm) = 1.6 (s, 6H), 5.95 (s, 2H), 6.76 (dd, 1H), 6.82 (t, 1H), 6.91 (dd, 1H)

25

4-(Benzo[1,3]dioxol-4-yl)-4-methyl-2-oxopentanoic acid

47 ml of tin(IV) chloride were added to 9.5 g of 1-(benzo[1,3]dioxol-4-yl)-1-methylethanol and 14.2 g of ethyl 2-trimethylsilyloxyacrylate in 200 ml of dichloromethane at -70°C. After 15 minutes, the solution was added to potassium carbonate solution. After extraction with diethyl ether, the organic phase was washed with water, dried and evaporated.

14.4 g of the ethyl 4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxopentanoate obtained in this way were stirred with 150 ml of 1 M sodium hydroxide and 300 ml of methanol at RT for 10 hours. The methanol was then removed in vacuo, and the remaining solution was extracted with diethyl ether. The aqueous phase was acidified with 1 M hydrochloric acid and extracted with diethyl ether. Drying and evaporation resulted in 11.1 g of

4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxopentanoic acid as yellowish oil.

MS (ei) m/e: $M^+ = 251$

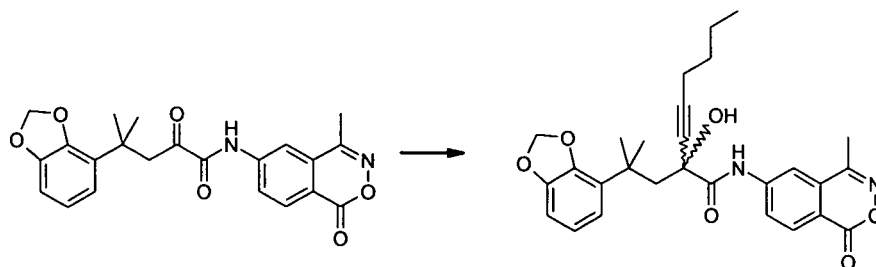
6-[4-(Benzo[1,3]dioxol-4-yl)-4-methyl-2-oxoaleroylamino]-4-methyl-2,3-benzoxazin-1-one

10 g of 4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxopentanoic acid were dissolved in 125 ml of dimethylacetamide and, at -0°C under argon, 3.5 ml of thionyl chloride were added. After stirring at -3 to $+3^\circ\text{C}$ for 20 minutes, 7.6 g of 6-amino-4-methyl-2,3-benzoxazin-1-one (WO 00/32584) were added. The mixture was stirred at room temperature for 96 hours and, after addition of water, extracted with ethyl acetate, the organic phase was washed with water and dried (Na_2SO_4), and evaporation of the solvent and chromatography of the crude product on silica gel with hexane/ethyl acetate (100:0 $\rightarrow$ 60:40) resulted in 6.56 g of 6-[4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxoaleroylamino]-4-methyl-2,3-benzoxazin-1-one as a beige solid.

m.p. = $165-166^\circ\text{C}$, MS (ei) m/e: $M^+ = 409$

Synthesis examples

(-)-6-{2-[2-(2,3-(Methylenedioxy)phenyl)-2-methylpropyl]-2-hydroxyoct-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one 1 and (+)-6-{2-[2-(2,3-(methylenedioxy)phenyl)-2-methylpropyl]-2-hydroxyoct-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one 2

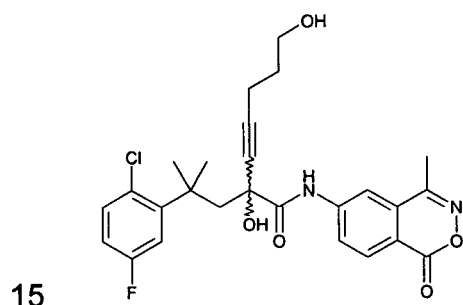


nBuLi (0.7 ml, 1.6M in hexane) was added to a solution of 1-hexyne (0.5 ml) in THF (4 ml) at -78°C . The mixture was stirred at -78°C for 20 min, 6-[4-(benzo[1,3]dioxol-4-yl)-4-methyl-2-oxoaleroylamino]-4-methyl-2,3-benzoxazin-1-one (192 mg) was added, and the mixture was stirred at -78°C for 4 h. Water was then added and the mixture was allowed to reach room temp. Extraction with ethyl acetate, washing with saturated sodium chloride solution, drying over sodium sulphate and purification by column chromatography on silica gel resulted in 82 mg of a white foam which was then converted by preparative chiral HPLC (Chiralpak AD 250 x 10 mm, eluent:

acetonitrile/water 55/45 v/v, flow rate 4.7 ml/min, temperature 40°C, retention times: 12.2 min (+)-enantiomer, 15.7 min (-)-enantiomer) into the compounds (-)-6-{2-[2-(2,3-(methylenedioxy)phenyl)-2-methylpropyl]-2-hydroxyoct-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one (Example 1) and (+)-6-{2-[2-(2,3-(methylenedioxy)phenyl)-2-methylpropyl]-2-hydroxyoct-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one (Example 2).

¹H-NMR (ppm, CDCl₃, 400 MHz): 0.91 (t, J = 7.2 Hz, 3H, CH₃), 1.32 – 1.49 (m, 4H), 1.55 (s, 3H), 1.58 (s, 3H), 2.17 (t, J = 7.2 Hz, 2H), 2.56 (s, 3H, CH₃), 2.59 (d, J = 14.4 Hz, 1H), 2.74 (d, J = 14.8 Hz, 1H), 2.80 (s, 1H, OH), 5.94 – 5.96 (m, 2H), 6.46 – 6.49 (m, 1H), 6.64 (t, J = 7.8 Hz, 1H), 7.47 – 7.49 (m, 1H), 8.25 – 8.28 (m, 1H), 8.76 (s, 1H, NH). C₂₈H₃₀N₂O₆ (490.6):

***rac*-6-{2-[2-(2-Chloro-5-fluorophenyl)-2-methylpropyl]-2,7-dihydroxyhept-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one 3**

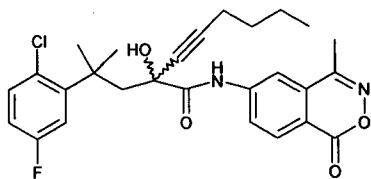


Stage A: Reaction of 5-(*tert*-butyldimethylsilyloxy)pent-1-yne (531 mg), *n*BuLi (0.7 ml, 1.6 M in hexane) and 6-[4-(2-chloro-5-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (207 mg) at -78°C as described for Example 1 gave, after column chromatography on silica gel, a colourless oil (86 mg).

20 Stage B: The resulting oil was stirred in THF (3 ml) at room temp. under argon (3 h). Addition of water, extraction with ethyl acetate and washing with saturated brine were followed by drying with sodium sulphate. Purification by column chromatography on silica gel led to the title compound as a white foam (43 mg).

¹H-NMR (ppm, CDCl₃, 400 MHz): 1.58 (s, 3H, Me), 1.59 (s, 3H, Me), 1.71 – 1.74 (m, 2H, CH₂), 2.2 – 2.3 (m, 2H), 2.56 (s, 3H, CH₃), 2.75 (d, J = 15.2 Hz, 1H, CH), 2.92 (d, J = 14.8 Hz, 1H, CH), 3.26 (s, 1H, OH), 3.74 – 3.78 (m, 2H), 6.67 – 6.78 (m, 1H), 7.09 – 7.19 (m, 2H), 7.66 – 7.69 (m, 2H), 8.20 – 8.21 (m, 1H), 8.27 – 8.29 (m, 1H), 8.99 (s, 1H, NH). C₂₆H₂₆ClFN₂O₅ (501.0): LC-MS: *m/z* = 501 [M + H⁺].

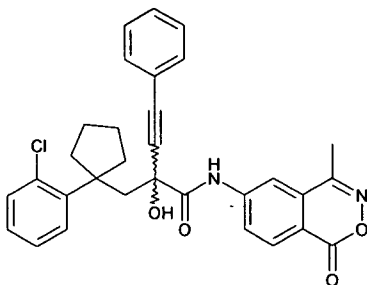
rac-6-{2-[2-(2-Chloro-5-fluorophenyl)-2-methylpropyl]-2-hydroxyoct-3-ynoyl}-4-methyl-2,3-benzoxazin-1-one 4



Reaction of 1-hexyne (0.6 ml), nBuLi (0.7 ml, 1.6 M in hexane) and 6-[4-(2-chloro-5-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (207 mg) at -78°C as described for Example 1 gave, after column chromatography on silica gel and preparative thin-layer chromatography a viscous oil (12 mg).

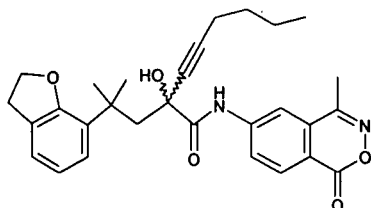
¹H-NMR (ppm, CDCl₃, 400 MHz): 0.90 (t, J = 7.2 Hz, 3H, Me), 1.32 – 1.47 (m, 4H), 1.57 (s, 3H, Me), 1.62 (s, 3H, Me), 2.13 (t, J = 7.2 Hz, CH₂C≡C), 2.56 (s, 3H, Me), 2.81 – 2.95 (m, 3H), 6.68 – 6.71 (m, 1H), 7.11 – 7.17 (m, 2H), 7.56 – 7.58 (m, 1H), 8.21 (d, J = 2.0 Hz, 1H), 8.29 (d, J = 12.6 Hz, 1H), 8.73 (br. s., 1H, NH). C₂₇H₂₈ClFN₂O₄ (499.0): LC-MS: m/z = 499 [M + H⁺].

rac-6-{2-[(2-Chlorophenyl)cyclopentyl]methyl-2-hydroxy-4-phenylbut-3-ynoyl-amino}-4-methyl-2,3-benzoxazin-1-one 5



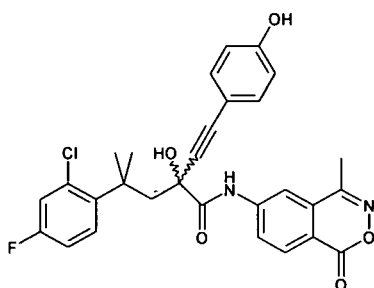
Lithiumphenylacetylide (0.65 ml, 1M in THF) was added to 6-{3-[1-(2-chlorophenyl)-cyclopentyl]-2-oxopropionylamino}-4-methyl-2,3-benzoxazin-1-one (110 mg) at -78°C and allowed to reach room temperature under argon during the night. Working up as described for Example 1 and column chromatography on silica gel resulted in the title compound as a foam (54 mg) after oil-pump drying. ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.59 – 1.85 (m, 5H), 2.18 – 2.35 (m, 3H), 2.54 (s, 3H, Me), 2.7 – 3.09 (3H), 6.94 – 7.58 (m, 10H), 8.18 (d, J = 1.1 Hz), 8.25 (d, J = 8.6 Hz, 1H), 8.81 (br. s., 1H, NH). C₃₁H₂₇ClN₂O₄ (526.0): HPLCMS: m/z = 526 [M], purity 97%.

6-{2-[2-(2,3-Dihydro-7-benzofuranyl)-2-methylpropyl]-2-hydroxy-3-octynoylamino}-4-methyl-2,3-benzoxazin-1-one 6



Reaction of 1-hexyne (0.4 ml), nBuLi (0.7 ml, 1.6 M in hexane) and 6-[4-(2,3-dihydro-7-benzofuranyl)-4-methyl-2-oxopentanoylamino]-4-methyl-2,3-benzoxazin-1-one (99.5 mg) at -78°C in THF (3 ml) as described for Example 1 gave, after column chromatography on silica gel and drying in vacuo, a solidified colourless oil (42 mg).
¹H NMR (ppm, CDCl₃, 400 MHz): 0.89 (t, J = 7.2 Hz, 3H, Me), 1.35 – 1.56 (m, 10H), 2.14 – 2.18 (m, 2H), 2.56 (s, 3H, Me), 2.66 (d, J = 14.8 Hz, 1H), 2.73 (d, J = 14.8 Hz, 1H), 3.0 – 3.2 (m, 2H), 3.27 (s, 1H), 4.57 (t, J = 9.3 Hz, 2H), 6.75 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 6.3 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 7.50 – 7.52 (m, 1H), 8.23 – 8.29 (m, 2H), 8.78 (br. s., NH). C₂₉H₃₂ClN₂O₅ (488): LC-MS: m/z = 489 [M + H⁺].

rac-6-{4-(2-Chloro-4-fluorophenyl)-2-hydroxy-2-[(4-hydroxyphenyl)ethynyl]-4-methylpentanoylamino}-4-methyl-2,3-benzoxazin-1-one 7



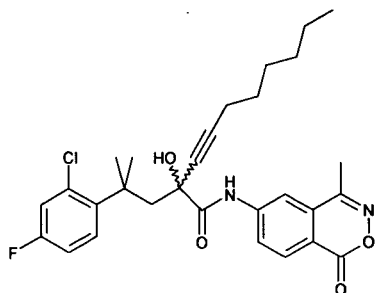
Stage A: a suspension of the compound of Example 10 (57.8 mg), triphenylphosphine (6.8 mg), copper iodide (5 mg), 4-iodophenyl acetate (51 mg), 5 mg of palladium acetate in THF (1 ml) and triethylamine (3 ml) was reacted in an ultrasonic bath under argon for 1 h. Addition of saturated aqueous ammonium chloride solution was followed by extraction with ethyl acetate and washing with water and brine. Drying with sodium sulphate was followed by concentration and purification by column chromatography on silica gel. A white solid (46.7 mg) was obtained. Stage B: A suspension of the compound from stage A (46.7 mg) and sodium bicarbonate (128 mg) in methanol was stirred at room temperature under argon for 6 h. A spatula tip of sodium bicarbonate was then added, and the mixture was stirred overnight. It was diluted with ethyl acetate,

water was added, and separation of the phases was followed by extraction with ethyl acetate. Washing of the combined organic phases with brine, drying over sodium sulphate, concentration and column chromatography on silica gel resulted in the title compound as a viscous oil (29 mg).

- 5 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.63 (s, 3H, Me), 1.69 (s, 3H, Me), 2.56 (s, 3H, Me), 2.94 – 3.01 (m, 3H), 5.48 (br. s, 1H, OH), 6.74 – 6.77 (m, 2H), 6.84 – 6.93 (m, 2H), 7.21 – 7.25 (m, 2H), 7.43 (dd, J = 9.0, 6.1 Hz, 1H), 7.57 – 7.59 (dd, J = 8.6, 2.3 Hz, 1H), 8.22 – 8.23 (m, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.80 (br. s, 1H, NH). C₂₉H₂₄ClFN₂O₅ (534.98): LC-MS: m/z = 535 [M + H⁺].

10

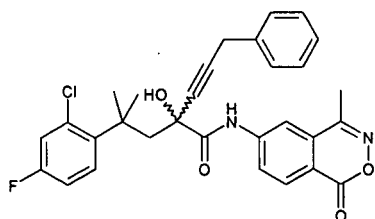
rac-6-{2-[2-(2-Chloro-4-fluorophenyl)-2-methylpropyl]-2-hydroxydec-3-ynoyl-amino}-4-methyl-2,3-benzoxazin-1-one 8



- 15 Reaction of 1-octyne (0.4 ml), nBuLi (0.6 ml, 1.6 M in hexane) and 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (110 mg) in THF (3 ml) at -78°C as described for Example 1 gave, after column chromatography on silica gel, a white solid (25 mg).

- ¹H-NMR (ppm, CDCl₃, 400 MHz): 0.87 (t, J = 7.0 Hz, 3H), 1.26 – 1.46 (m, 8H), 1.58 (s, 3H, Me), 1.63 (s, 3H, Me), 2.12 (t, J = 7.0 Hz, CH₂C≡C), 2.56 (s, 3H, Me), 2.79 – 2.91 (m, 3H), 6.92 – 6.95 (m, 2H), 7.40 (dd, J = 8.9, 6.3 Hz, 1H), 7.53 (dd, J = 8.6, 1.9 Hz, 1H), 8.21 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.71 (br. s., 1H, NH); C₂₉H₃₂ClFN₂O₄ (527.0): LC-MS: m/z = 527 [M + H⁺].
- 20

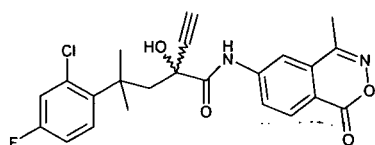
rac-6-{2-[2-(2-Chloro-4-fluorophenyl)-2-methylpropyl]-2-hydroxy-5-phenylpent-3-ynoylamino}-4-methyl-2,3-benzoxazin-1-one 9



- 5 Reaction of 3-phenyl-1-propyne (0.17 ml), nBuLi (0.51 ml, 1.6 M in hexane) and 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (140 mg) in THF (3 ml) at -78°C as described for Example 1 gave, after column chromatography on silica gel and drying in vacuo, a white foam (116 mg).

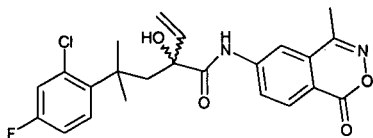
1H-NMR (ppm, CDCl₃, 400 MHz): 1.59 (s, 3H, Me), 1.61 (s, 3H, Me), 2.55 (s, 3H, Me),
 10 2.79 – 2.95 (m, 3H), 3.4 – 3.6 (m, 2H, CH₂C≡C), 6.8 – 6.93 (m, 2H), 7.23 – 7.42 (m, 7H), 8.15 (d, J = 2.3 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.64 (br. s., 1H, NH).
 C₃₀H₂₆ClFN₂O₄ (533.0): LC-MS: m/z = 533 [M + H⁺].

