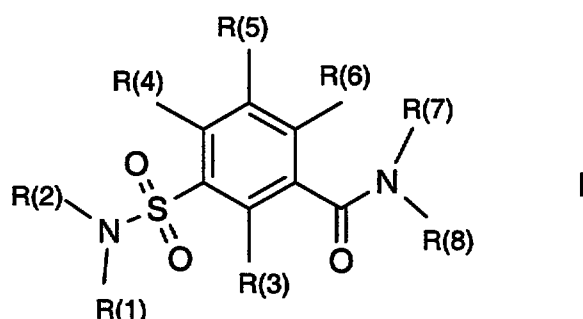


Description

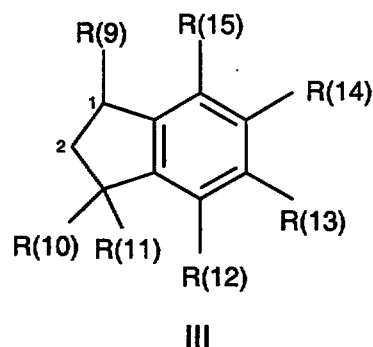
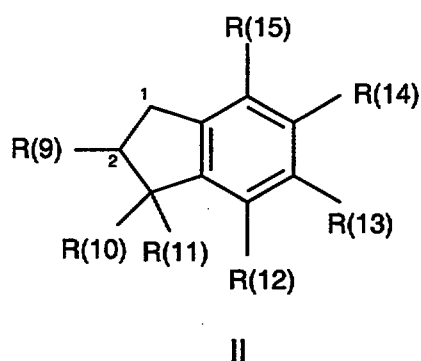
Indanyl-substituted benzenecarboxamides, processes for their preparation,
their use as a medicament and pharmaceutical formulations containing
5 them

The invention relates to compounds of the formula I



10

in which R(8) is either a 1-indanyl radical of the formula II or a 2-indanyl
radical of the formula III



15

and in which R(1), R(2), R(3), R(4), R(5), R(6), R(7), R(9), R(10), R(11),
R(12), R(13), R(14) and R(15) have the meanings stated below, their
preparation and their use, in particular in medicaments.

20 The compounds according to the invention act on the so-called Kv1.5
potassium channel and inhibit a potassium current, referred to as "ultra-
rapidly activating delayed rectifier", in the human atrium. The compounds
are therefore very particularly suitable as novel antiarrhythmic active
substances, in particular for the treatment and prophylaxis of atrial
25 arrhythmias, e.g. atrial fibrillation (AF) or atrial flutter.

Atrial fibrillation (AF) and atrial flutter are the most frequent persistent cardiac arrhythmias. They occur increasingly with increasing age and frequently lead to fatal consequences, such as, for example, a cerebrovascular accident. AF affects about 1 million Americans annually and leads to more than 80,000 strokes every year in the USA. The class I and III antiarrhythmic drugs commonly used at present reduce the rate of recurrence of AF but, owing to their potential proarrhythmic side effects, are used only to a limited extent. There is therefore a considerable medical necessity for the development of better medicaments for the treatment of atrial arrhythmias (S. Nattel, *Am. Heart J.* 130, 1995, 1094 - 1106; "Newer developments in the management of atrial fibrillation").

It was found that most supraventricular arrhythmias are based on so-called "re-entry" excitation thresholds. Such re-entries occur when the heart tissue has slow conductivity and at the same time very short refractory periods. Increasing the myocardial refractory time by lengthening the action potential is a recognized mechanism for terminating arrhythmias and for preventing their occurrence (T.J. Colatsky et al., *Drug Dev. Res.* 19, 1990, 129 - 140; "Potassium channels as targets for antiarrhythmic drug action"). The length of the action potential is essentially determined by the extent of repolarizing K^+ currents which flow out of the cell via various K^+ channels. Particularly great importance here is attributed to the so-called "delayed rectifier" I_K , which consists of 3 different components: I_{K_r} , I_{K_s} and $I_{K_{ur}}$.

Most known class III antiarrhythmic drugs (e.g. Dofetilide, E4031 and d-Sotalol) predominantly or exclusively block the fast-activating potassium channel I_{K_r} , which is detectable both in the cells of the human ventricle and in the atrium. However, it has been found that these compounds give rise to a high proarrhythmic risk at low or normal heart rates, in particular arrhythmias referred to as "Torsades de pointes" having been observed (D. M. Roden, *Am. J. Cardiol.* 72, 1993, 44B-49B; "Current status of class III antiarrhythmic drug therapy"). In addition to this high, sometimes fatal risk at low rate, the I_{K_r} blockers were found to decline in activity under the conditions of tachycardia, precisely where the activity is required ("negative use-dependence").