- 15 **rac-6-{4-(2-Chloro-4-fluorophenyl)-2-ethynyl-2-hydroxy-4-methylpentanoylamino}-4-methyl-2,3-benzoxazin-1-one 10**



- Ethynylmagnesium bromide (2.2 ml, 0.5 M in THF) was added to an ice-cold solution of
 20 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (208 mg) in THF (4 ml). Under argon, the reaction solution was allowed to reach room temperature over the course of 3 h. Working up as described in Example 1 and column chromatography on silica gel resulted in the title compound as a foam (84 mg) after oil-pump drying. 1H-NMR (ppm, CDCl₃, 400 MHz): 0.8 – 0.9 (m, 1H), 1.58 (s, 3H, Me), 1.65 (s, 3H, Me), 2.56 – 2.96 (6H), 6.86 – 6.94 (m, 2H), 7.41 (dd, J = 9.0, 6.2 Hz, 1H), 7.56 (dd, J = 8.6, 1.9 Hz, 1H), 8.19 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.63 (br. s., 1H, NH).
 25 C₂₃H₂₀ClFN₂O₄ (542.9): LC-MS: m/z = 543 [M + H⁺].

rac-6-{4-(2-Chloro-4-fluorophenyl)-2-hydroxy-4-methyl-2-vinyl-pentanoylamino}-4-methyl-2,3-benzoxazin-1-one 11

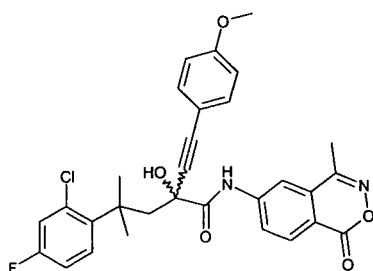


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A vinylmagnesium bromide solution (0.5 ml, 1M in THF) was injected into 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (103 mg) in THF (3 ml) at -78°C, and the mixture was allowed to reach room temp. under argon overnight. Addition of aqueous ammonium chloride solution was followed by extraction with ethyl acetate and washing with sat. sodium chloride solution. Drying with sodium sulphate was followed by concentration in a rotary evaporator and purification by column chromatography on silica gel to result in the title compound as solidified oil (18 mg). 1H-NMR (ppm, CDCl₃, 400 MHz, selected signals): 1.53 (s, 3H, Me), 1.57 (s, 3H, Me), 2.35 (s, 1H), 2.56 (s, 3H, Me), 2.74 (d, J = 15.3 Hz, 1H), 2.89 (d, J = 15.3 Hz, 1H), 5.15 (d, J = 10.5 Hz, 1H), 5.27 (d, J = 17.6 Hz, 1H), 6.10 (dd, J = 17.2, 10.6 Hz, 1H), 6.81 – 6.86 (m, 1H),

rac-6-{4-(2-Chloro-4-fluorophenyl)-2-hydroxy-2-[(4-methoxyphenyl)ethynyl]-4-methylpentanoylamino}-4-methyl-2,3-benzoxazin-1-one 12

20



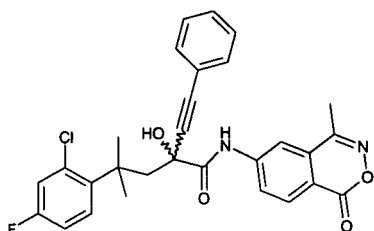
Reaction of 4-methoxyphenylacetylene (0.4 ml), nBuLi (0.6 ml, 1.6 M in hexane) and 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (110 mg) at -78°C as described for Example 1 gave, after column chromatography on silica gel, the title compound as a white solid (44 mg).

25

1H-NMR (ppm, CDCl₃, 400 MHz): 1.63 (s, 3H, Me), 1.69 (s, 3H, Me), 2.91 – 3.01 (m, 3H), 3.81 (s, 3H, Me), 6.81 – 6.94 (m, 3H), 7.25 – 7.29 (m, 3H), 7.43 (dd, J = 8.4, 6.3

Hz, 1H), 7.58 (dd, J = 8.6, 2.3 Hz, 1H), 8.24 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.79 (br. s., 1H, NH). C₃₀H₂₆ClFN₂O₅ (549.0): LC-MS: m/z = 549 [M + H⁺].

5 **rac-6-{4-(2-Chloro-4-fluorophenyl)-2-hydroxy-4-methyl-2-(phenylethynyl)-pentanoylamino}-4-methyl-2,3-benzoxazin-1-one 13**

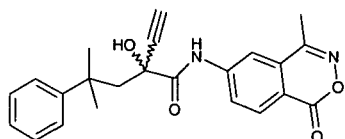


10 Lithium phenylacetylide (0.65 ml, 1M in THF) was added to 6-[4-(2-chloro-4-fluorophenyl)-4-methyl-2-oxovaleroylamino]-4-methyl-2,3-benzoxazin-1-one (136 mg) at -78°C and the mixture was stirred at -78°C under argon for 2.5 h. Working up as described for Example 1 and column chromatography on silica gel resulted in the title compound as a white foam (102 mg) after oil-pump drying.

1H-NMR (ppm, CDCl₃, 400 MHz): 1.64 (s, 3H, Me), 1.70 (s, 3H, Me), 2.57 (s, 3H, Me),
15 2.92 – 3.03 (m, 3H), 6.82 – 6.86 (m, 1H), 6.91 – 6.93 (m, 1H), 7.30 – 7.36 (m, 5H), 7.44 (dd, J = 9.0, 6.2 Hz, 1H), 7.59 (dd, J = 8.6, 2.0 Hz, 1H), 8.23 (d, J = 2.0 Hz, 1H), 8.31 (d, J = 8.2 Hz, 1H), 8.79 (br. s., NH); C₂₉H₂₄ClFN₂O₄ (519.0): HPLC-MS: m/z = 518 [M].

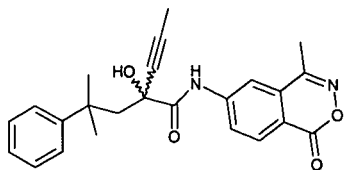
20 The compounds 14 and 15 were prepared in analogy to Example 10 from 6-(4-methyl-4-phenyl-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one and the alkynyl-magnesium halide:

25 **rac-6-[2-Ethynyl-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 14**



1H-NMR (ppm, CDCl₃, 400 MHz): 1.42 (3H), 1.59 (3H), 2.57 (3H), 2.64 (4H), 7.15 (1H),
30 7.31 (2H), 7.46 (2H), 7.58 (1H), 8.25 (1H), 8.30 (1H), 8.81 (1H).

rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-propynylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 15

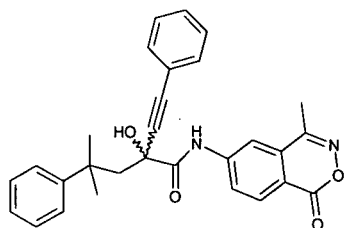


- 5 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.42 (3H), 1.59 (3H), 2.50-2.65 (6H), 7.11 (1H), 7.30 (2H), 7.43 (2H), 7.58 (1H), 8.29 (2H), 8.85 (1H).

The compounds 15-28 were prepared in analogy to Example 1 from 6-(4-methyl-4-phenyl-2-oxoaleroylamino)-4-methyl-2,3-benzoxazin-1-one and the respective lithium
10 arylacetylide:

rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-(phenylethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 16

15

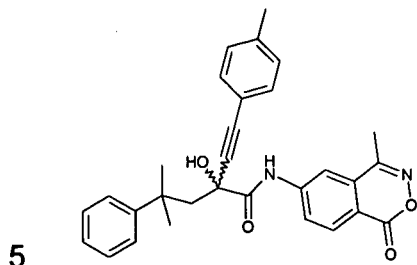


- ¹H-NMR (ppm, CDCl₃, 300 MHz): 1.47 (3H), 1.65 (3H), 2.57 (3H), 2.62-2.78 (3H), 7.15 (1H), 7.27-7.37 (5H), 7.40 (2H), 7.50 (2H), 7.59 (1H), 8.29 (2H), 8.90 (1H).

20

(+)-6-[2-Hydroxy-4-methyl-2-[(4-methylphenyl)ethynyl]-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 17a and

(-)-6-[2-Hydroxy-4-methyl-2-[(4-methylphenyl)ethynyl]-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 17b

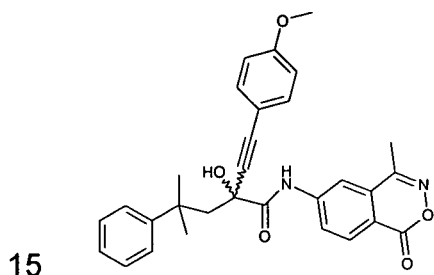


¹H-NMR (ppm, CDCl₃, 300 MHz): 1.48 (3H), 1.64 (3H), 2.36 (3H), 2.57 (3H), 2.60-2.80 (3H), 7.08-7.20 (3H), 7.30 (4H), 7.49 (2H), 7.60 (1H), 8.29 (2H), 8.90 (1H).

16a: [α]₂₀^D: +28.4° (CHCl₃, 1.03 g/100 ml; λ =589 nm)

10 **16b:** [α]₂₀^D: -28.6° (CHCl₃, 1.01 g/100 ml; λ =589 nm)

rac-6-[2-Hydroxy-2-[(4-methoxyphenyl)ethynyl]-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 18



¹H-NMR (ppm, CDCl₃, 300 MHz): 1.47 (3H), 1.63 (3H), 2.56 (3H), 2.60-2.78 (3H), 3.80 (3H), 6.81 (2H), 7.13 (1H), 7.25-7.38 (4H), 7.48 (2H), 7.60 (1H), 8.28 (2H), 8.89 (1H).

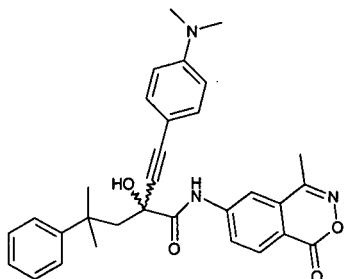
20 **(+)-6-[2-Hydroxy-2-[(4-methoxyphenyl)ethynyl]-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 18a and**
(-)-6-[2-Hydroxy-2-[(4-methoxyphenyl)ethynyl]-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 18b

25 The racemic mixture which was described in example 18 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 18a and 18b.

18a: [α]₂₀^D: + 29.3° (CHCl₃, 1.12 g/100 ml; λ =589 nm)

18b: [α]₂₀^D: - 30.0° (CHCl₃, 1.14 g/100 ml; λ =589 nm)

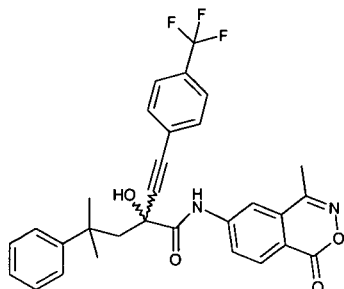
rac-6-[2-Hydroxy-2-[(4-(N,N-dimethylamino)phenyl)ethynyl]-4-methyl-4-phenyl-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 19



5

¹H-NMR (ppm, CDCl₃, 400 MHz): 1.48 (3H), 1.62 (3H), 2.57 (3H), 2.60-2.75 (3H), 2.98 (6H), 6.58 (2H), 7.12 (1H), 7.23-7.38 (4H), 7.48 (2H); 7.57 (1H), 8.28 (2H), 8.90 (1H).

10 rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 20



15 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.48 (3H), 1.63 (3H), 2.57 (3H), 2.64-2.80 (3H), 7.17 (1H), 7.33 (2H), 7.48 (4H), 7.56 (2H), 7.61 (1H), 8.30 (2H), 8.92 (1H).

(+)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 20a and

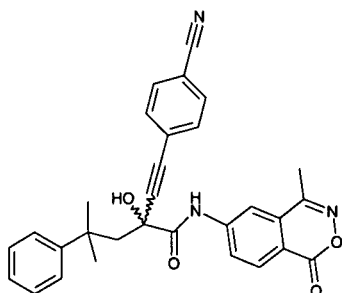
20 (-)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 20b

The racemic mixture which was described in example 20 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 20a and 20b.

20a : [α]_D²⁰: + 19.9° (CHCl₃, 1.05 g/100 ml; λ=589 nm)

25 **20b** : [α]_D²⁰: - 20.4° (CHCl₃, 1.01 g/100 ml; λ=589 nm)

rac-6-[2-[(4-Cyanophenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 21



5

¹H-NMR (ppm, CDCl₃, 400 MHz): 1.50 (3H), 1.62 (3H), 2.57 (3H), 2.63-2.82 (3H), 7.18 (1H), 7.35 (2H), 7.48 (4H), 7.55-7.68 (2H), 7.62 (1H), 8.30 (2H), 8.94 (1H).

- 10 **(+)-6-[2-[(4-Cyanophenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 21a and**
(-)-6-[2-[(4-Cyanophenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 21b

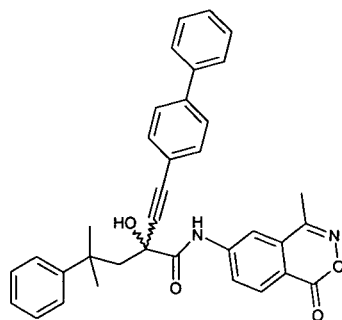
The racemic mixture which was described in example 21 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 21a and 21b.

15

21a : $[\alpha]_{20}^D$: + 26.6° (CHCl₃, 1.12 g/100 ml; λ=589 nm)

21b : $[\alpha]_{20}^D$: - 26.8° (CHCl₃, 1.02 g/100 ml; λ=589 nm)

- 20 **rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-phenylphenyl)ethynyl]pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 22**



- 25 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.50 (3H), 1.68 (3H), 2.58 (3H), 2.64-2.81 (3H), 7.18

(1H), 7.30-7.40 (3H), 7.41-7.61 (11H), 8.30 (2H), 8.92 (1H).

(+)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-phenylphenyl)ethynyl]pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 22a and

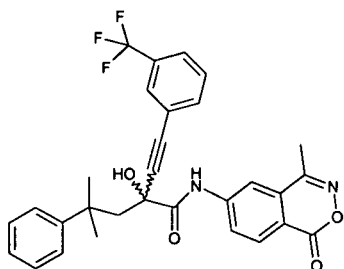
- 5 **(-)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(4-phenylphenyl)ethynyl]pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 22b**

The racemic mixture which was described in example 22 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 22a and 22b.

22a : $[\alpha]_{20}^D$: + 38.4° (CHCl₃, 1.06 g/100 ml; λ =589 nm)

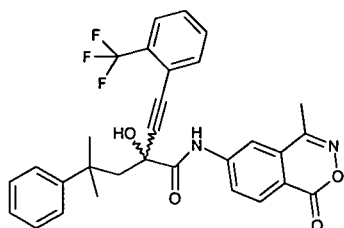
- 10 **22b** : $[\alpha]_{20}^D$: - 30.6° (CHCl₃, 1.12 g/100 ml; λ =589 nm)

- 15 **rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(3-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 23**



- 20 **1H-NMR** (ppm, CDCl₃, 300 MHz): 1.52 (3H), 1.68 (3H), 2.60 (3H), 2.65-2.88 (3H), 7.21 (1H), 7.49 (2H), 7.42-7.70 (7H), 8.34 (2H), 8.96 (1H).

- 25 **rac-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(2-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 24**



1H-NMR (ppm, CDCl₃, 600 MHz): 1.52 (3H), 1.65 (3H), 2.62 (3H), 2.69 (1H), 2.78 (1H),

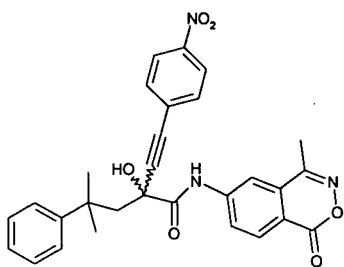
2.91 (1H), 7.11 (1H), 7.32 (3H), 7.51 (3H), 7.57 (2H), 7.70 (1H), 8.20 (1H), 8.45 (1H), 8.75 (1H).

- 5 **(+)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(2-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 24a** and
(-)-6-[2-Hydroxy-4-methyl-4-phenyl-2-[(2-trifluoromethylphenyl)ethynyl]-pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 24b

The racemic mixture which was described in example 24 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 24a and 24b.

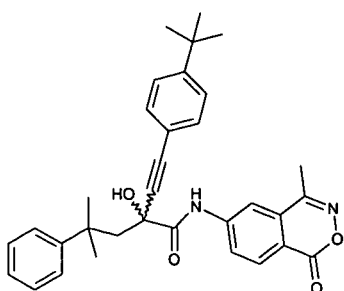
- 10 **24a** : $[\alpha]_{20}^D$: + 21.3° (CHCl₃, 1.00 g/100 ml; λ =589 nm)
24b : $[\alpha]_{20}^D$: - 19.4° (CHCl₃, 1.00 g/100 ml; λ =589 nm)

- 15 **rac-6-[2-Hydroxy-4-methyl-2-[(4-nitrophenyl)ethynyl]-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 25**



- 20 ¹H-NMR (ppm, CDCl₃, 600 MHz): 1.47 (3H), 1.62 (3H), 2.55 (3H), 2.79 (1H), 2.81 (2H), 7.18 (1H), 7.34 (2H), 7.50 (4H), 7.63 (1H), 8.17 (2H), 8.80 (2H), 8.94 (1H).

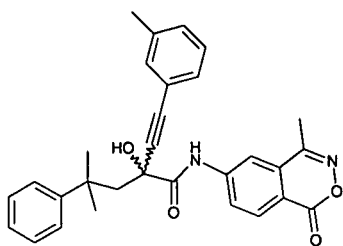
- 25 **rac-6-[2-[[4-(1,1-Dimethylethyl)phenyl]ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 26**



¹H-NMR (ppm, CDCl₃, 300 MHz): 1.32 (9H), 1.51 (3H), 1.68 (3H), 2.62 (3H), 2.65-2.82 (3H), 7.18 (1H), 7.30-7.40 (6H), 7.52 (2H), 7.63 (1H), 8.32 (2H), 8.93 (1H).

5

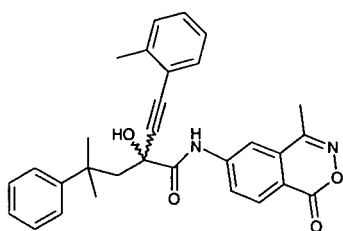
rac-6-[2-Hydroxy-4-methyl-2-[(3-methylphenyl)ethynyl]-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 27



10

¹H-NMR (ppm, CDCl₃, 400 MHz): 1.47 (3H), 1.63 (3H), 2.30 (3H), 2.58 (3H), 2.62-2.80 (3H), 7.12-7.26 (5H), 7.32 (2H), 7.50 (2H), 7.60 (1H), 8.30 (2H), 8.90 (1H).

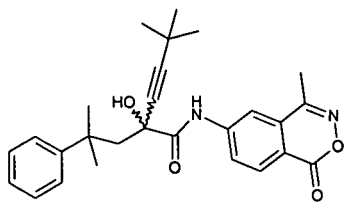
15 **rac-6-[2-Hydroxy-4-methyl-2-[(2-methylphenyl)ethynyl]-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 28**



20 ¹H-NMR (ppm, CDCl₃, 300 MHz): 1.47 (3H), 1.65 (3H), 2.38 (3H), 2.58 (3H), 2.62-2.80 (3H), 7.08-7.42 (7H), 7.49 (2H), 7.60 (1H), 8.22-8.36 (2H), 8.90 (1H).

rac-6-[2-(3,3-Dimethylbutynyl)-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 29

25

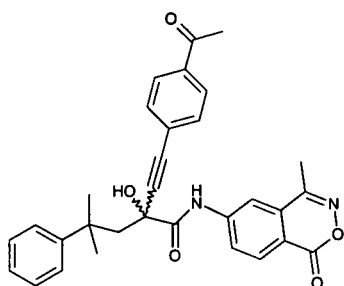


¹H-NMR (ppm, CDCl₃, 300 MHz): 1.20 (9H), 1.43 (3H), 1.60 (3H), 2.46 (1H), 2.50-2.63 (5H), 7.11 (1H), 7.28 (2H), 7.43 (2H), 7.54 (1H), 8.22 (1H), 8.29 (1H), 8.32 (1H).

5

The following compound was prepared in analogy to Example 7 from the compound described in Example 13 and 4'-iodoacetophenone:

- 10 **rac-6-[2-[(4-Acetylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 30**



- 15 ¹H-NMR (ppm, CDCl₃, 300 MHz): 1.48 (3H), 1.63 (3H), 2.56 (3H), 2.60 (3H), 2.63-2.82 (3H), 7.18 (1H), 7.33 (2H), 7.40-7.56 (4H), 7.62 (1H), 7.90 (2H), 8.30 (2H), 8.93 (1H).

(+)-6-[2-[(4-Acetylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 30a and

- 20 **(-)-6-[2-[(4-Acetylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 30b**

The racemic mixture which was described in example 30 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 30a and 30b.

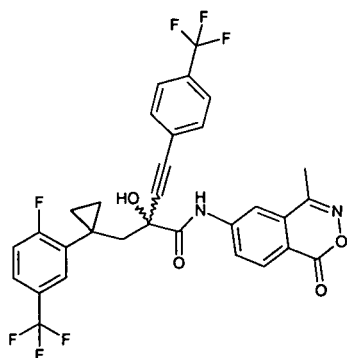
30a : [α]₂₀^D: + 31.3° (CHCl₃, 1.09 g/100 ml; λ=589 nM)

- 25 **30b** : [α]₂₀^D: - 28.4° (CHCl₃, 1.09 g/100 ml; λ=589 nM)

The compounds 30 and 31 were prepared in analogy to Example 1 from 6-[3-[1-(2-fluoro-5-trifluoromethylphenyl)cyclopropyl]-2-oxopropionylamino]-4-methyl-2,3-benzoxazin-1-one

5

rac-6-[2-[(2-Fluoro-5-trifluoromethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluoromethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 31



10

¹H-NMR (ppm, CDCl₃, 400 MHz): 0.90 (1H), 1.00-1.15 (3H), 2.51 (1H), 2.55 (3H), 2.68 (1H), 3.18 (1H), 7.01 (1H), 7.30 (1H), 7.41 (2H), 7.56 (2H), 7.63 (1H), 7.68 (1H), 8.19 (1H), 8.31 (1H), 8.98 (1H).

15

(+)-6-[2-[(2-Fluor-5-trifluormethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluormethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 31a and (-)-6-[2-[(2-Fluor-5-trifluormethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluormethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 31b

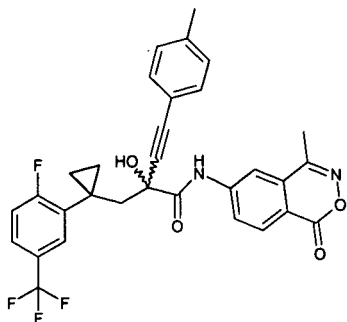
The racemic mixture which was described in example 31 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 31a and 31b.

31a : [α]₂₀^D: + 2.3° (CHCl₃, 1.00 g/100 ml; λ=589 nm)

31b : [α]₂₀^D: - 1.9° (CHCl₃, 1.00 g/100 ml; λ=589 nm)

25

rac-6-[2-[(2-Fluoro-5-trifluoromethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-ynoylamino]-4-methyl-2,3-benzoxazin-1-one 32



5

¹H-NMR (ppm, CDCl₃, 400 MHz): 0.88 (1H), 0.98-1.13 (3H), 2.34 (3H), 2.44 (1H), 2.55 (3H), 2.70 (1H), 3.02 (1H), 7.01 (1H), 7.10 (2H), 7.22 (2H), 7.30 (1H), 7.64 (2H), 8.19 (1H), 8.31 (1H), 8.98 (1H).

- 10 **(+)-6-[2-[(2-Fluor-5-trifluormethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 32a and (-)-6-[2-[(2-Fluor-5-trifluormethylphenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 32b**

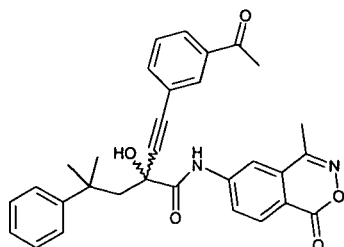
15 The racemic mixture which was described in example 32 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 32a and 32b.

32a : [α]_D²⁰: + 8.6° (CHCl₃, 1.00 g/100 ml; λ=589 nm)

32b : [α]_D²⁰: - 8.7° (CHCl₃, 1.00 g/100 ml; λ=589 nm)

20 The following compound was prepared in analogy to example 7 from compound which was described in example 14 and 3'-Iodacetophenon:

rac-6-[2-[(3-Acetylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 33

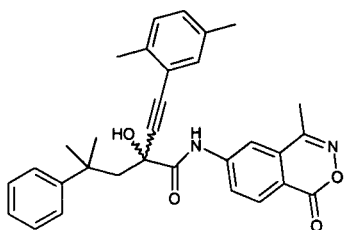


25 ¹H-NMR (ppm, CDCl₃, 300 MHz): 1.49 (3H), 1.63 (3H), 2.57 (6H), 2.62-2.81 (3H), 7.16 (8H), 7.28-7.70 (7H), 7.90-8.00 (2H), 8.30 (2H), 8.94 (1H).

Compounds 34 and 35 were prepared in analogy to example 1 from 6-(4-Methyl-4-phenyl-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one and the according Lithium arylacetylide.

5

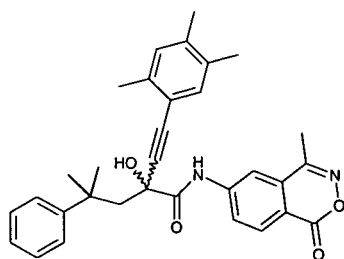
rac-6-[2-[(2,5-Dimethylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 34



10

¹H-NMR (ppm, CDCl₃, 400 MHz): 1.49 (3H), 1.62 (3H), 2.27 (3H), 2.33 (3H), 2.57 (3H), 2.65-2.78 (3H), 7.03 (2H), 7.13 (2H), 7.30 (2H), 7.50 (2H), 7.61 (1H), 8.22 (1H), 8.30 (1H), 8.89 (1H).

15 **rac-6-[2-[(2,4,5-Trimethylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 35**



20 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.47 (3H), 1.64 (3H), 2.18 (3H), 2.21 (3H), 2.30 (3H), 2.56 (3H), 2.65-2.77 (3H), 6.93 (1H), 7.12 (2H), 7.30 (2H), 7.48 (2H), 7.59 (1H), 8.22 (1H), 8.29 (1H), 8.90 (1H).

25 **(+)-6-[2-[(2,4,5-Trimethylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 35a and (-)-6-[2-[(2,4,5-Trimethylphenyl)ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 35b**

The racemic mixture which was described in example **35** was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers **35a** and **35b**.

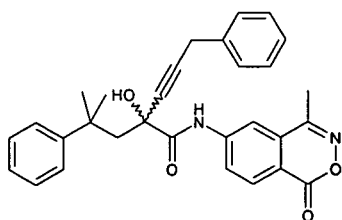
35a : $[\alpha]_{20}^D$: + 30.6° (CHCl₃, 0.97 g/100 ml; λ =589 nm)

35b : $[\alpha]_{20}^D$: - 28.0° (CHCl₃, 0.96 g/100 ml; λ =589 nm)

5

The following compound was prepared in analogy to example 9 from 3-Phenyl-1-propine, nBuLi and 6-(4-Methyl-4-phenyl-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one:

10 **rac-6-{2-(2-phenyl)-2-methylpropyl}-2-hydroxy-5-phenylpent-3-inoylamino}-4-methyl-2,3-benzoxazin-1-one **36****

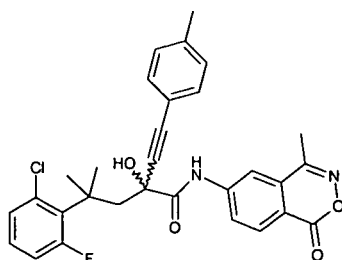


15 ¹H-NMR (ppm, CDCl₃, 400 MHz): 1.42 (3H), 1.53 (3H), 2.55-2.70 (6H), 3.58 (2H), 7.11 (1H), 7.20-7.35 (7H), 7.41 (2H), 7.48 (1H), 8.20 (1H), 8.28 (1H), 8.80 (1H).

Compounds 37 and 38 were prepared in analogy to example 1 from 6-(4-Methyl-4-(2-chlor-6-fluorophenyl)-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one and the according Lithium arylacetylide.

20

rac-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorophenyl)-2-(4-methylphenyl)ethynyl]pentanoylamino}-4-methyl-2,3-benzoxazin-1-one **37**



25

¹H-NMR (ppm, CDCl₃, 300 MHz): 1.73 (3H), 1.82 (3H), 2.33 (3H), 2.57 (3H), 2.88-3.02 (3H), 6.75-6.96 (2H), 7.01 (1H), 7.09 (2H), 7.27 (2H), 7.60 (1H), 8.22-8.35 (2H), 8.96 (1H).

(+)-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorphenyl)-2-(4-methylphenyl-ethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 37a and

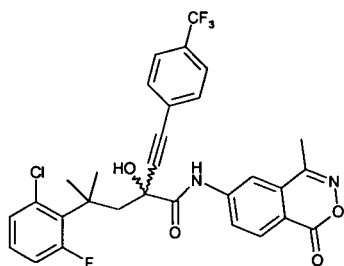
(-)-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorphenyl)-2-(4-methylphenyl-ethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 37b

The racemic mixture which was described in example 37 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 37a and 37b.

37a : $[\alpha]_{20}^D$: + 21.5° (CHCl₃, 1.00 g/100 ml; λ =589 nm)

37b : $[\alpha]_{20}^D$: - 21.0° (CHCl₃, 1.04 g/100 ml; λ =589 nm)

rac-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorphenyl)-2-(4-(trifluormethyl)phenyl-ethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 38



¹H-NMR (ppm, CDCl₃, 400 MHz): 1.60 (3H), 1.93 (3H), 2.36 (1H), 2.56-2.72 (5H), 7.04 (1H), 7.14 (2H), 7.45 (2H), 7.53 (2H), 7.80 (1H), 8.35-8.45 (2H), 8.90 (1H).

(+)-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorphenyl)-2-(4-(trifluormethyl)phenyl-ethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 38a and

(-)-6-[2-Hydroxy-4-methyl-4-(2-chlor-6-fluorphenyl)-2-(4-(trifluormethyl)phenyl-ethynyl)pentanoylamino]-4-methyl-2,3-benzoxazin-1-one 38b

The racemic mixture which was described in example 38 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 38a and 38b.

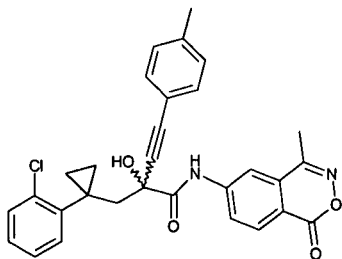
38a : $[\alpha]_{20}^D$: + 143.2° (CHCl₃, 1.05 g/100 ml; λ =589 nm)

38b : $[\alpha]_{20}^D$: - 137.8° (CHCl₃, 1.12 g/100 ml; λ =589 nm)

Compounds 39 and 40 were prepared in analogy to example 1 from 6-(4-Methyl-4-(2-chlorophenyl)-2-oxovaleroylamino)-4-methyl-2,3-benzoxazin-1-one and the according Lithium arylacetylide.

rac-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 39

5



¹H-NMR (ppm, CDCl₃, 400 MHz): 0.84 (1H), 1.00 (1H), 1.08-1.22 (2H), 2.36 (3H), 2.53 (3H), 2.90 (1H), 7.03-7.18 (4H), 7.23-7.38 (3H), 7.50 (1H), 7.60 (1H), 8.22 (1H), 8.29 (1H), 8.91 (1H).

10

(+)-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 39a and

(-)-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-methylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 39b

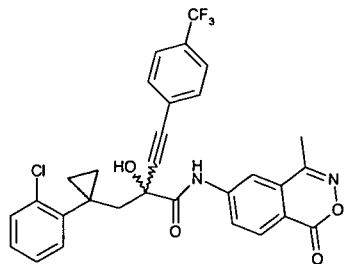
15 The racemic mixture which was described in example 39 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 39a and 39b.

39a : [α]₂₀^D: + 30.8° (CHCl₃, 1.00 g/100 ml; λ =589 nm)

39b : [α]₂₀^D: - 28.3° (CHCl₃, 1.00 g/100 ml; λ =589 nm)

20

rac-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluoromethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 40



25

¹H-NMR (ppm, CDCl₃, 300 MHz): 0.91 (1H), 1.02 (1H), 1.08-1.25 (2H), 2.53 (3H), 3.00 (1H), 7.02-7.18 (2H), 7.28 (1H), 7.42-7.54 (3H), 7.55-7.67 (3H), 8.22 (1H), 8.32 (1H), 8.91 (1H).

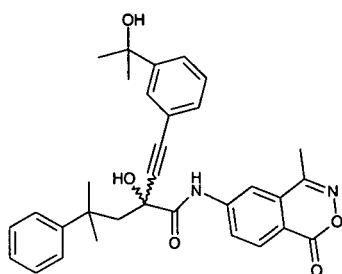
- 5 **(+)-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluoromethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 40a and (-)-6-[2-(2-Chlorophenyl)cyclopropylmethyl]-2-hydroxy-4-(4-trifluoromethylphenyl)but-3-inoylamino]-4-methyl-2,3-benzoxazin-1-one 40b**

The racemic mixture which was described in example 40 was separated by preparative chiral HPLC (column Chiralpak AD 250x10 mm) into the enantiomers 40a and 40b.

40a : $[\alpha]_{20}^D$: + 20.9° (CHCl₃, 1.06 g/100 ml; λ=589 nm)

40b : $[\alpha]_{20}^D$: - 20.6° (CHCl₃, 1.05 g/100 ml; λ=589 nm)

- 15 **rac-6-[2-[[3-(1-Hydroxy-1-methylethyl)phenyl]ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 41**



- 20 59 µl of 3 molar solution of Methylmagnesium chloride was diluted with 1 ml of pure Tetrahydrofuran. The solution was cooled to -70°C and a solution of 30 mg of the compound which was described in example 33 in 0,5 ml of pure Tetrahydrofuran was added. After stirring for 2,5 hours at -70°C the mixture was given to a saturated solution of ammonium chloride. After extracting the mixture with Ethyl acetate the combined organic phases were washed with saturated sodium chloride and dried over sodium sulphate. After column chromatography 16 mg of the product was obtained.

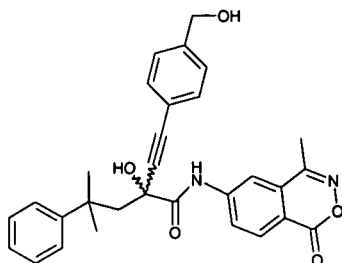
¹H-NMR (ppm, CDCl₃, 400 MHz): 1.46 (3H), 1.53 (6H), 1.62 (3H), 1.80 (1H), 2.55 (3H), 2.65-2.90 (3H), 7.12 (1H), 7.30 (3H), 7.40-7.52 (3H), 7.53 (1H), 7.60 (1H), 8.27 (2H), 8.95 (1H).

30

The following compound was prepared in analogy to example 7 from the compound which was described in example 14 and 4-Iodobenzylalcohol:

rac-6-[2-[[4-(Hydroxymethyl)phenyl]ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 42

5



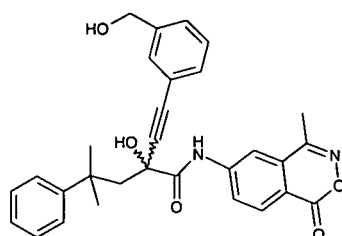
1H-NMR (ppm, CDCl₃, 300 MHz): 1.47 (3H), 1.60 (3H), 1.80 (1H), 2.57 (3H), 2.62-2.83 (3H), 4.68 (2H), 7.13 (1H), 7.25-7.43 (6H), 7.48 (2H), 7.59 (1H), 8.25-8.32 (2H), 8.91 (1H).

10

The following compound was prepared in analogy to example 7 from the compound which was described in example 14 and 4-Iodobenzylalcohol:

rac-6-[2-[[3-(Hydroxymethyl)phenyl]ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 43

15



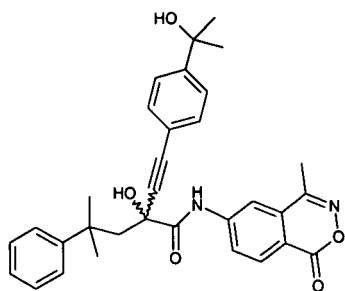
1H-NMR (ppm, CDCl₃, 400 MHz): 1.48 (3H), 1.62 (3H), 1.79 (1H), 2.57 (3H), 2.62-2.80 (3H), 4.68 (2H), 7.15 (1H), 7.25-7.39 (5H), 7.40 (1H), 7.49 (2H), 7.60 (1H), 8.29 (2H), 8.91 (1H).