While some of these disadvantages can possibly be overcome by blockers of the slowly activating component (I_{K_s}), their activity has not been

demonstrated to date, since no clinical studies with IK_S channel blockers are known.

5 The "particularly rapidly" activating and very slowly inactivating component of the delayed rectifier IK_{ur} (= ultra-rapidly activating delayed rectifier), which corresponds to the $Kv1.5$ channel, plays a particularly major role for the repolarization time in the human atrium. Compared with the inhibition of IK_r or IK_S , inhibition of the IK_{ur} potassium outward current is thus a particularly effective method for lengthening the atrial action potential and
10 hence for terminating or preventing atrial arrhythmias.

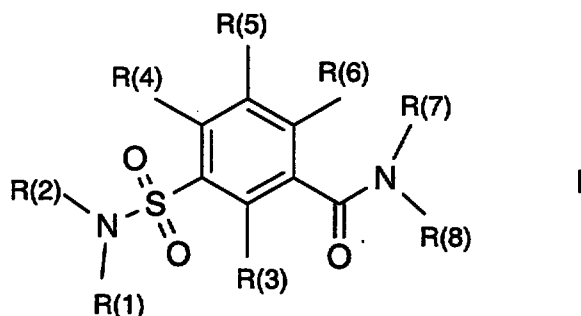
In contrast to IK_r and IK_S , which also occur in the human ventricle, the IK_{ur} plays an important role in the human atrium but not in the ventricle. For this reason, on inhibition of the IK_{ur} current, in contrast to the blockage of IK_r or
15 IK_S , the risk of a proarrhythmic effect on the ventricle is ruled out from the outset. (Z. Wang et al., *Circ. Res.* 73, 1993, 1061 - 1076: "Sustained Depolarisation-Induced Outward Current in Human Atrial Myocytes"; G.-R. Li et al., *Circ. Res.* 78, 1996, 689 - 696: "Evidence for Two Components of Delayed Rectifier K^+ -Current in Human Ventricular Myocytes"; G.J. Amos et al., *J. Physiol.* 491, 1996, 31 - 50: "Differences between outward currents of human atrial and subepicardial ventricular myocytes").
20

Selective blockers of the IK_{ur} or $Kv1.5$ channel have not been described to date in the literature. Although a blocking effect on the $Kv1.5$ channel has
25 been described for numerous pharmaceutical active substances (e.g. Tedisamil, Bupivacaine or Sertindole), the $Kv1.5$ blockage in each case constitutes only a side effect here, alongside other principal effects of the substances. WO 98 04 521 claims, as potassium channel blockers, aminoindanes which block the $Kv1.5$ channel. However, an equipotent
30 action on the $Kv1.3$ channel is also described for these compounds. Blockage of the $Kv1.3$ channel, which plays a role in human T-lymphocytes, has an immunosuppressive effect, which is undesirable as a side effect of an antiarrhythmic drug to be administered for a chronic condition. Applications WO 98 18 475 and WO 98 18 476 claim the use of
35 various pyridazinones and phosphine oxides as antiarrhythmic drugs, which are said to act by blocking the IK_{ur} . However, these compounds were originally (WO 96 25 936) also described as immunosuppressive drugs, so that their medical usability for the treatment of atrial arrhythmias appears doubtful.

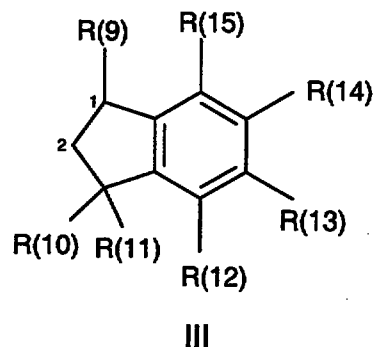
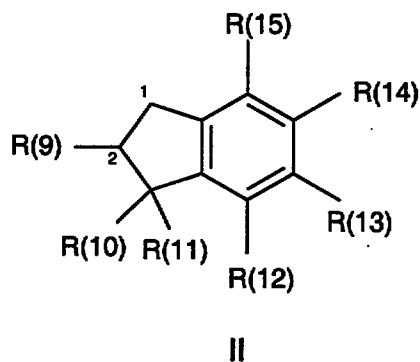
It has now been found that the compounds according to the invention are potent blockers of the human Kv1.5 channel. They can therefore be used as novel antiarrhythmic drugs having a particularly advantageous safety profile. In particular, the compounds are suitable for the treatment of supraventricular arrhythmias, e.g. atrial fibrillation or atrial flutter.

The compounds according to the invention, of the formula I, were not previously known. Some structurally related indane derivatives are described in the applications EP 258 096 and EP 374 054. However, the compounds claimed there differ from the compounds according to the invention in this application in that, in said applications, R(9) is a basic amino substituent. Moreover, only unsubstituted sulfonamides (R^1 and $R^2 = H$) are described there, whereas it has been found here that it is precisely substituted sulfonamides that are particularly effective blockers of the Kv1.5 channel.

The present invention relates to compounds of the formula I



in which R(8) is either a 1-indanyl radical of the formula II or a 2-indanyl radical of the formula III



and in which:

R(1) and R(2),

independently of one another, are R(20)-C_rH_{2r},

5 where a CH₂ group of the group C_rH_{2r} may be replaced by
-O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-,
-SO₂-, -NR(21)- or -CONR(21);

R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

10 R(20) is H, CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl
having 3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23),
-CONR(22)R(23), -OR(24), -COOR(24), phenyl or an
N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9
carbon atoms,

15 where phenyl and the N-containing heterocycle are
unsubstituted or substituted by 1 or 2 substituents,
selected from the group consisting of F, Cl, Br, I,
CF₃, NO₂, CN, NH₂, OH, methyl, ethyl,
hydroxymethyl, hydroxyethyl, methoxy, dimethyl-
20 amino, sulfamoyl, methylsulfonyl and methyl-
sulfonylamino;

R(22) and R(23),

independently of one another, are hydrogen or
alkyl having 1, 2, 3 or 4 carbon atoms;

or

25 R(22) and R(23)

together form a chain of 4 or 5 methylene groups,
of which one CH₂ group can be replaced by -O-,
-S-, -NH-, -N(methyl)- or -N(benzyl)- ;

30 R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
r is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

or

R(1) and R(2)

35 together form a chain of 4 or 5 methylene groups, of which one
CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or
-N(benzyl)- ;

R(3), R(4), R(5) and R(6),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl
having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7
or 8 carbon atoms, CN, CF₃, NO₂, OR(25) or NR(26)R(27);

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a fluorinated alkyl radical of the formula $-C_xH_{2x}CF_yH_{3-y}$ or phenyl,

5 which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , NO_2 , CN, NH_2 , OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

10 x is 0, 1, 2 or 3;
y is 1, 2 or 3;

R(26) and R(27),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

15 R(26) and R(27)

together form a chain of 4 or 5 methylene groups, of which one CH_2 group can be replaced by $-O-$, $-S-$, $-NH-$, $-N(methyl)-$ or $-N(benzyl)-$;

R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

20 R(9) is hydrogen, OR(28) or OCOR(28);

R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) and R(11),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

25 R(12), R(13), R(14) and R(15),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, $-CN$, $-CF_3$, $-C_2F_5$, $-C_3F_7$, $-N_3$, $-NO_2$, $-Y-C_5H_2s-$ R(29), phenyl, thienyl, furyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

30 where phenyl, thienyl, furyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF_3 , NO_2 , CN, NH_2 , OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

35 Y is $-O-$, $-CO-$, $-CO-O-$, $-O-CO-$, $-S-$, $-SO-$, $-SO_2-$, $-O-SO_2-$, $-SO_2NR(30)-$, $-CONR(30)-$ or $-NR(30)CO-$, where the link to the backbone is in each case via the atom on the left;

R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 s is zero, 1, 2, 3, 4, 5 or 6;
 R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3,
 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31),
 5 -NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing
 heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
 where phenyl and the N-containing heterocycle are
 unsubstituted or substituted by 1 or 2 substituents,
 selected from the group consisting of F, Cl, Br, I,
 10 CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy,
 dimethylamino, sulfamoyl, methylsulfonyl and
 methylsulfonylamino;
 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 R(32) and R(33),
 15 independently of one another, are hydrogen or
 alkyl having 1, 2, 3 or 4 carbon atoms;
 or
 R(32) and R(33)
 together form a chain of 4 or 5 methylene groups,
 20 of which one CH₂ group can be replaced by -O-,
 -S-, -NH-, -N(CH₃)- or -N(benzyl)-;
 and their physiologically tolerated salts.

25 Compounds of the formula I having the abovementioned meanings, but
 where at least one of the radicals R(1) and R(2) is other than hydrogen are
 preferred.