20

The following compound was prepared in analogy to example 41 from the compound which was described in example 30 and a solution of Methyl magnesium chloride:

rac-6-[2-[[4-(1-Hydroxy-1-methylethyl)phenyl]ethynyl]-2-hydroxy-4-methyl-4-phenylpentanoylamino]-4-methyl-2,3-benzoxazin-1-one 44

25



1H-NMR (ppm, CDCl₃, 400 MHz): 1.47 (3H), 1.55 (6H), 1.62 (3H), 1.70 (1H), 2.55 (3H),
2.60-2.80 (3H), 7.14 (1H), 7.28-7.40 (4H), 7.41 (2H), 7.48 (2H), 7.60 (1H), 8.25-8.32
5 (2H), 8.90 (1H).

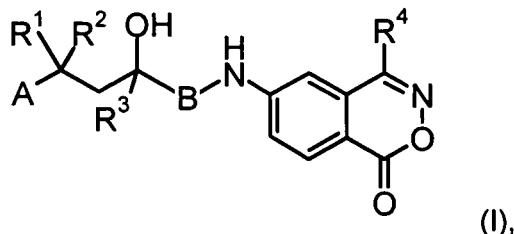
10

15

20

Claims

1. Compounds of the general formula I



5

R^1 and R^2 are independently of one another a hydrogen atom, a linear or nonlinear, branched or unbranched C_1 - C_5 -alkyl group, further forming together with the C atom of the chain a ring having a total of 3-7 members,

10

R^3 is a radical $C\equiv C-R^a$, where

15

R^a is a hydrogen or a C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl, C_2 - C_8 -alkynyl, C_3 - C_{10} -cycloalkyl, heterocycloalkyl optionally substituted one or more times, identically or differently, by K, or an aryl or heteroaryl optionally substituted one or more times, identically or differently by L,

20

K is a cyano, halogen, hydroxy, nitro, $-C(O)R^b$, CO_2R^b , $-O-R^b$, $-S-R^b$, $SO_2NR^cR^d$, $-C(O)-NR^cR^d$, $-OC(O)-NR^cR^d$, $-C=NOR^b$ $-NR^cR^d$ or C_3 - C_{10} -cycloalkyl, heterocycloalkyl optionally substituted one or more times, identically or differently, by M, or aryl or heteroaryl optionally substituted one or more times by L,

25

L is C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl, C_2 - C_8 -alkynyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -perfluoroalkoxy, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, $(CH_2)_p$ - C_3 - C_{10} -cycloalkyl, $(CH_2)_p$ -heterocycloalkyl, $(CH_2)_p$ CN, $(CH_2)_p$ Hal, $(CH_2)_p$ NO₂, $(CH_2)_p$ - C_6 - C_{12} -aryl, $(CH_2)_p$ -heteroaryl, $-(CH_2)_pPO_3(R^b)_2$,

30

$-(CH_2)_pNR^cR^d$, $-(CH_2)_pNR^cCOR^b$, $-(CH_2)_pNR^cSR^b$, $-(CH_2)_pNR^cS(O)R^b$, $-(CH_2)_pNR^cS(O)_2R^b$, $-(CH_2)_pNR^cCONR^cR^d$,

5 $-(CH_2)_pNR^eCOOR^b$, $-(CH_2)_pNR^eC(NH)NR^cR^d$,
 $-(CH_2)_pNR^eCSNR^cR^d$, $-(CH_2)_pNR^eS(O)NR^cR^d$,
 $-(CH_2)_pNR^eS(O)_2NR^cR^d$, $-(CH_2)_pCOR^b$,
 $-(CH_2)_pCSR^b$, $-(CH_2)_pS(O)R^b$,
 $-(CH_2)_pS(O)(NH)R^b$, $-(CH_2)_pS(O)_2R^b$,
 $-(CH_2)_pS(O)_2NR^cR^d$, $-(CH_2)_pSO_2OR^b$,
 $-(CH_2)_pCO_2R^b$, $-(CH_2)_pCONR^cR^d$,
 $-(CH_2)_pCSNR^cR^d$, $-(CH_2)_pOR^b$, $-(CH_2)_pSR^b$, -
 10 $(CH_2)_pCR^b(OH)-R^e$, $-(CH_2)_p-C=NOR^b$,
 $-O-(CH_2)_n-O-$, $-O-(CH_2)_n-CH_2-$, $-O-CH=CH-$ or
 $-(CH_2)_{n+2}-$, where n is 1 or 2, and the terminal
 oxygen atoms and/or carbon atoms are linked
 to directly adjacent ring carbon atoms,
 M is C_1-C_6 -alkyl or a group $-COR^b$, CO_2R^b , $-O-R^b$,
 15 or $-NR^cR^d$, where

20 R^b is a hydrogen or a C_1-C_6 -alkyl, C_2-C_8 -
 alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -
 cycloalkyl, C_6-C_{12} -aryl or C_1-C_3 -
 perfluoroalkyl and
 R^c and R^d are independently of one another a
 hydrogen, C_1-C_6 -alkyl, C_2-C_8 -alkenyl,
 C_2-C_8 -alkynyl, C_3-C_{10} -cycloalkyl,
 C_6-C_{12} -aryl, $C(O)R^b$ or a hydroxy
 25 group, where if
 R^c is a hydroxy group, then R^d can only
 be a hydrogen, a C_1-C_6 -alkyl, C_2-C_8 -
 alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -
 cycloalkyl or C_6-C_{12} -aryl and vice
 30 versa, and
 R^e is a hydrogen, C_1-C_6 -alkyl, C_2-C_8 -
 alkenyl, C_2-C_8 -alkynyl, C_3-C_{10} -cyclo-
 alkyl or C_6-C_{12} -aryl, and
 p can be a number from 0-6,

35

or

- R^3 is a radical $C=C-R^gR^h$, where
 R^g and R^h are independently of one another a hydrogen or a
 C_1 - C_8 -alkyl, C_2 - C_8 -alkenyl or C_2 - C_8 -alkynyl
optionally substituted one or more times, identically
or differently, by X, in which
X is a cyano, halogen, hydroxy, nitro,
 $-C(O)R^b$, CO_2R^b , $-O-R^b$, $-C(O)-NR^cR^d$,
 $-NR^cR^d$ with the meanings already
mentioned before for R^b , R^c and R^d , and
- R^4 is a hydrogen atom, a methyl or an ethyl group or a partly or
completely fluorinated C_1 - C_3 -alkyl group,
- A is a mono- or bicyclic carbocyclic or heterocyclic aromatic ring which
may optionally be substituted one or more times by C_1 - C_8 -alkyl, C_2 - C_8 -
alkenyl, C_2 - C_8 -alkynyl, C_1 - C_6 -perfluoroalkyl, C_1 - C_6 -perfluoroalkoxy,
 C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy, $(CH_2)_p$ - C_3 - C_{10} -
cycloalkyl, $(CH_2)_p$ -heterocycloalkyl, $(CH_2)_p$ CN, $(CH_2)_p$ Hal, $(CH_2)_p$ NO₂,
 $(CH_2)_p$ - C_6 - C_{12} -aryl, $(CH_2)_p$ -heteroaryl,
 $-(CH_2)_pPO_3(R^b)_2$, $-(CH_2)_pNR^cR^d$, $-(CH_2)_pNR^cCOR^b$, $-(CH_2)_pNR^cCSR^b$,
 $-(CH_2)_pNR^cS(O)R^b$, $-(CH_2)_pNR^cS(O)_2R^b$, $-(CH_2)_pNR^cCONR^cR^d$,
 $-(CH_2)_pNR^cCOOR^b$, $-(CH_2)_pNR^cC(NH)NR^cR^d$, $-(CH_2)_pNR^cCSNR^cR^d$,
 $-(CH_2)_pNR^cS(O)NR^cR^d$, $-(CH_2)_pNR^cS(O)_2NR^cR^d$, $-(CH_2)_pCOR^b$,
 $-(CH_2)_pCSR^b$, $-(CH_2)_pS(O)R^b$, $-(CH_2)_pS(O)(NH)R^b$, $-(CH_2)_pS(O)_2R^b$,
 $-(CH_2)_pS(O)_2NR^cR^d$, $-(CH_2)_pSO_2OR^b$, $-(CH_2)_pCO_2R^b$, $-(CH_2)_pCONR^cR^d$,
 $-(CH_2)_pCSNR^cR^d$, $-(CH_2)_pOR^b$, $-(CH_2)_pSR^b$, $-(CH_2)_pCR^b(OH)-R^d$,
 $-(CH_2)_pC=NOR^b$, $-O-(CH_2)_n-O-$, $-O-(CH_2)_n-CH_2-$, $-O-CH=CH-$ or
 $-(CH_2)_{n+2}-$, where n is 1 or 2, and the terminal oxygen atoms and/or
carbon atoms are linked to directly adjacent ring carbon atoms, or
- A is a radical $-CO_2R^b$, $C(O)NR^cR^d$, COR^b ,
- or
- A is an alkenyl group $-CR^5=CR^6R^7$, where
 R^5 , R^6 and R^7 are identical or different and are independently of
one another hydrogen atoms, halogen atoms, aryl

radicals or an unsubstituted or partly or completely fluorinated C₁-C₅-alkyl group, or

A is an alkynyl group -C≡CR⁵, with the meaning stated above for R⁵, and

5 B is a carbonyl or a CH₂ group

and their pharmaceutically acceptable salts.

10 2. Compounds according to Claim 1, in which R¹ and R² are preferably a hydrogen atom, a methyl or ethyl group.

3. Compounds according to Claim 1, in which R¹ and R² preferably form together with the C atom of the chain a ring having a total of 3-7 members.

15 4. Compounds according to Claim 1 to 3, in which R³ is preferably alkenyl, alkynyl, arylalkynyl, heteroarylalkynyl, cycloalkylalkynyl, heterocycloalkylalkynyl.

5. Compounds according to any of the preceding claims, in which R³ is preferably a vinyl, ethynyl, propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, hydroxypropynyl, hydroxybutynyl, 3-hydroxy-3-methylbutynyl, hydroxypentynyl, carboxypropynyl, t-butylcarboxypropynyl, phenylethynyl, (hydroxyphenyl)ethynyl, (methoxyphenyl)ethynyl, (dimethylaminophenyl)ethynyl, (methylphenyl)ethynyl, (cyanophenyl)ethynyl, (trifluoromethyl)ethynyl, (diphenyl)ethynyl, (nitrophenyl)ethynyl, (tert-butylphenyl)ethynyl, (acetylphenyl)ethynyl, (acetoxyphe-
25 nyl)ethynyl, (carboxyphenyl)ethynyl or a benzylethynyl group.

6. Compounds according to any of the preceding claims, in which A is preferably an aromatic ring.

30 7. Compounds according to any of the preceding claims, in which A is preferably a phenyl or naphthyl radical.

8. Compounds according to Claim 7, in which A is preferably an unsubstituted or optionally mono- or polysubstituted phenyl radical.

35

9. Compounds according to Claim 8, where the phenyl radical is preferably substituted

by one or two halogen atoms or one trifluoromethyl group.

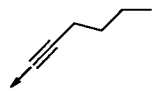
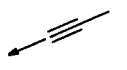
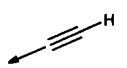
10. Compounds according to Claim 9, in which the halogen atoms are preferably chlorine and/or fluorine.

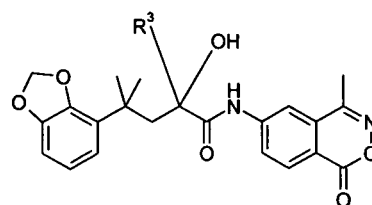
5

11. Compounds according to Claims 1-8, in which A is preferably a phenyl ring substituted by $-O-(CH_2)_n-O-$ or $-O-(CH_2)_n-CH_2-$, where the respectively directly adjacent ring carbon atoms are linked.

10 12. Compounds according to any of the preceding claims, in which R^4 is a hydrogen atom, a methyl or a trifluoromethyl radical.

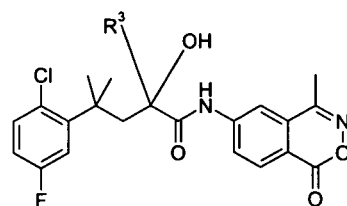
13. Compounds according to Claim 1 to 5, namely

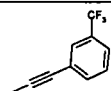
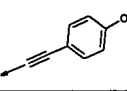
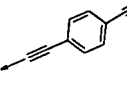
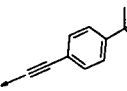
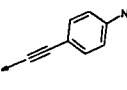
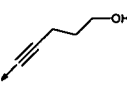
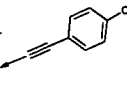
No.	Racemic or enantiomer	R3
1	rac	
2	-	
3	+	
4	rac	
5	+	
6	-	
7	rac	
8	+	
9	-	
10	rac	
11	+	
12	-	
13	rac	
14	+	
15	-	
16	rac	
17	+	
18	-	
19	rac	
20	+	
21	-	
22	rac	
23	+	
24	-	
25	rac	
26	+	
27	-	
28	rac	
29	+	
30	-	

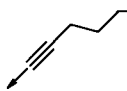
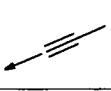
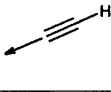
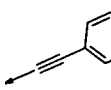
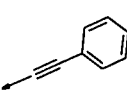
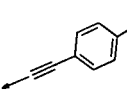
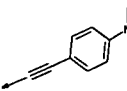


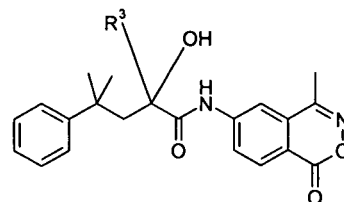
31	rac	
32	+	
33	-	
34	rac	
35	+	
36	-	
37	rac	
38	+	
39	-	
40	rac	
41	+	
42	-	
43	rac	
44	+	
45	-	
46	rac	
47	+	
48	-	
49	rac	
50	+	
51	-	

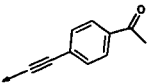
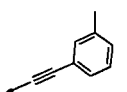
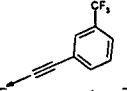
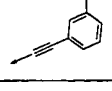
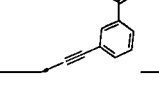
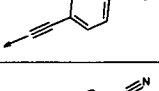
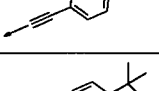
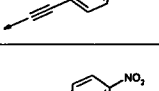
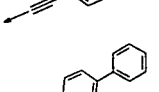
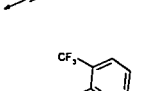
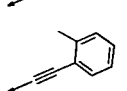
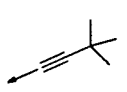
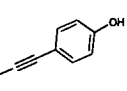
No.	Racemic or enantiomer	R3
52	rac	
53	-	
54	+	
55	rac	
56	+	
57	-	
58	rac	
59	+	
60	-	
61	rac	
62	+	
63	-	
64	rac	
65	+	
66	-	
67	rac	
68	+	
69	-	
70	rac	
71	+	
72	-	
73	rac	
74	+	
75	-	
76	rac	
77	+	
78	-	

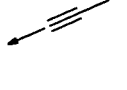


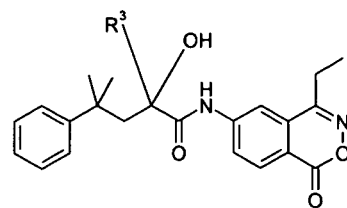
79	rac	
80	+	
81	-	
82	rac	
83	+	
84	-	
85	rac	
86	+	
87	-	
88	rac	
89	+	
90	-	
91	rac	
92	+	
93	-	
94	rac	
95	+	
96	-	
97	rac	
98	+	
99	-	
100	rac	
101	+	
102	-	
103	rac	
104	+	
105	-	

No.	Racemic or enantiomer	R3
106	rac	
107	-	
108	+	
109	rac	
110	+	
111	-	
112	rac	
113	+	
114	-	
115	rac	
116	+	
117	-	
118	rac	
119	+	
120	-	
121	rac	
122	+	
123	-	
124	rac	
125	+	
126	-	

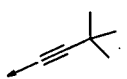
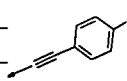


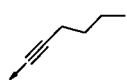
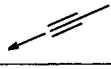
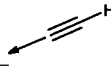
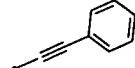
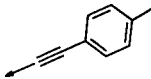
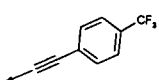
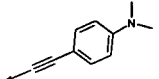
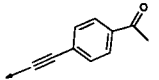
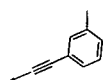
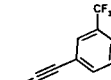
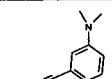
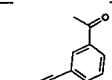
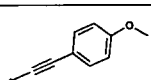
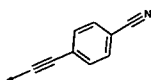
127	rac	
128	+	
129	-	
130	rac	
131	+	
132	-	
133	rac	
134	+	
135	-	
136	rac	
137	+	
138	-	
139	rac	
140	+	
141	-	
142	rac	
143	+	
144	-	
145	rac	
146	+	
147	-	
148	rac	
149	+	
150	-	
151	rac	
152	+	
153	-	
154	rac	
155	+	
156	-	
157	rac	
158	+	
159	-	
160	rac	
161	+	
162	-	
163	rac	
164	+	
165	-	
166	rac	
167	+	
168	-	

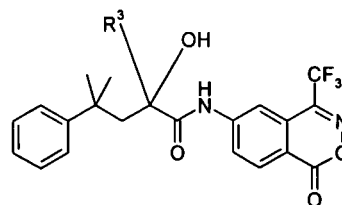
No.	Racemic or enantiomer	R3
169	rac	
170	-	
171	+	
172	rac	
173	+	
174	-	



175	rac	
176	+	
177	-	
178	rac	
179	+	
180	-	
181	rac	
182	+	
183	-	
184	rac	
185	+	
186	-	
187	rac	
188	+	
189	-	
190	rac	
191	+	
192	-	
193	rac	
194	+	
195	-	
196	rac	
197	+	
198	-	
199	rac	
200	+	
201	-	
202	rac	
203	+	
204	-	
205	rac	
206	+	
207	-	
208	rac	
209	+	
210	-	
211	rac	
212	+	
213	-	
214	rac	
215	+	
216	-	
217	rac	
218	+	
219	-	
220	rac	
221	+	
222	-	
223	rac	
224	+	
225	-	

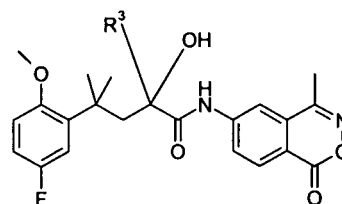
226	rac	
227	+	
228	-	
229	rac	
230	+	
231	-	

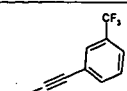
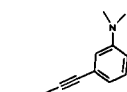
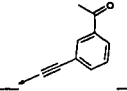
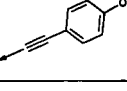
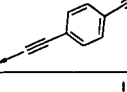
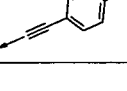
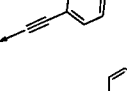
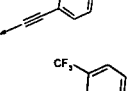
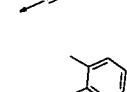
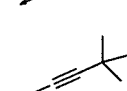
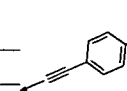
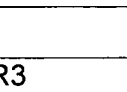
No.	Racemic or enantiomer	R3
232	rac	
233	-	
234	+	
235	rac	
236	+	
237	-	
238	rac	
239	+	
240	-	
241	rac	
242	+	
243	-	
244	rac	
245	+	
246	-	
247	rac	
248	+	
249	-	
250	rac	
251	+	
252	-	
253	rac	
254	+	
255	-	
256	rac	
257	+	
258	-	
259	rac	
260	+	
261	-	
262	rac	
263	+	
264	-	
265	rac	
266	+	
267	-	
268	rac	
269	+	
270	-	
271	rac	
272	+	
273	-	

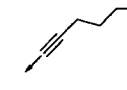
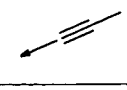
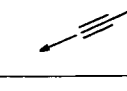
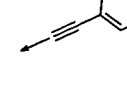


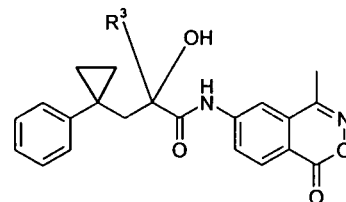
274	rac	
275	+	
276	-	
277	rac	
278	+	
279	-	
280	rac	
281	+	
282	-	
283	rac	
284	+	
285	-	
286	rac	
287	+	
288	-	
289	rac	
290	+	
291	-	
292	rac	
293	+	
294	-	

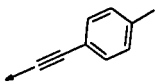
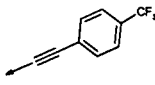
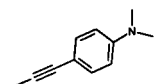
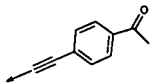
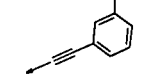
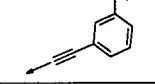
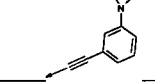
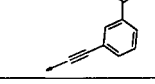
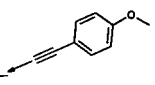
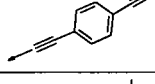
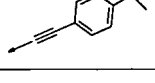
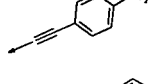
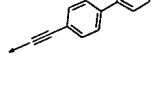
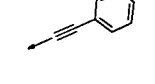
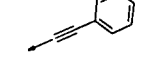
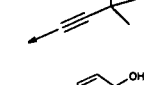
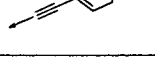
No.	Racemic or enantiomer	R3
295	rac	
296	-	
297	+	
298	rac	
299	+	
300	-	
301	rac	
302	+	
303	-	
304	rac	
305	+	
306	-	
307	rac	
308	+	
309	-	
310	rac	
311	+	
312	-	
313	rac	
314	+	
315	-	
316	rac	
317	+	
317	-	
319	rac	
320	+	
321	-	

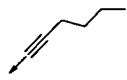
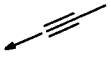
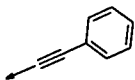
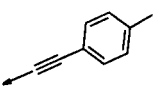
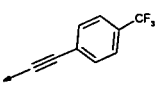
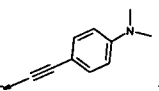
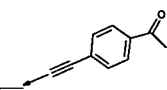
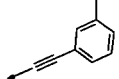
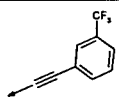
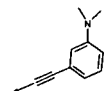
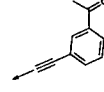
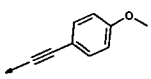
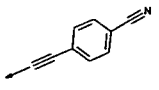
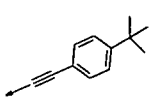
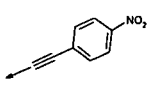
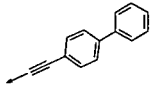


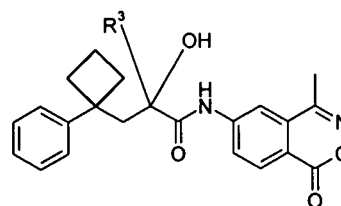
322	rac	
323	+	
324	-	
325	rac	
326	+	
327	-	
328	rac	
329	+	
330	-	
331	rac	
332	+	
333	-	
334	rac	
335	+	
336	-	
337	rac	
338	+	
339	-	
340	rac	
341	+	
342	-	
343	rac	
344	+	
345	-	
346	rac	
347	+	
348	-	
349	rac	
350	+	
351	-	
352	rac	
353	+	
354	-	
355	rac	
356	+	
357	-	

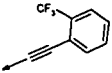
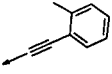
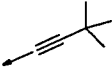
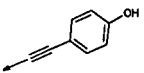
No.	Racemic or enantiomer	R3
358	rac	
359	-	
360	+	
361	rac	
362	+	
363	-	
364	rac	
365	+	
366	-	
367	rac	
368	+	
369	-	

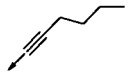
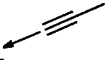
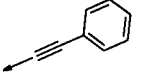
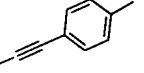
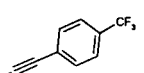
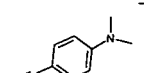
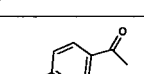
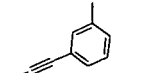
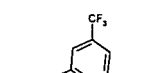
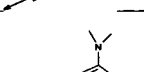
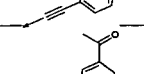


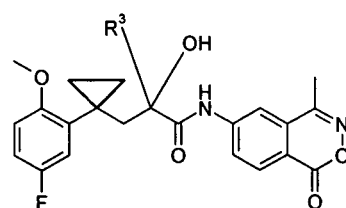
370	rac	
371	+	
372	-	
373	rac	
374	+	
375	-	
376	rac	
377	+	
378	-	
379	rac	
380	+	
381	-	
382	rac	
383	+	
384	-	
385	rac	
386	+	
387	-	
388	rac	
389	+	
390	-	
391	rac	
392	+	
393	-	
394	rac	
395	+	
396	-	
397	rac	
398	+	
399	-	
400	rac	
401	+	
402	-	
403	rac	
404	+	
405	-	
406	rac	
407	+	
408	-	
409	rac	
410	+	
411	-	
412	rac	
413	+	
414	-	
415	rac	
416	+	
417	-	
418	rac	
419	+	
420	-	

No.	Racemic or enantiomer	R3
421	rac	
422	-	
423	+	
424	rac	
425	+	
426	-	
427	rac	
428	+	
429	-	
430	rac	
431	+	
432	-	
433	rac	
434	+	
435	-	
436	rac	
437	+	
438	-	
439	rac	
440	+	
441	-	
442	rac	
443	+	
444	-	
445	rac	
446	+	
447	-	
448	rac	
449	+	
450	-	
451	rac	
452	+	
453	-	
454	rac	
455	+	
456	-	
457	rac	
458	+	
459	-	
460	rac	
461	+	
462	-	
463	rac	
464	+	
465	-	
466	rac	
467	+	
468	-	
469	rac	
470	+	
471	-	



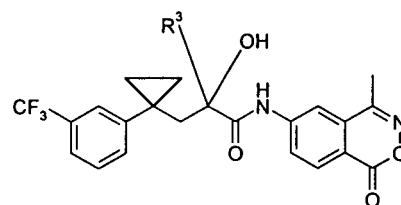
472	rac	
473	+	
474	-	
475	rac	
476	+	
477	-	
478	rac	
479	+	
480	-	
481	rac	
482	+	
483	-	

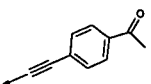
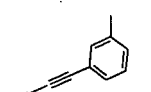
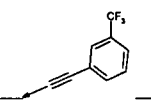
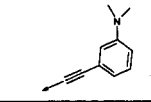
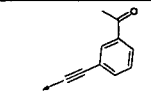
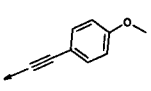
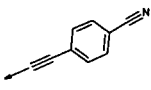
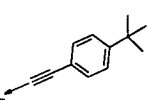
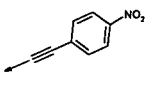
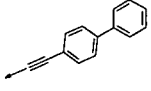
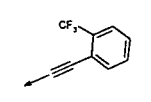
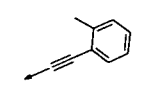
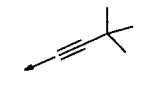
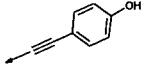
No.	Racemic or enantiomer	R3
484	rac	
485	-	
486	+	
487	rac	
488	+	
489	-	
490	rac	
491	+	
492	-	
493	rac	
494	+	
495	-	
496	rac	
497	+	
498	-	
499	rac	
500	+	
501	-	
502	rac	
503	+	
504	-	
505	rac	
506	+	
507	-	
508	rac	
509	+	
510	-	
511	rac	
512	+	
513	-	
514	rac	
515	+	
516	-	
517	rac	
518	+	
519	-	

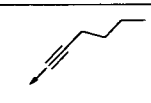
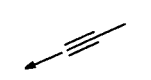


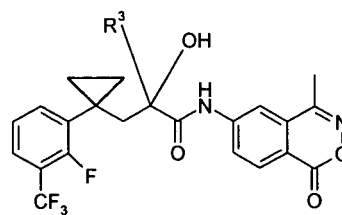
520	rac	
521	+	
522	-	
523	rac	
524	+	
525	-	
526	rac	
527	+	
528	-	
529	rac	
530	+	
531	-	
532	rac	
533	+	
534	-	
535	rac	
536	+	
537	-	
538	rac	
539	+	
540	-	
541	rac	
542	+	
543	-	
544	rac	
545	+	
546	-	

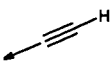
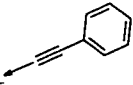
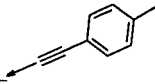
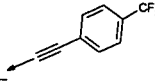
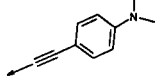
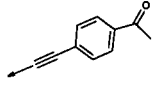
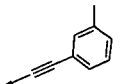
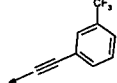
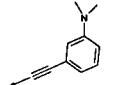
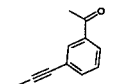
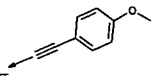
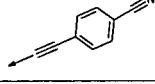
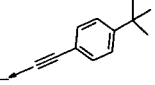
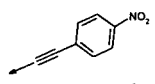
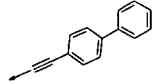
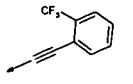
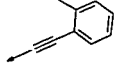
No.	Racemic or enantiomer	R3
547	rac	
548	-	
549	+	
550	rac	
551	+	
552	-	
553	rac	
554	+	
555	-	
556	rac	
557	+	
558	-	
559	rac	
560	+	
561	-	
562	rac	
563	+	
564	-	
565	rac	
566	+	
567	-	

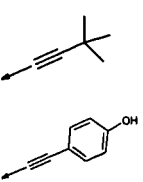


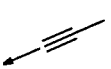
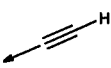
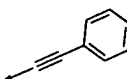
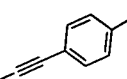
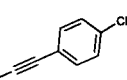
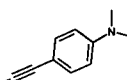
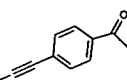
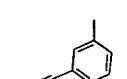
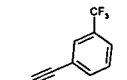
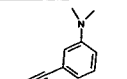
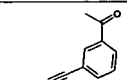
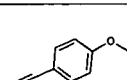
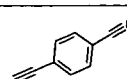
568	rac	
569	+	
570	-	
571	rac	
572	+	
573	-	
574	rac	
575	+	
576	-	
577	rac	
578	+	
579	-	
580	rac	
581	+	
582	-	
583	rac	
584	+	
585	-	
586	rac	
587	+	
588	-	
589	rac	
590	+	
591	-	
592	rac	
593	+	
594	-	
595	rac	
596	+	
597	-	
598	rac	
599	+	
600	-	
601	rac	
602	+	
603	-	
604	rac	
605	+	
606	-	
607	rac	
608	+	
609	-	

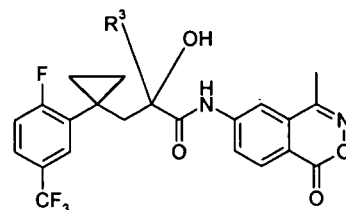
No.	Racemic or enantiomer	R3
610	rac	
611	-	
612	+	
613	rac	
614	+	
615	-	



616	rac	
617	+	
618	-	
619	rac	
620	+	
621	-	
622	rac	
623	+	
624	-	
625	rac	
626	+	
627	-	
628	rac	
629	+	
630	-	
631	rac	
632	+	
633	-	
634	rac	
635	+	
636	-	
637	rac	
638	+	
639	-	
640	rac	
641	+	
642	-	
643	rac	
644	+	
645	-	
646	rac	
647	+	
648	-	
649	rac	
650	+	
651	-	
652	rac	
653	+	
654	-	
655	rac	
656	+	
657	-	
658	rac	
659	+	
660	-	
661	rac	
662	+	
663	-	
664	rac	
665	+	
666	-	

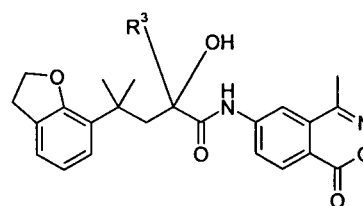
667	rac	
668	+	
669	-	
670	rac	
671	+	
672	-	

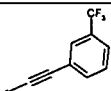
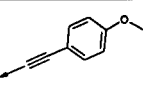
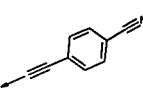
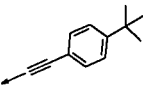
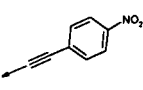
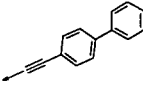
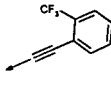
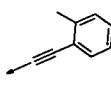
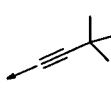
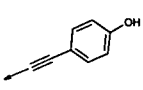
No.	Racemic or enantiomer	R3
673	rac	
674	-	
675	+	
676	rac	
677	+	
678	-	
679	rac	
680	+	
681	-	
682	rac	
683	+	
684	-	
685	rac	
686	+	
687	-	
688	rac	
689	+	
690	-	
691	rac	
692	+	
693	-	
694	rac	
695	+	
696	-	
697	rac	
698	+	
699	-	
700	rac	
701	+	
702	-	
703	rac	
704	+	
705	-	
706	rac	
707	+	
708	-	
709	rac	
710	+	
711	-	
712	rac	
713	+	
714	-	

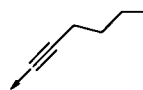
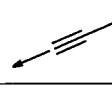
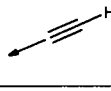
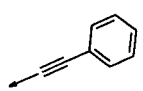


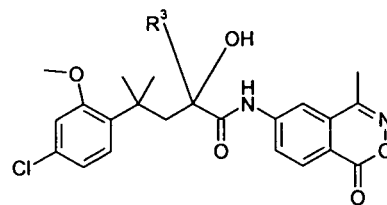
715	rac	
716	+	
717	-	
718	rac	
719	+	
720	-	
721	rac	
722	+	
723	-	
724	rac	
725	+	
726	-	
727	rac	
728	+	
729	-	
730	rac	
731	+	
732	-	
733	rac	
734	+	
735	-	

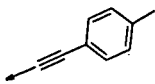
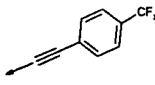
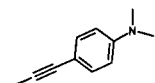
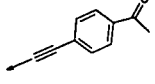
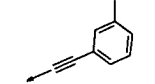
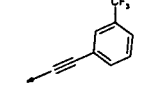
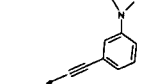
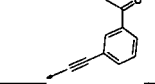
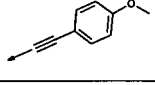
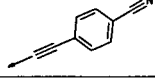
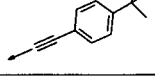
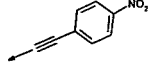
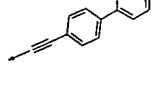
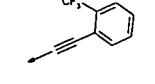
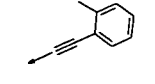
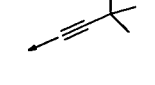
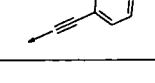
No.	Racemic or enantiomer	R3
736	rac	
737	-	
738	+	
739	rac	
740	+	
741	-	
742	rac	
743	+	
744	-	
745	rac	
746	+	
747	-	
748	rac	
749	+	
750	-	
751	rac	
752	+	
753	-	
754	rac	
755	+	
756	-	
757	rac	
758	+	
759	-	
760	rac	
761	+	
762	-	

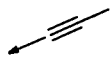
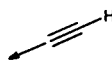
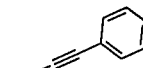
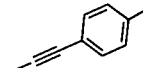
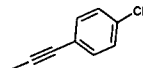
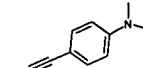
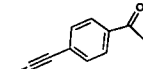
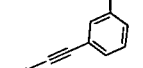
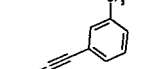
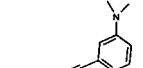
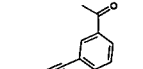
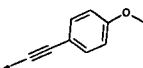
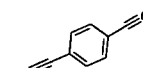
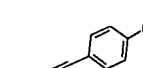
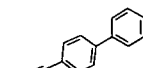