Particularly preferred are compounds of the formula I in which R(8) is either
 a 1-indanyl radical of the formula II or a 2-indanyl radical of the formula III
 30 and in which:

R(1) is hydrogen;
 R(2) is R(20)-C_rH_{2r},
 where one CH₂ group of the group C_rH_{2r} may be replaced
 by -O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-,
 35 -SO₂-, -NR(21)- or -CONR(21);
 R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 R(20) is CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl having
 3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23),
 -CONR(22)R(23), -OR(24), -COOR(24), phenyl or an

N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, hydroxymethyl, hydroxyethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

5

10

R(22) and R(23),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(22) and R(23)

15

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)-;

R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

r is zero, 1, 2, 3, 4, 5, 6, 7 or 8;

20 R(3), R(4), R(5) and R(6),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂, OR(25) or NR(26)R(27);

25

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or phenyl,

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

30

x is 0, 1, 2 or 3;

y is 1, 2 or 3;

R(26) and R(27),

35

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(26) and R(27)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)-;

- R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- 5 R(9) is hydrogen, OR(28) or OCOR(28);
R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- R(10) and R(11),
independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- 10 R(12), R(13), R(14) and R(15),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CN, -CF₃, -C₂F₅, -C₃F₇, -N₃, -NO₂, -Y-C₈H₂s-R(29), phenyl, thienyl, furyl or an N-containing heterocycle having
- 15 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where phenyl, thienyl, furyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 20 Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-, -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left;
- 25 R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
- s is zero, 1, 2, 3, 4, 5 or 6;
- R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31), -NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing
- 30 heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 35 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
- R(32) and R(33),
independently of one another, are hydrogen or

alkyl having 1, 2, 3 or 4 carbon atoms;

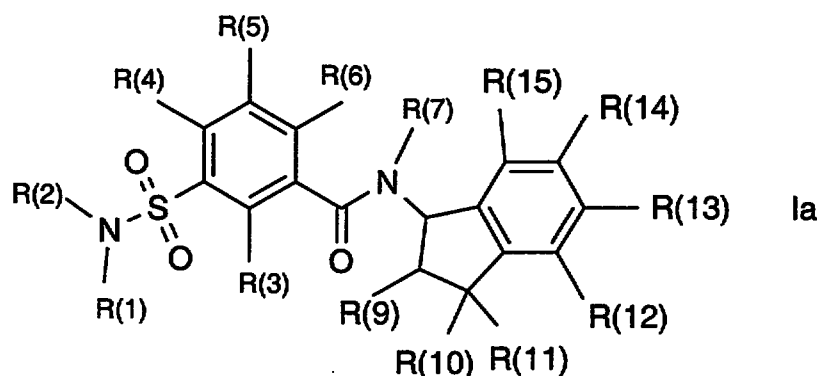
or

R(32) and R(33)

together form a chain of 4 or 5 methylene groups,
of which one CH₂ group can be replaced by -O-,
-S-, -NH-, -N(CH₃)- or -N(benzyl)-;

and their physiologically tolerated salts.

Very particularly preferred are compounds of the formula I in which R(8) is
a 1-indanyl radical of the formula II, i.e. compounds of the formula Ia



in which:

R(1) is hydrogen;

R(2) is R(20)-CY_rH_{2r},

where one CH₂ group of the group C_rH_{2r} may be replaced
by -O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-,
-SO₂-, -NR(21)- or -CONR(21);

R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

R(20) is CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl having
3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23),
-CONR(22)R(23), -OR(24), -COOR(24), phenyl or an
N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9
carbon atoms,

where phenyl and the N-containing heterocycle are
unsubstituted or substituted by 1 or 2 substituents
selected from the group consisting of F, Cl, Br, I,
CF₃, NO₂, CN, NH₂, OH, methyl, ethyl,
hydroxymethyl, hydroxyethyl, methoxy, dimethyl-
amino, sulfamoyl, methylsulfonyl and methyl-
sulfonylamino;

R(22) and R(23),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

5

R(22) and R(23)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)-;

R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

10

r is zero, 1, 2, 3, 4, or 5;

R(3), R(4), R(5) and R(6),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂ or OR(25);

15

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or phenyl,

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethyl-amino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

20

x is 0, 1, 2 or 3;

25

y is 1, 2 or 3;

R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(9) is hydrogen, OR(28) or OCOR(28);

R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) and R(11),

30

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(12), R(13), R(14) and R(15),

35

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CN, -CF₃, -C₂F₅, -C₃F₇, -NO₂, -Y-C₈H₂₈-R(29), phenyl, thienyl, furyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

where phenyl, thienyl, furyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2

substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

5 Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-, -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left;

R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

s is zero, 1, 2, 3, 4, 5 or 6;

10 R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31), -NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

15 where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

20 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(32) and R(33),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

25 R(32) and R(33)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(CH₃)- or -N(benzyl)-;

and their physiologically tolerated salts.