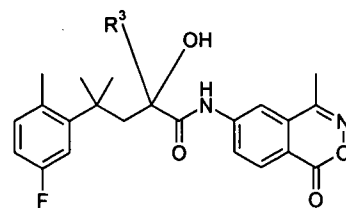
763	rac	
764	+	
765	-	
766	rac	
767	+	
768	-	
769	rac	
770	+	
771	-	
772	rac	
773	+	
774	-	
775	rac	
776	+	
777	-	
778	rac	
779	+	
780	-	
781	rac	
782	+	
783	-	
784	rac	
785	+	
786	-	
787	rac	
788	+	
789	-	
790	rac	
791	+	
792	-	
793	rac	
794	+	
795	-	
796	rac	
797	+	
798	-	

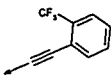
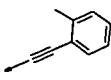
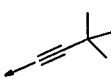
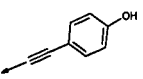
No.	Racemic or enantiomer	R3
799	rac	
800	-	
801	+	
802	rac	
803	+	
804	-	
805	rac	
806	+	
807	-	
808	rac	
809	+	
810	-	

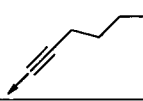
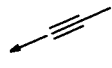
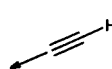
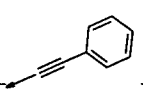
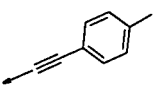
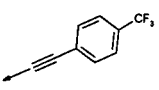
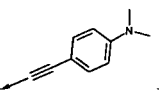
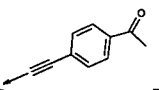
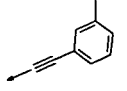
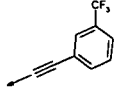
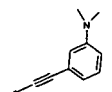
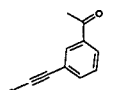


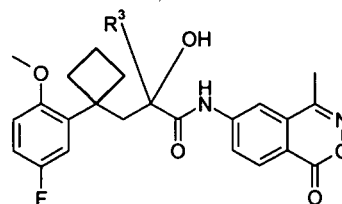
811	rac	
812	+	
813	-	
814	rac	
815	+	
816	-	
817	rac	
818	+	
819	-	
820	rac	
821	+	
822	-	
823	rac	
824	+	
825	-	
826	rac	
827	+	
828	-	
829	rac	
830	+	
831	-	
832	rac	
833	+	
834	-	
835	rac	
836	+	
837	-	
838	rac	
839	+	
840	-	
841	rac	
842	+	
843	-	
844	rac	
845	+	
846	-	
847	rac	
848	+	
849	-	
850	rac	
851	+	
852	-	
853	rac	
854	+	
855	-	
856	rac	
857	+	
858	-	
859	rac	
860	+	
861	-	

No.	Racemic or enantiomer	R3
862	rac	
863	-	
864	+	
865	rac	
866	+	
867	-	
868	rac	
869	+	
870	-	
871	rac	
872	+	
873	-	
874	rac	
875	+	
876	-	
877	rac	
878	+	
879	-	
880	rac	
881	+	
882	-	
883	rac	
884	+	
885	-	
886	rac	
887	+	
888	-	
889	rac	
890	+	
891	-	
892	rac	
893	+	
894	-	
895	rac	
896	+	
897	-	
898	rac	
899	+	
900	-	
901	rac	
902	+	
903	-	
904	rac	
905	+	
906	-	
907	rac	
908	+	
909	-	
910	rac	
911	+	



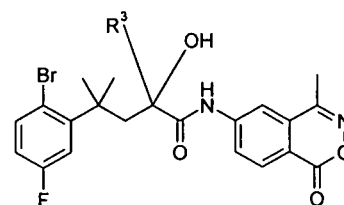
912	-	
913	rac	
914	+	
915	-	
916	rac	
917	+	
918	-	
919	rac	
920	+	
921	-	
922	rac	
923	+	
924	-	

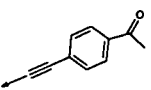
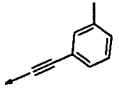
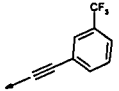
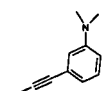
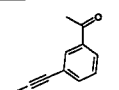
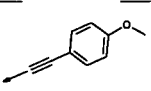
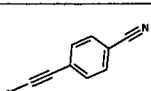
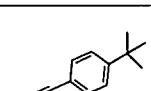
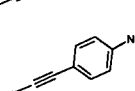
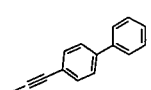
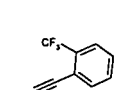
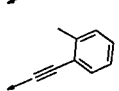
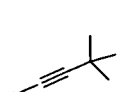
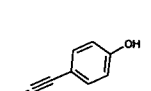
No.	Racemic or enantiomer	R3
925	rac	
926	-	
927	+	
928	rac	
929	+	
930	-	
931	rac	
932	+	
933	-	
934	rac	
935	+	
936	-	
937	rac	
938	+	
939	-	
940	rac	
941	+	
942	-	
943	rac	
944	+	
945	-	
946	rac	
947	+	
948	-	
949	rac	
950	+	
951	-	
952	rac	
953	+	
954	-	
955	rac	
956	+	
957	-	
958	rac	
959	+	
960	-	

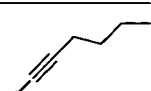
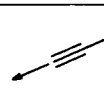


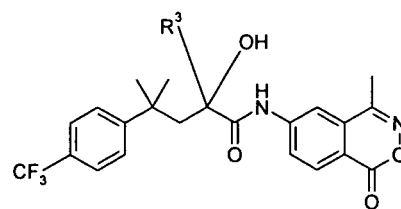
961	rac	
962	+	
963	-	
964	rac	
965	+	
966	-	
967	rac	
968	+	
969	-	
970	rac	
971	+	
972	-	
973	rac	
974	+	
975	-	
976	rac	
977	+	
978	-	
979	rac	
980	+	
981	-	
982	rac	
983	+	
984	-	
985	rac	
986	+	
987	-	

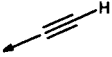
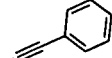
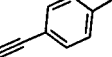
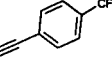
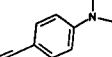
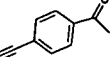
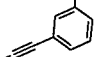
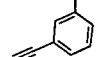
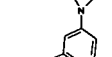
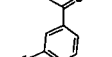
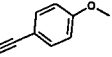
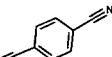
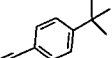
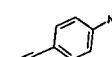
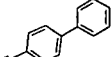
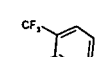
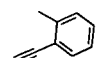
No.	Racemic or enantiomer	R3
988	rac	
989	-	
990	+	
991	rac	
992	+	
993	-	
994	rac	
995	+	
996	-	
997	rac	
998	+	
999	-	
1000	rac	
1001	+	
1002	-	
1003	rac	
1004	+	
1005	-	
1006	rac	
1007	+	
1008	-	



1009	rac	
1010	+	
1011	-	
1012	rac	
1013	+	
1014	-	
1015	rac	
1016	+	
1017	-	
1018	rac	
1019	+	
1020	-	
1021	rac	
1022	+	
1023	-	
1024	rac	
1025	+	
1026	-	
1027	rac	
1028	+	
1029	-	
1030	rac	
1031	+	
1032	-	
1033	rac	
1034	+	
1035	-	
1036	rac	
1037	+	
1038	-	
1039	rac	
1040	+	
1041	-	
1042	rac	
1043	+	
1044	-	
1045	rac	
1046	+	
1047	-	
1048	rac	
1049	+	
1050	-	

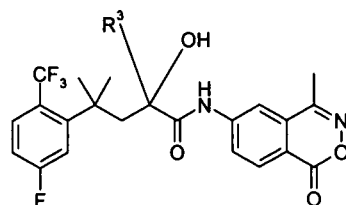
No.	Racemic or enantiomer	R3
1051	rac	
1052	-	
1053	+	
1054	rac	
1055	+	
1056	-	



1057	rac	
1058	+	
1059	-	
1060	rac	
1061	+	
1062	-	
1063	rac	
1064	+	
1065	-	
1066	rac	
1067	+	
1068	-	
1069	rac	
1070	+	
1071	-	
1072	rac	
1073	+	
1074	-	
1075	rac	
1076	+	
1077	-	
1078	rac	
1079	+	
1080	-	
1081	rac	
1082	+	
1083	-	
1084	rac	
1085	+	
1086	-	
1087	rac	
1088	+	
1089	-	
1090	rac	
1091	+	
1092	-	
1093	rac	
1094	+	
1095	-	
1096	rac	
1097	+	
1098	-	
1099	rac	
1100	+	
1101	-	
1102	rac	
1103	+	
1104	-	
1105	rac	
1106	+	
1107	-	

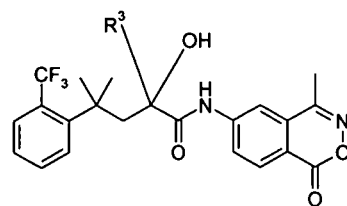
1108	rac	
1109	+	
1110	-	
1111	rac	
1112	+	
1113	-	

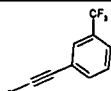
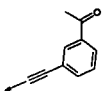
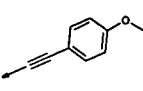
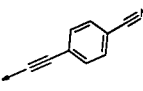
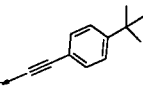
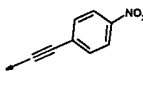
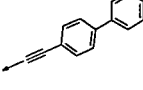
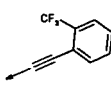
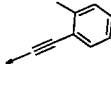
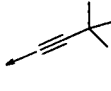
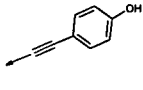
No.	Racemic or enantiomer	R3
1114	rac	
1115	-	
1116	+	
1117	rac	
1118	+	
1119	-	
1120	rac	
1121	+	
1122	-	
1123	rac	
1124	+	
1125	-	
1126	rac	
1127	+	
1128	-	
1129	rac	
1130	+	
1131	-	
1132	rac	
1133	+	
1134	-	
1135	rac	
1136	+	
1137	-	
1138	rac	
1139	+	
1140	-	
1141	rac	
1142	+	
1143	-	
1144	rac	
1145	+	
1146	-	
1147	rac	
1148	+	
1149	-	
1150	rac	
1151	+	
1152	-	
1153	rac	
1154	+	
1155	-	

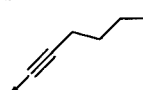
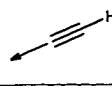
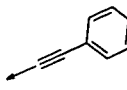


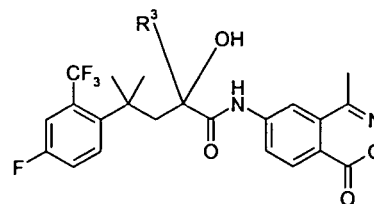
1156	rac	
1157	+	
1158	-	
1159	rac	
1160	+	
1161	-	
1162	rac	
1163	+	
1164	-	
1165	rac	
1166	+	
1167	-	
1168	rac	
1169	+	
1170	-	
1171	rac	
1172	+	
1173	-	
1174	rac	
1175	+	
1176	-	

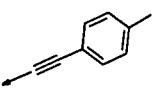
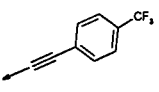
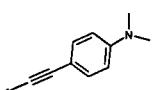
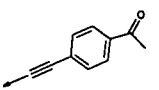
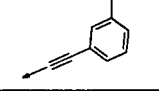
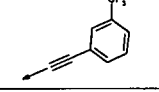
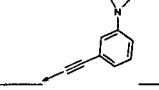
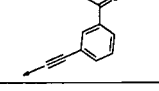
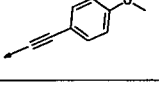
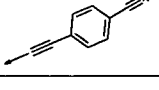
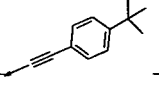
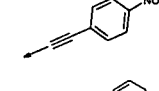
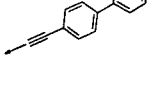
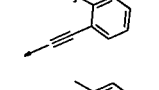
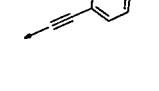
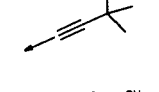
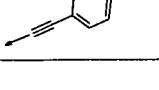
No.	Racemic or enantiomer	R3
1177	rac	
1178	-	
1179	+	
1180	rac	
1181	+	
1182	-	
1183	rac	
1184	+	
1185	-	
1186	rac	
1187	+	
1188	-	
1189	rac	
1190	+	
1191	-	
1192	rac	
1193	+	
1194	-	
1195	rac	
1196	+	
1197	-	
1198	rac	
1199	+	
1200	-	
1202	rac	
1202	+	
1203	-	

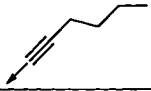
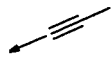
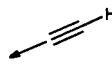
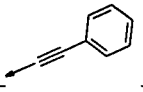
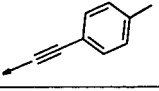
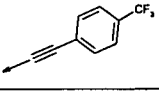
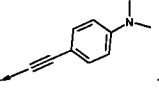
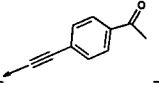
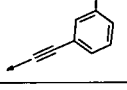
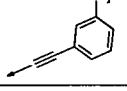
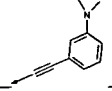
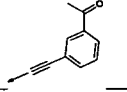
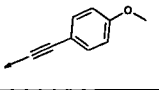
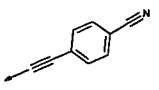
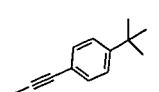
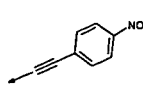


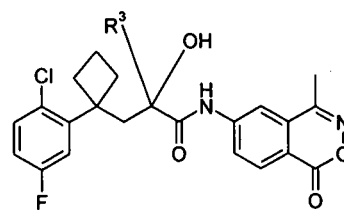
1204	rac	
1205	+	
1206	-	
1207	rac	
1208	+	
1209	-	
1210	rac	
1211	+	
1212	-	
1213	rac	
1214	+	
1215	-	
1216	rac	
1217	+	
1218	-	
1219	rac	
1220	+	
1221	-	
1222	rac	
1223	+	
1224	-	
1225	rac	
1226	+	
1227	-	
1228	rac	
1229	+	
1230	-	
1231	rac	
1232	+	
1233	-	
1234	rac	
1235	+	
1236	-	
1237	rac	
1238	+	
1239	-	

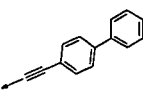
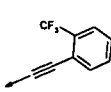
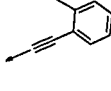
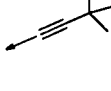
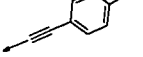
No.	Racemic or enantiomer	R3
1240	rac	
1241	-	
1242	+	
1243	rac	
1244	+	
1245	-	
1246	rac	
1247	+	
1248	-	
1249	rac	
1250	+	
1251	-	

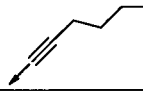
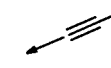
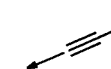
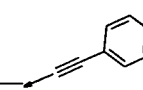
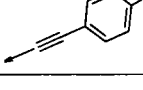
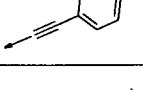
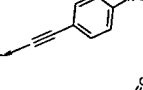
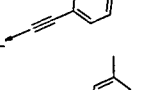
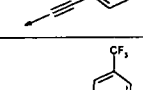
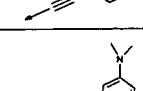


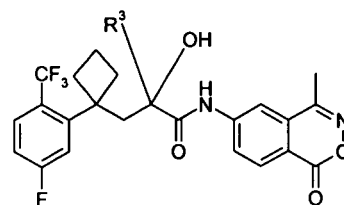
1252	rac	
1253	+	
1254	-	
1255	rac	
1256	+	
1257	-	
1258	rac	
1259	+	
1260	-	
1261	rac	
1262	+	
1263	-	
1264	rac	
1265	+	
1266	-	
1267	rac	
1268	+	
1269	-	
1270	rac	
1271	+	
1272	-	
1273	rac	
1274	+	
1275	-	
1276	rac	
1277	+	
1278	-	
1279	rac	
1280	+	
1281	-	
1282	rac	
1283	+	
1284	-	
1285	rac	
1286	+	
1287	-	
1288	rac	
1289	+	
1290	-	
1291	rac	
1292	+	
1293	-	
1294	rac	
1295	+	
1296	-	
1297	rac	
1298	+	
1299	-	
1300	rac	
1301	+	
1302	-	

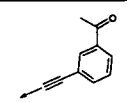
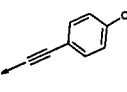
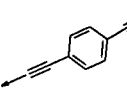
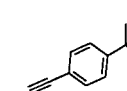
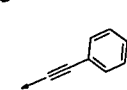
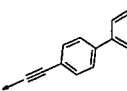
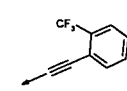
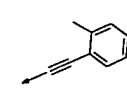
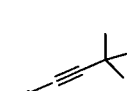
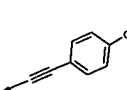
No.	Racemic or enantiomer	R3
1303	rac	
1304	-	
1305	+	
1306	rac	
1307	+	
1308	-	
1309	rac	
1310	+	
1311	-	
1312	rac	
1313	+	
1314	-	
1315	rac	
1316	+	
1317	-	
1318	rac	
1319	+	
1320	-	
1321	rac	
1322	+	
1323	-	
1324	rac	
1325	+	
1326	-	
1327	rac	
1328	+	
1329	-	
1330	rac	
1331	+	
1332	-	
1333	rac	
1334	+	
1335	-	
1336	rac	
1337	+	
1338	-	
1339	rac	
1340	+	
1341	-	
1342	rac	
1343	+	
1344	-	
1345	rac	
1346	+	
1347	-	
1348	rac	
1349	+	
1350	-	

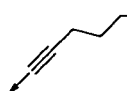
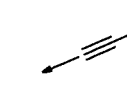
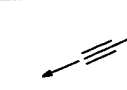
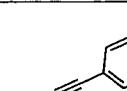
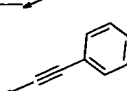
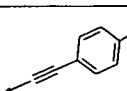


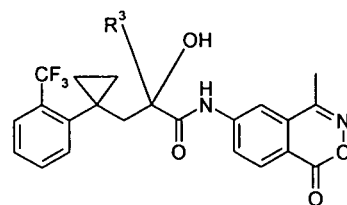
1351	rac	
1352	+	
1353	-	
1354	rac	
1355	+	
1356	-	
1357	rac	
1358	+	
1359	-	
1360	rac	
1361	+	
1362	-	
1362	rac	
1364	+	
1365	-	

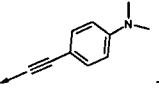
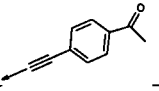
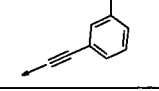
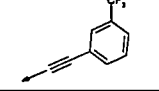
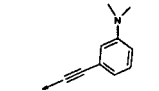
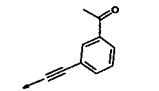
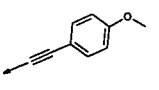
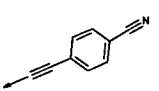
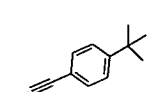
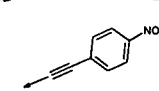
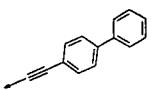
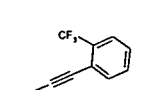
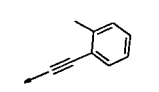
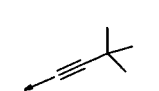
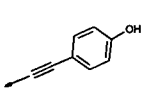
No.	Racemic or enantiomer	R3
1366	rac	
1367	-	
1368	+	
1369	rac	
1370	+	
1371	-	
1372	rac	
1373	+	
1374	-	
1375	rac	
1376	+	
1377	-	
1378	rac	
1379	+	
1380	-	
1381	rac	
1382	+	
1383	-	
1384	rac	
1385	+	
1386	-	
1387	rac	
1388	+	
1389	-	
1390	rac	
1391	+	
1392	-	
1393	rac	
1394	+	
1395	-	
1396	rac	
1397	+	
1398	-	



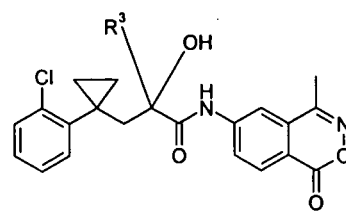
1399	rac	
1400	+	
1401	-	
1402	rac	
1403	+	
1404	-	
1405	rac	
1406	+	
1407	-	
1408	rac	
1409	+	
1410	-	
1411	rac	
1412	+	
1413	-	
1414	rac	
1415	+	
1416	-	
1417	rac	
1418	+	
1419	-	
1420	rac	
1421	+	
1422	-	
1423	rac	
1424	+	
1425	-	
1426	rac	
1427	+	
1428	-	

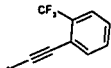
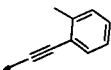
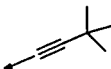
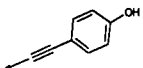
No.	Racemic or enantiomer	R3
1429	rac	
1430	-	
1431	+	
1432	rac	
1433	+	
1434	-	
1435	rac	
1436	+	
1437	-	
1438	rac	
1439	+	
1440	-	
1441	rac	
1442	+	
1443	-	
1444	rac	
1445	+	
1446	-	

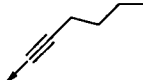
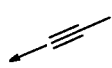
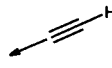
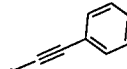
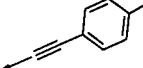
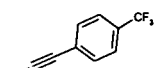
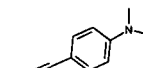
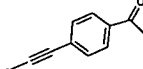
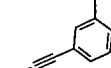
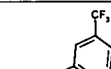
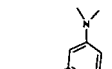
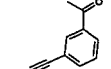


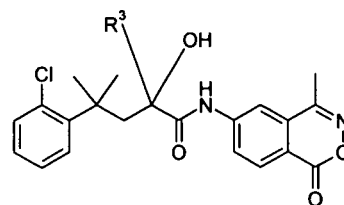
1447	rac	
1448	+	
1449	-	
1450	rac	
1451	+	
1452	-	
1453	rac	
1454	+	
1455	-	
1456	rac	
1457	+	
1458	-	
1459	rac	
1460	+	
1461	-	
1462	rac	
1463	+	
1464	-	
1465	rac	
1466	+	
1467	-	
1468	rac	
1469	+	
1470	-	
1471	rac	
1472	+	
1473	-	
1474	rac	
1475	+	
1476	-	
1477	rac	
1478	+	
1479	-	
1480	rac	
1481	+	
1482	-	
1483	rac	
1484	+	
1485	-	
1486	rac	
1487	+	
1488	-	
1489	rac	
1490	+	
1491	-	

No.	Racemic or enantiomer	R3
1492	rac	
1493	-	
1494	+	
1495	rac	
1496	+	
1497	-	
1498	rac	
1499	+	
1500	-	
1501	rac	
1502	+	
1503	-	
1504	rac	
1505	+	
1506	-	
1507	rac	
1508	+	
1509	-	
1510	rac	
1511	+	
1512	-	
1513	rac	
1514	+	
1515	-	
1516	rac	
1517	+	
1518	-	
1519	rac	
1520	+	
1521	-	
1522	rac	
1523	+	
1524	-	
1525	rac	
1526	+	
1527	-	
1528	rac	
1529	+	
1530	-	
1531	rac	
1532	+	
1533	-	
1534	rac	
1535	+	
1536	-	
1537	rac	
1538	+	
1539	-	
1540	rac	
1541	+	
1542	-	



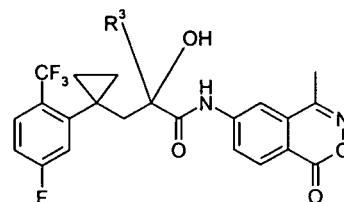
1543	rac	
1544	+	
1545	-	
1546	rac	
1547	+	
1548	-	
1549	rac	
1550	+	
1551	-	
1552	rac	
1553	+	
1554	-	

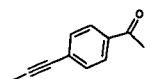
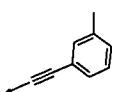
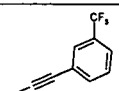
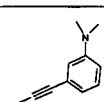
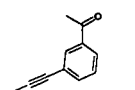
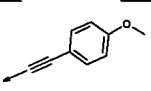
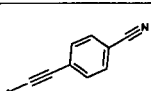
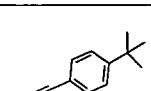
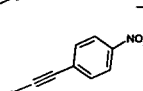
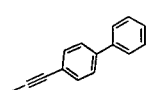
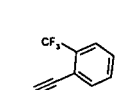
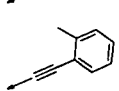
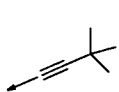
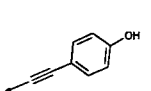
No.	Racemic or enantiomer	R3
1555	rac	
1556	-	
1557	+	
1558	rac	
1559	+	
1560	-	
1561	rac	
1562	+	
1563	-	
1564	rac	
1565	+	
1566	-	
1567	rac	
1568	+	
1569	-	
1570	rac	
1571	+	
1572	-	
1573	rac	
1574	+	
1575	-	
1576	rac	
1577	+	
1578	-	
1579	rac	
1580	+	
1581	-	
1582	rac	
1583	+	
1584	-	
1585	rac	
1586	+	
1587	-	
1588	rac	
1589	+	
1590	-	

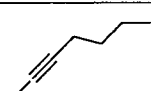


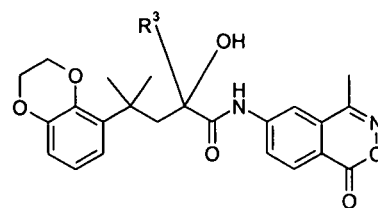
1591	rac	
1592	+	
1593	-	
1594	rac	
1595	+	
1596	-	
1597	rac	
1598	+	
1599	-	
1600	rac	
1601	+	
1602	-	
1603	rac	
1604	+	
1605	-	
1606	rac	
1607	+	
1608	-	
1609	rac	
1610	+	
1611	-	
1612	rac	
1613	+	
1614	-	
1615	rac	
1616	+	
1617	-	

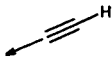
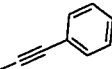
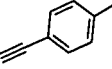
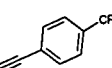
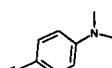
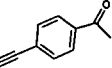
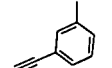
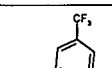
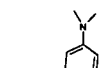
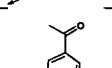
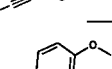
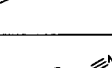
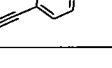
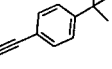
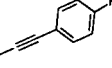
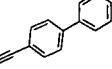
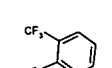
No.	Racemic or enantiomer	R3
1618	rac	
1619	-	
1620	+	
1621	rac	
1622	+	
1623	-	
1624	rac	
1625	+	
1626	-	
1627	rac	
1628	+	
1629	-	
1630	rac	
1631	+	
1632	-	
1633	rac	
1634	+	
1635	-	
1636	rac	
1637	+	
1638	-	



1639	rac	
1640	+	
1641	-	
1642	rac	
1643	+	
1644	-	
1645	rac	
1646	+	
1647	-	
1648	rac	
1649	+	
1650	-	
1651	rac	
1652	+	
1653	-	
1654	rac	
1655	+	
1656	-	
1657	rac	
1658	+	
1659	-	
1660	rac	
1661	+	
1662	-	
1663	rac	
1664	+	
1665	-	
1666	rac	
1667	+	
1668	-	
1669	rac	
1670	+	
1671	-	
1672	rac	
1673	+	
1674	-	
1675	rac	
1676	+	
1677	-	
1678	rac	
1679	+	
1680	-	

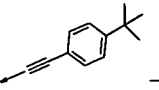
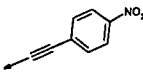
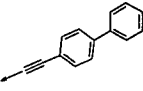
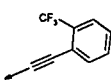
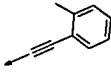
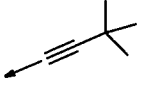
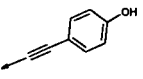
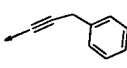
No.	Racemic or enantiomer	R3
1681	rac	
1682	-	
1683	+	
1684	rac	
1685	+	
1686	-	

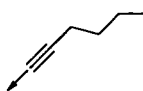
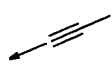
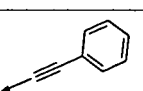
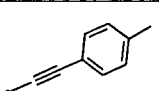
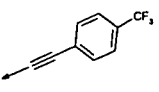
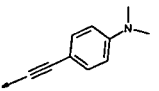


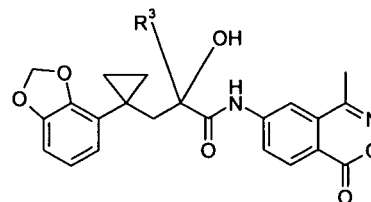
1687	rac	
1688	+	
1689	-	
1690	rac	
1691	+	
1692	-	
1693	rac	
1694	+	
1695	-	
1696	rac	
1697	+	
1698	-	
1699	rac	
1700	+	
1701	-	
1702	rac	
1703	+	
1704	-	
1705	rac	
1706	+	
1707	-	
1708	rac	
1709	+	
1710	-	
1711	rac	
1712	+	
1713	-	
1714	rac	
1715	+	
1716	-	
1717	rac	
1718	+	
1719	-	
1720	rac	
1721	+	
1722	-	
1723	rac	
1724	+	
1725	-	
1726	rac	
1727	+	
1728	-	
1729	rac	
1730	+	
1731	-	
1732	rac	
1733	+	
1734	-	
1735	rac	
1736	+	
1737	-	

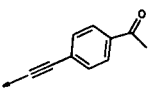
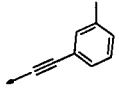
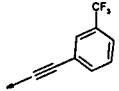
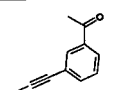
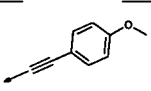
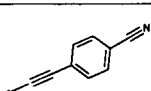
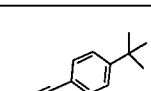
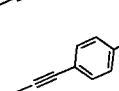
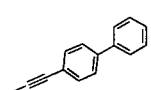
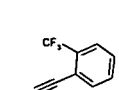
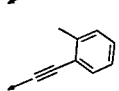
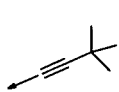
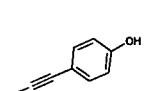
1738	rac	
1739	+	
1740	-	
1741	rac	
1742	+	
1743	-	

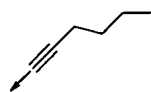
No.	Racemic or enantiomer	R3
1744	rac	
1745	-	
1746	+	
1747	rac	
1748	+	
1749	-	
1750	rac	
1751	+	
1752	-	
1753	rac	
1754	+	
1755	-	
1756	rac	
1757	+	
1758	-	
1759	rac	
1760	+	
1761	-	
1762	rac	
1763	+	
1764	-	
1765	rac	
1766	+	
1767	-	
1768	rac	
1769	+	
1770	-	
1771	rac	
1772	+	
1773	-	
1774	rac	
1775	+	
1776	-	
1777	rac	
1778	+	
1779	-	
1780	rac	
1781	+	
1782	-	
1783	rac	
1784	+	
1785	-	

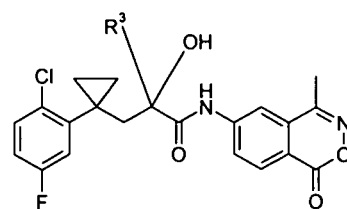
1786	rac	
1787	+	
1788	-	
1789	rac	
1790	+	
1791	-	
1792	rac	
1793	+	
1794	-	
1795	rac	
1796	+	
1797	-	
1798	rac	
1799	+	
1800	-	
1801	rac	
1802	+	
1803	-	
1804	rac	
1805	+	
1806	-	
1807	rac	
1808	+	
1809	-	
1810	rac	
1811	+	
1812	-	

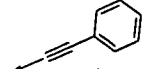
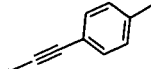
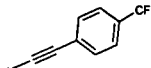
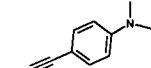
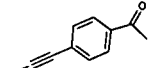
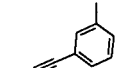
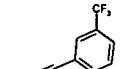
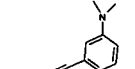
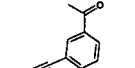
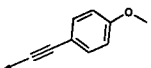
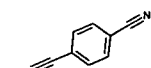
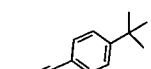
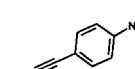
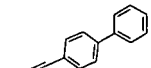
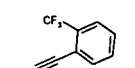
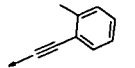
No.	Racemic or enantiomer	R3
1813	rac	
1814	-	
1815	+	
1816	rac	
1817	+	
1818	-	
1819	rac	
1820	+	
1821	-	
1822	rac	
1823	+	
1824	-	
1825	rac	
1826	+	
1827	-	
1828	rac	
1829	+	
1830	-	
1831	rac	
1832	+	
1833	-	

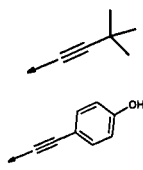


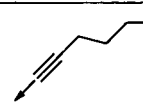
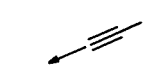
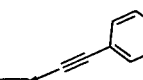
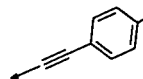
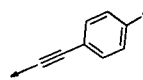
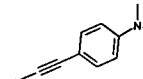
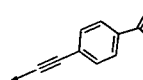
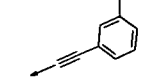
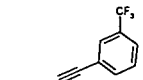
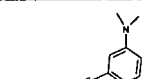
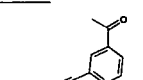
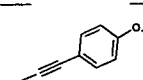
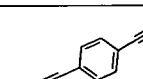
1834	rac	
1835	+	
1836	-	
1837	rac	
1838	+	
1839	-	
1840	rac	
1841	+	
1842	-	
1843	rac	
1844	+	
1845	-	
1846	rac	
1847	+	
1848	-	
1849	rac	
1850	+	
1851	-	
1852	rac	
1853	+	
1854	-	
1855	rac	
1856	+	
1857	-	
1858	rac	
1859	+	
1860	-	
1861	rac	
1862	+	
1863	-	
1864	rac	
1865	+	
1866	-	
1867	rac	
1868	+	
1869	-	
1870	rac	
1871	+	
1872	-	
1873	rac	
1874	+	
1875	-	

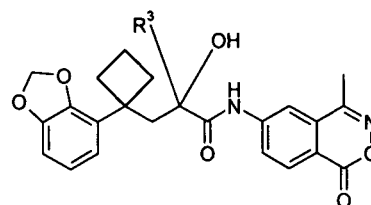
No.	Racemic or enantiomer	R3
1876	rac	
1877	-	
1878	+	
1879	rac	
1880	+	
1881	-	



1882	rac	
1883	+	
1884	-	
1885	rac	
1886	+	
1887	-	
1888	rac	
1889	+	
1890	-	
1891	rac	
1892	+	
1893	-	
1894	rac	
1895	+	
1896	-	
1897	rac	
1898	+	
1899	-	
1900	rac	
1901	+	
1902	-	
1903	rac	
1904	+	
1905	-	
1906	rac	
1907	+	
1908	-	
1909	rac	
1910	+	
1911	-	
1912	rac	
1913	+	
1914	-	
1915	rac	
1916	+	
1917	-	
1918	rac	
1919	+	
1920	-	
1921	rac	
1922	+	
1923	-	
1924	rac	
1925	+	
1926	-	
1927	rac	
1928	+	
1929	-	
1930	rac	
1931	+	
1932	-	

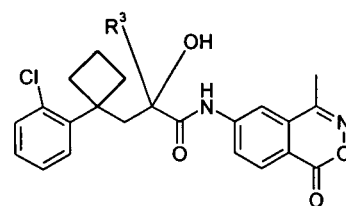
1933	rac	
1934	+	
1935	-	
1936	rac	
1937	+	
1938	-	