30

Especially preferred are compounds of the formula Ia in which:

R(1) is hydrogen;

R(2) is R(20)-C_rH_{2r};

35 R(20) is CH₃, CH₂F, CHF₂, CF₃, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CONR(22)R(23), -OR(24), -COOR(24) or phenyl,

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of

F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl, hydroxymethyl, hydroxyethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

5 R(22) and R(23),
independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(22) and R(23)
10 together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)-;

R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
r is zero, 1, 2, 3, 4, or 5;

15 R(3), R(4), R(5) and R(6),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂ or OR(25);

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms,
20 a fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or phenyl,
which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl,
25 methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

x is 0, 1, 2 or 3;

y is 1, 2 or 3;

R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

30 R(9) is hydrogen or OR(28);

R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) and R(11),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

35 R(12), R(13), R(14) and R(15),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, -NO₂ or -Y-C₅H_{2s}-R(29);

Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-,

-SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left; R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; s is zero, 1, 2, 3, 4 or 5;

5 R(29) is hydrogen, methyl, CF₃, -OR(31), -COOR(31), -NR(32)R(33), -CONR(32)R(33) or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

10 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(32) and R(33), independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

15 or R(32) and R(33) together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(CH₃)- or -N(benzyl)-;

20 and their physiologically tolerated salts.

Alkyl radicals and alkylene radicals may be straight-chain or branched. This also applies to the alkylene radicals of the formulae C_rH_{2r}, C_sH_{2s} and C_xH_{2x}.

25 Alkyl radicals and alkylene radicals may also be straight-chain or branched if they are substituted or are contained in other radicals, e.g. in an alkoxy radical or in an alkylmercapto radical or in a fluorinated alkyl radical. Examples of alkyl radicals are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3,3-dimethylbutyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl, nonadecyl and eicosyl. The divalent radicals derived from these radicals, e.g. methylene, 1,1-ethylene, 1,2-ethylene, 1,1-propylene, 1,2-propylene, 2,2-propylene, 1,3-propylene, 1,4-butylene, 1,5-pentylene, 2,2-dimethyl- 1,3-propylene, 1,6-hexylene, etc., are examples of alkylene radicals.

35

Cycloalkyl radicals can likewise be branched. Examples of cycloalkyl radicals having 3 to 8 carbon atoms are cyclopropyl, cyclobutyl, 1-methylcyclopropyl, 2-methylcyclopropyl, cyclopentyl, 2-methylcyclobutyl, 3-methyl-

cyclobutyl, cyclopentyl, cyclohexyl, 2-methylcyclohexyl, 3-methylcyclohexyl, 4-methylcyclohexyl, cycloheptyl, cyclooctyl, etc.

N-containing heterocycles having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms are in particular the aromatic systems 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 1,2,3-triazol-1-, -4- or -5-yl, 1,2,4-triazol-1-, -3- or -5-yl, 1- or 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 1,2,3-oxadiazol-4- or -5-yl, 1,2,4-oxadiazol-3- or -5-yl, 1,3,4-oxadiazol-2-yl or -5-yl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or -5-yl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, 3- or 4-pyridazinyl, pyrazinyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-indazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl, 2-, 3-, 5-, 6-, 7- or 8-quinoxalinyll or 1-, 4-, 5-, 6-, 7- or 8-phthalazinyl.

The N-containing heterocycles pyrrolyl, imidazolyl, quinolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl and pyridazinyl are particularly preferred.

Thienyl is both 2- and 3-thienyl.

Monosubstituted phenyl radicals may be substituted in the 2-, 3- or 4-position or disubstituted in the 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-position.

The same applies in context to the N-containing heterocycles or the thiophene radical.

In the case of disubstitution of a radical, the substituents may be identical or different.

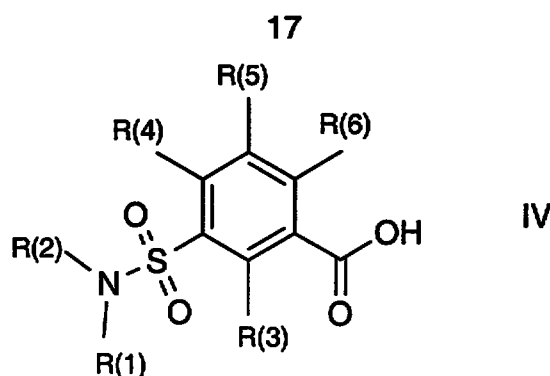
If the compounds of the formula I contain one or more acidic or basic groups or one or more basic heterocycles, the corresponding physiologically or toxicologically tolerated salts are also the subject of the invention, in particular the pharmaceutically usable salts. Thus, the compounds of the formula I which carry acidic groups, e.g. one or more COOH groups, for example as alkali metal salts, preferably sodium or potassium salts, or as alkaline earth metal salts, e.g. calcium or magnesium salts, or as ammonium salts, e.g. as salts with ammonia or organic amines or amino acids, can be used. Compounds of the formula I

which carry one or more basic, i.e. pronotatable, groups or contain one or more basic heterocyclic rings can also be used in the form of their physiologically tolerated acid addition salts with inorganic or organic acids, for example as hydrochlorides, phosphates, sulfates, methanesulfonates, acetates, lactates, maleates, fumarates, malates, gluconates, etc. If the compounds of the formula I simultaneously contain acidic and basic groups in the molecule, internal salts, so-called betaines, are also subjects of the invention, in addition to the salt forms described. Salts can be obtained from the compounds of the formula I by customary methods, for example by combination with an acid or base in a solvent or dispersant or by anion exchange from other salts.

With appropriate substitution, the compounds of the formula I may be present in stereoisomeric forms. If the compounds of the formula I contain one or more centers of asymmetry, they can, independently of one another, have the S-configuration or the R-configuration. The invention relates to all possible stereoisomers, e.g. enantiomers or diastereomers, and mixtures of two or more stereoisomeric forms, e.g. enantiomers and/or diastereomers, in any ratios. The invention thus relates to enantiomers, for example, in the form of pure enantiomers, both as levorotatory and dextrorotatory antipodes and also in the form of mixtures of the two enantiomers in different ratios or in the form of racemates. When cis/trans isomerism is present, the invention relates both to the cis form and to the trans form and mixtures of these forms. The preparation of individual stereoisomers can be carried out, if desired, by separating a mixture by customary methods or, for example, by stereoselective synthesis. When mobile hydrogen atoms are present, the present invention also comprises all tautomeric forms of the compounds of the formula I.

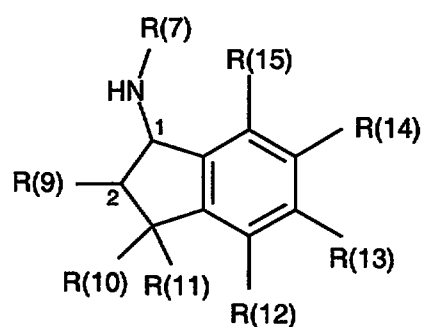
The compounds of the formula I can be prepared by different chemical processes, which likewise form subjects of the present invention. Thus, for example, a compound of the formula I is obtained by reacting

a carboxylic acid of the formula IV,

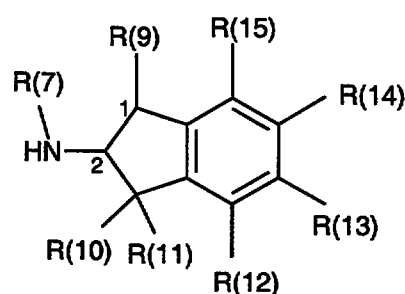


in which R(1), R(2), R(3), R(4), R(5) and R(6) have the abovementioned meanings, with an amine of the formula V a or V b

5



Va



Vb

in which R(7), R(9), R(10), R(11), R(12), R(13), R(14) and R(15) have the abovementioned meanings, in a manner known per se, in an amidation reaction.

10

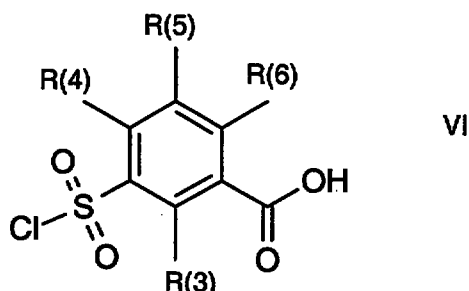
Numerous methods for carrying out these reactions have been described in the literature. They can be particularly advantageously carried out by activating the carboxylic acid, for example with dicyclohexylcarbodiimide (DCC), if required with the addition of hydroxybenzotriazole (HOBT) or dimethylaminopyridine (DMAP), or with O-[(cyano(ethoxycarbonyl)methylene)amino]-1,1,3,3-tetramethyluronium tetrafluoroborate (TOTU). However, it is also possible first to synthesize reactive acid derivatives by known methods, for example acid chlorides by reacting carboxylic acids of the formula IV with inorganic acid halides, such as, for example, SOCl_2 , or acid imidazolides by reaction with carbonyldiimidazole, which are then reacted with the amines of the formulae V a or V b, if required with addition of an auxiliary base.