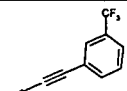
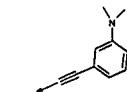
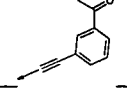
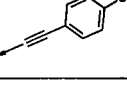
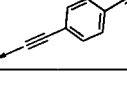
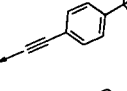
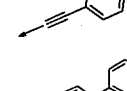
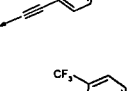
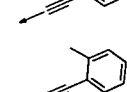
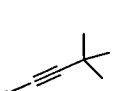
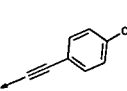
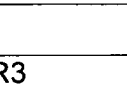
No.	Racemic or enantiomer	R3
1939	rac	
1940	-	
1941	+	
1942	rac	
1943	+	
1944	-	
1945	rac	
1946	+	
1947	-	
1948	rac	
1949	+	
1950	-	
1951	rac	
1952	+	
1953	-	
1954	rac	
1955	+	
1956	-	
1957	rac	
1958	+	
1959	-	
1960	rac	
1961	+	
1962	-	
1963	rac	
1964	+	
1965	-	
1966	rac	
1967	+	
1968	-	
1969	rac	
1970	+	
1971	-	
1972	rac	
1973	+	
1974	-	
1975	rac	
1976	+	
1977	-	
1978	rac	
1979	+	
1980	-	

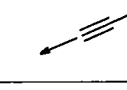
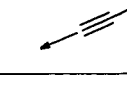
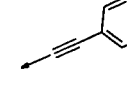


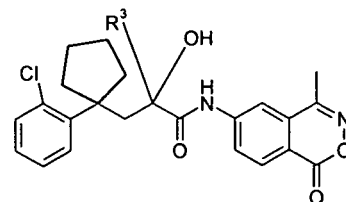
1981	rac	
1982	+	
1983	-	
1984	rac	
1985	+	
1986	-	
1987	rac	
1988	+	
1989	-	
1990	rac	
1991	+	
1992	-	
1993	rac	
1994	+	
1995	-	
1996	rac	
1997	+	
1998	-	
1999	rac	
2000	+	
2001	-	

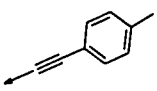
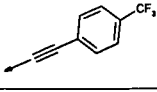
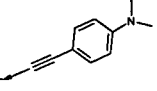
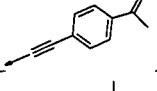
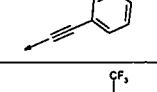
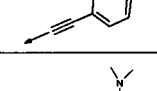
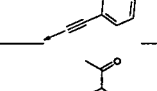
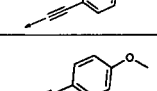
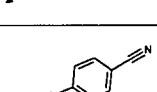
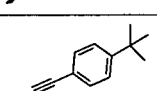
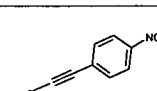
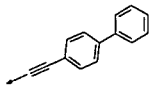
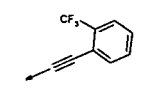
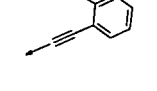
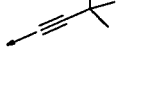
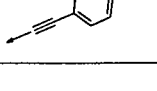
No.	Racemic or enantiomer	R3
2002	rac	
2003	-	
2004	+	
2005	rac	
2006	+	
2007	-	
2008	rac	
2009	+	
2010	-	
2011	rac	
2012	+	
2013	-	
2014	rac	
2015	+	
2016	-	
2017	rac	
2018	+	
2019	-	
2020	rac	
2021	+	
2022	-	
2023	rac	
2024	+	
2025	-	
2026	rac	
2027	+	
2028	-	

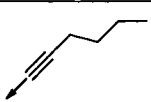
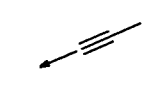
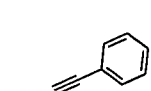
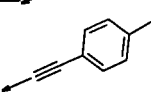
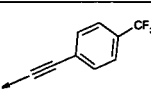
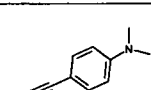
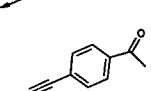
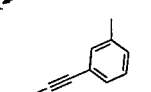
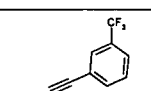
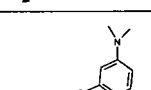
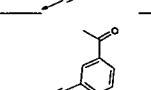
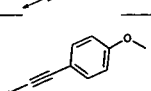
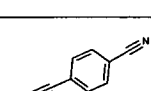
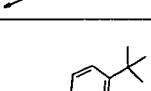
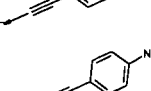
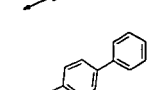


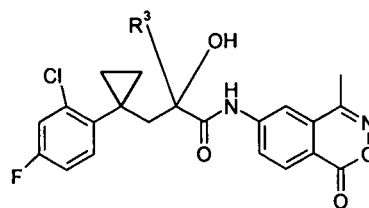
2029	rac	
2030	+	
2031	-	
2032	rac	
2033	+	
2034	-	
2035	rac	
2036	+	
2037	-	
2038	rac	
2039	+	
2040	-	
2041	rac	
2042	+	
2043	-	
2044	rac	
2045	+	
2046	-	
2047	rac	
2048	+	
2049	-	
2050	rac	
2051	+	
2052	-	
2053	rac	
2054	+	
2055	-	
2056	rac	
2057	+	
2058	-	
2059	rac	
2060	+	
2061	-	
2062	rac	
2063	+	
2064	-	

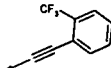
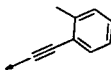
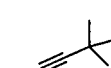
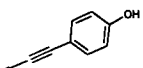
No.	Racemic or enantiomer	R3
2065	rac	
2066	-	
2067	+	
2068	rac	
2069	+	
2070	-	
2071	rac	
2072	+	
2073	-	
2074	rac	
2075	+	
2076	-	

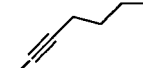
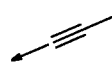
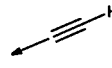
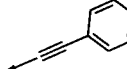
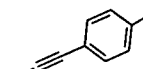
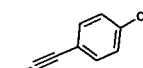
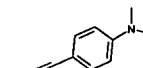
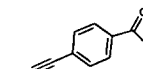
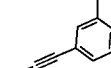
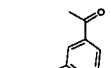


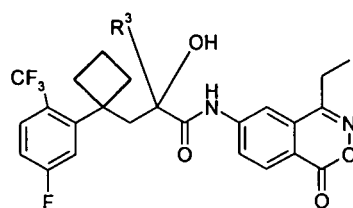
2077	rac	
2078	+	
2079	-	
2080	rac	
2081	+	
2082	-	
2083	rac	
2084	+	
2085	-	
2086	rac	
2087	+	
2088	-	
2089	rac	
2090	+	
2091	-	
2092	rac	
2093	+	
2094	-	
2095	rac	
2096	+	
2097	-	
2098	rac	
2099	+	
2100	-	
2101	rac	
2102	+	
2103	-	
2104	rac	
2105	+	
2106	-	
2107	rac	
2108	+	
2109	-	
2110	rac	
2111	+	
2112	-	
2113	rac	
2114	+	
2115	-	
2116	rac	
2117	+	
2118	-	
2119	rac	
2120	+	
2121	-	
2122	rac	
2123	+	
2124	-	
2125	rac	
2126	+	
2127	-	

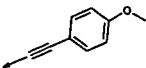
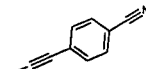
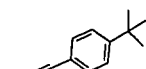
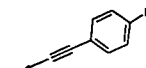
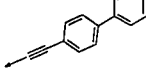
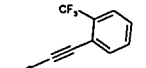
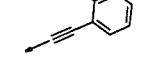
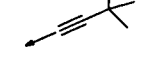
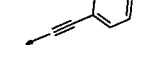
No.	Racemic or enantiomer	R3
2128	rac	
2129	-	
2130	+	
2131	rac	
2132	+	
2133	-	
2134	rac	
2135	+	
2136	-	
2137	rac	
2138	+	
2139	-	
2140	rac	
2141	+	
2142	-	
2143	rac	
2144	+	
2145	-	
2146	rac	
2147	+	
2148	-	
2149	rac	
2150	+	
2151	-	
2152	rac	
2153	+	
2154	-	
2155	rac	
2156	+	
2157	-	
2158	rac	
2159	+	
2160	-	
2161	rac	
2163	+	
2163	-	
2164	rac	
2165	+	
2166	-	
2167	rac	
2168	+	
2169	-	
2170	rac	
2171	+	
2172	-	
2173	rac	
2174	+	
2175	-	
2176	rac	
2177	+	
2178	-	

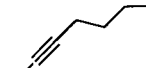
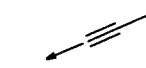
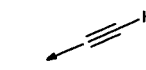
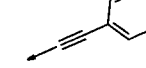
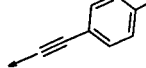
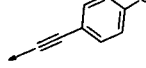
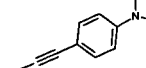


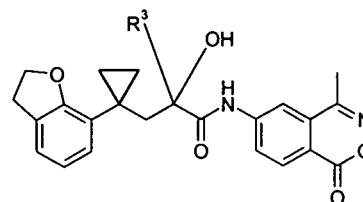
2179	rac	
2180	+	
2181	-	
2182	rac	
2183	+	
2184	-	
2185	rac	
2186	+	
2187	-	
2188	rac	
2189	+	
2190	-	

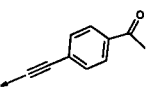
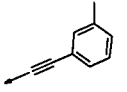
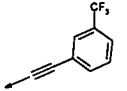
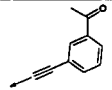
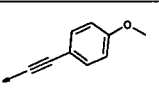
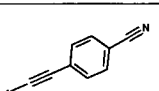
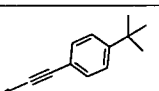
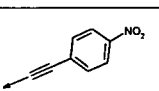
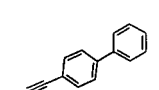
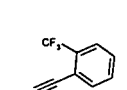
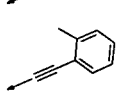
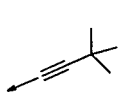
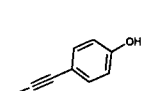
No.	Racemic or enantiomer	R3
2191	rac	
2192	-	
2193	+	
2194	rac	
2195	+	
2196	-	
2197	rac	
2198	+	
2199	-	
2200	rac	
2201	+	
2202	-	
2203	rac	
2204	+	
2205	-	
2206	rac	
2207	+	
2208	-	
2209	rac	
2210	+	
2211	-	
2212	rac	
2213	+	
2214	-	
2215	rac	
2216	+	
2217	-	
2218	rac	
2219	+	
2220	-	
2221	rac	
2222	+	
2223	-	
2224	rac	
2225	+	
2226	-	

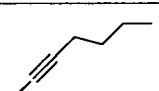
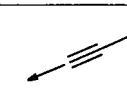


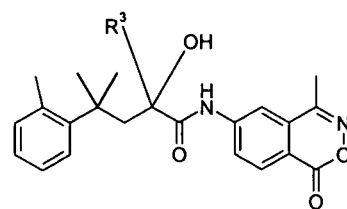
2227	rac	
2228	+	
2229	-	
2230	rac	
2231	+	
2232	-	
2233	rac	
2234	+	
2235	-	
2236	rac	
2237	+	
2238	-	
2239	rac	
2240	+	
2241	-	
2242	rac	
2243	+	
2244	-	
2245	rac	
2246	+	
2247	-	
2248	rac	
2249	+	
2250	-	
2251	rac	
2252	+	
2253	-	

No.	Racemic or enantiomer	R3
2254	rac	
2255	-	
2256	+	
2257	rac	
2258	+	
2259	-	
2260	rac	
2261	+	
2262	-	
2263	rac	
2264	+	
2265	-	
2266	rac	
2267	+	
2268	-	
2269	rac	
2270	+	
2271	-	
2272	rac	
2273	+	
2274	-	



2273	rac	
2276	+	
2277	-	
2278	rac	
2279	+	
2280	-	
2281	rac	
2282	+	
2283	-	
2284	rac	
2285	+	
2286	-	
2287	rac	
2288	+	
2289	-	
2290	rac	
2291	+	
2292	-	
2293	rac	
2294	+	
2295	-	
2296	rac	
2297	+	
2298	-	
2299	rac	
2300	+	
2301	-	
2302	rac	
2303	+	
2304	-	
2305	rac	
2306	+	
2307	-	
2308	rac	
2309	+	
2310	-	
2311	rac	
2312	+	
2313	-	
2314	rac	
2315	+	
2316	-	

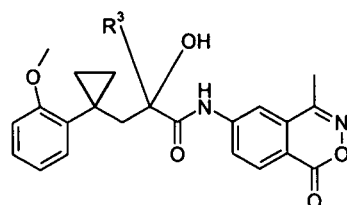
No.	Racemic or enantiomer	R3
2317	rac	
2318	-	
2319	+	
2320	rac	
2321	+	
2322	-	

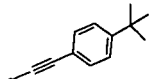
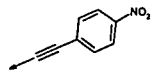
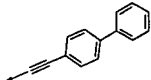
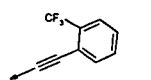
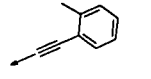
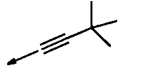
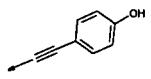


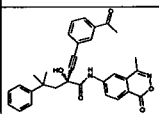
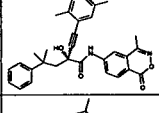
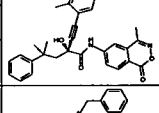
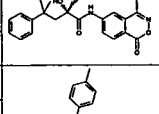
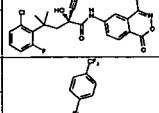
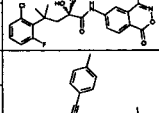
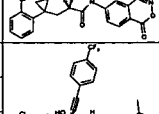
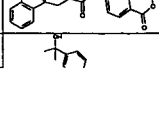
2323	rac	
2324	+	
2325	-	
2326	rac	
2327	+	
2328	-	
2329	rac	
2330	+	
2331	-	
2332	rac	
2333	+	
2334	-	
2335	rac	
2336	+	
2337	-	
2338	rac	
2339	+	
2340	-	
2341	rac	
2342	+	
2343	-	
2344	rac	
2345	+	
2346	-	
2347	rac	
2348	+	
2349	-	
2350	rac	
2351	+	
2652	-	
2353	rac	
2354	+	
2355	-	
2356	rac	
2357	+	
2358	-	
2359	rac	
2360	+	
2361	-	
2362	rac	
2363	+	
2364	-	
2365	rac	
2366	+	
2367	-	
2368	rac	
2369	+	
2370	-	
2371	rac	
2372	+	
2373	-	

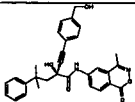
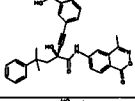
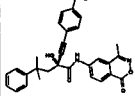
2374	rac	
2375	+	
2376	-	
2377	rac	
2378	+	
2379	-	

No.	Racemic or enantiomer	R3
2380	rac	
2381	-	
2382	+	
2383	rac	
2384	+	
2385	-	
2386	rac	
2387	+	
2388	-	
2389	rac	
2390	+	
2391	-	
2392	rac	
2393	+	
2394	-	
2395	rac	
2396	+	
2397	-	
2398	rac	
2399	+	
2400	-	
2401	rac	
2402	+	
2403	-	
2404	rac	
2405	+	
2406	-	
2407	rac	
2408	+	
2409	-	
2410	rac	
2411	+	
2412	-	
2413	rac	
2414	+	
2415	-	
2416	rac	
2417	+	
2418	-	
2419	rac	
2420	+	
2421	-	



2422	rac	
2423	+	
2424	-	
2425	rac	
2426	+	
2427	-	
2428	rac	
2429	+	
2430	-	
2431	rac	
2432	+	
2433	-	
2434	rac	
2435	+	
2436	-	
2437	rac	
2438	+	
2439	-	
2440	rac	
2441	+	
2442	-	
		
		
		
		

No.	Racemic or enantiomer	Structure
2443	rac	
2444	-	
2445	+	
2446	rac	
2447	+	
2448	-	
2449	rac	
2450	+	
2451	-	
2452	rac	
2453	+	
2454	-	
2455	rac	
2456	+	
2457	-	
2458	rac	
2459	+	
2460	-	
2461	rac	
2462	+	
2463	-	
2464	rac	
2465	+	
2466	-	
2467	rac	

2468	+	
2469	-	
2470	rac	
2471	+	
2472	-	
2473	rac	
2474	+	
2475	-	
2476	rac	
2477	+	
2478	-	

14. Pharmaceutical composition comprising at least one compound of the general formula I according to any of Claims 1 to 13 and, where appropriate, at least one further active ingredient together with pharmaceutically suitable excipients and/or carriers.
15. Pharmaceutical composition according to Claim 14, where the further active ingredient is a SERM (selective estrogen receptor modulator), an aromatase inhibitor, an antiestrogen or a prostaglandin.
16. Pharmaceutical composition according to Claim 14, where the active ingredient may be tamoxifen, 5-(4-{5-[(RS)-(4,4,5,5,5-pentafluoropentyl)sulphinyl]pentyloxy}phenyl)-6-phenyl-8,9-dihydro-7H-benzocyclohepten-2-ol, ICI 182 780 (7alpha-[9-(4,4,5,5-pentafluoropentylsulphinyl)nonyl]estra-1,3,5(10)-triene-3,17beta-diol), 11beta-fluoro-7alpha-[5-(methyl{3-[(4,4,5,5,5-pentafluoropentyl)sulphanyl]-propyl}amino)pentyl]estra-1,3,5(10)-triene-3,17beta-diol, 11beta-fluoro-7alpha-[5-[methyl(7,7,8,8,9,9,10,10,10-nonafluorodecyl)amino]pentyl]estra-1,3,5(10)-triene-3,17beta-diol, 11beta-fluoro-17alpha-methyl-7alpha-[5-[methyl(8,8,9,9,9-pentafluorononyl)amino]pentyl]estra-1,3,5(10)-triene-3,17beta-diol, clomifen, raloxifen, fadrozole, formestane, letrozole, anastrozole or atamestane.
17. Use of compounds according to any of Claims 1 to 13 for producing a medicament.
18. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of gynaecological disorders such as endometriosis, leiomyomas of the uterus, dysfunctional bleeding and dysmenorrhoea.
19. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of hormone-dependent tumours.
20. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of breast carcinomas.
21. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of endometrial carcinoma.

22. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of ovarian carcinomas.
- 5 23. Use of compounds according to Claim 17 for producing a medicament for the therapy and prophylaxis of prostate carcinomas.
24. Use of compounds according to Claim 17 for producing a medicament for female hormone replacement therapy.
- 10 25. Use of compounds according to Claim 17 for female fertility control.
26. Process for the selective addition of lithium alkynyl and magnesium haloalkynyl compounds onto a keto amide.