The amines of the formulae V a or V b are either known from the literature or can be prepared analogously to known methods, for example by

25

reductive amination of the corresponding 1-indanones or by epoxidation of the corresponding 1H-indenes and subsequent epoxide opening with an amine of the formula $R(7)-NH_2$.

- 5 The carboxylic acids of the formula (IV) can be obtained, for example, from the chlorosulfonyl compounds of the formula VI



- 10 by reaction with an amine of the formula $R(1)R(2)NH$ in a suitable inert solvent, such as, for example, diethyl ether, THF or acetone, and, if required, in the presence of an auxiliary base, such as, for example, triethylamine.
- 15 The chlorosulfonyl compounds of the formula VI are either known from the literature or can be prepared analogously to known methods, for example by chlorosulfonation of correspondingly substituted benzoic acids with chlorosulfonic acid.
- 20 In all procedures, it may be appropriate temporarily to protect functional groups in the molecule in specific reaction steps. Such protective group techniques are familiar to a person skilled in the art. The choice of a protective group for suitable groups and the processes for their introduction and elimination are described in the literature and, if required, can be
- 25 adapted to the specific case without difficulties.

- The compounds, according to the invention, of the formula I and their physiologically tolerated salts can thus be used as a medicament alone, in mixtures with one another or in the form of pharmaceutical formulations, in
- 30 animals, preferably in mammals, and in particular in humans. The present invention also relates to the compounds of the formula I and their physiologically tolerated salts for use as medicaments, their use in the therapy and prophylaxis of said pathological states and their use for the preparation of medicaments for this purpose and of medicaments having a

K⁺-channel-blocking effect. Furthermore, the present invention relates to pharmaceutical formulations which contain, as an active ingredient, an effective dose of at least one compound of the formula I and/or of one physiologically tolerated salt thereof in addition to customary, pharmaceutically satisfactory carriers and auxiliaries. The pharmaceutical formulations usually contain from 0.1 to 90% by weight of the compounds of the formula I and/or of their physiologically tolerated salts. The preparation of the pharmaceutical formulations can be carried out in a manner known per se. For this purpose, the compounds of the formula I and/or their physiologically tolerated salts, together with one or more solid or liquid pharmaceutical carriers and/or auxiliaries and, if desired, in combination with other pharmaceutical active substances, are brought into a suitable administration form or dosage form, which can then be used as a medicament in human medicine or veterinary medicine.

Medicaments which contain compounds, according to the invention, of the formula I and/or their physiologically tolerated salts can be administered orally, parenterally, e.g. intravenously, rectally, by inhalation or topically, the preferred administration depending on the specific case, for example the respective symptom of the disease to be treated.

Auxiliaries which are suitable for the desired medicament formulation are familiar to the person skilled in the art on the basis of his technical knowledge. In addition to solvents, gel formers, suppository bases, tablet auxiliaries and other active substance carriers, it is possible to use, for example, antioxidants, dispersants, emulsifiers, antifoams, flavoring agents, preservatives, solubilizers, compositions for achieving a depot effect, buffer substances or colorants.

The compounds of the formula I can also be combined with other pharmaceutical active ingredients in order to achieve an advantageous therapeutic effect. Thus, combinations with substances having cardiovascular activity, which combinations are advantageous in the treatment of cardiovascular diseases, are possible. Suitable combination partners of this type which are advantageous for cardiovascular diseases are, for example, other antiarrhythmic drugs, for example class I, class II or class III antiarrhythmic drugs, such as, for example, IK_S- or IK_r-channel blockers, e.g. dofetilide, or furthermore hypotensive substances, such as ACE inhibitors (for example enalapril, captopril, ramipril), angiotensin

antagonists, K^+ -channel activators and alpha- and beta-receptor blockers, as well as sympathomimetic and adrenergic compounds, and Na^+/H^+ exchange inhibitors, calcium channel antagonists, phosphodiesterase inhibitors and other substances having positive inotropic activity, such as,
5 for example, digitalis glycosides, or diuretics.

For an oral application form, the active compounds are mixed with the additives suitable for this purpose, such as carriers, stabilizers or inert diluents, and brought by the customary methods into the suitable dosage
10 forms, such as tablets, coated tablets, capsules or aqueous, alcoholic or oily solutions. For example, gum arabic, magnesia, magnesium carbonate, potassium phosphate, lactose, glucose or starch, in particular corn starch, can be used as inert carriers. The formulation may be in the form of both
15 dry granules and moist granules. Suitable oily carriers or suitable solvents are, for example, vegetable or animal oils, such as sunflower oil or cod-liver oil. Suitable solvents for aqueous or alcoholic solutions are, for example, water, ethanol or sugar solutions or mixtures thereof. Further auxiliaries, also for other application forms are, for example, polyethylene glycols and
polypropylene glycols.

20

For subcutaneous or intravenous application, the active compounds, if desired for the substances customary for this purpose, such as solubilizers, emulsifiers or further auxiliaries, are brought into solution, suspension or emulsion. The compounds of the formula I and their physiologically
25 tolerated salts may also be lyophilized and the resulting lyophilized products may be used, for example, for the preparation of injection or infusion preparations. Suitable solvents are, for example, water, physiological saline solution or alcohols, e.g. ethanol, propanol or glycerol, as well as sugar solutions, such as glucose or mannitol solutions, or
30 mixtures of the various solvents mentioned.

Suitable pharmaceutical formulations for administration in the form of aerosols or sprays are, for example, solutions, suspensions or emulsions of the active substances of the formula I or their physiologically tolerated salts
35 in a pharmaceutically acceptable solvent, such as, in particular, ethanol or water, or a mixture of such solvents. If required, the formulation may also contain other pharmaceutical auxiliaries, such as surfactants, emulsifiers and stabilizers as well as a propellant. Such a formulation contains the active substance usually in a concentration of from about 0.1 to 10, in

particular from about 0.3 to 3, % by weight.

The dosage of the active substance of the formula I to be administered or of the physiologically tolerated salts depends on the specific case and, as usual, should be adapted to the circumstances of the specific case for optimum effect. Thus, it does of course depend on the frequency of administration and on the intensity of action and duration of action of the compounds used in each case for therapy or prophylaxis, as well as on the type and intensity of the disease to be treated and on sex, age, weight and individual responsiveness of the human or animal to be treated and on whether acute or prophylactic treatment is being carried out. Usually, the daily dose of a compound of the formula I when administered to a patient weighing about 75 kg is from 0.001 mg/kg body weight to 100 mg/kg body weight, preferably from 0.01 mg/kg body weight to 20 mg/kg body weight. The dose can be administered in the form of a single dose or divided into several, for example two, three or four, single doses. Particularly in the treatment of acute cases of cardiac arrhythmias, for example in an intensive care ward, a parenteral administration by injection or infusion, for example by a continuous intravenous infusion, may also be advantageous.

20

Experimental Section

List of abbreviations

25	DMF	N,N-dimethylformamide
	EA	ethyl acetate
	m.p.	melting point (unless stated otherwise, the melting points of the unpurified crude products are stated; it is quite possible that the melting points of the respective pure substances are substantially higher)
30	HOBT	1-hydroxy-1H-benzotriazole
	i. vac.	in vacuo
	solv	solvent
	RT	room temperature
35	THF	tetrahydrofuran
	TOTU	O-[(cyano(ethoxycarbonyl)methylene)amino]-1,1,3,3-tetramethyluronium tetrafluoroborate

General method for the synthesis of 3-chlorosulfonylbenzoic acids (formula

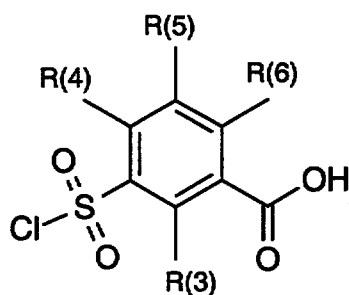
VI)

0.2 mol of a substituted benzoic acid is introduced into 135 ml of chlorosulfonic acid and the reaction mixture is heated to 120°C for 4 hours.

- 5 After cooling, it is poured onto 800 g of ice and stirred for 1 h, and the precipitated product is filtered off with suction.

Inter alia, the following 3-chlorosulfonylbenzoic acids were synthesized in this manner:

10



VI

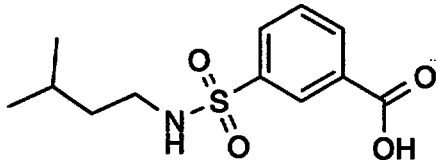
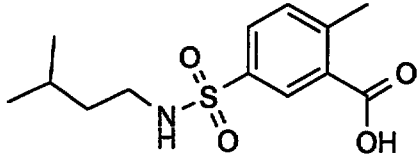
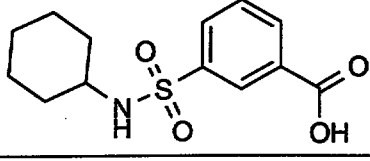
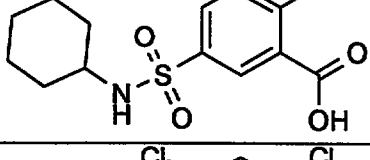
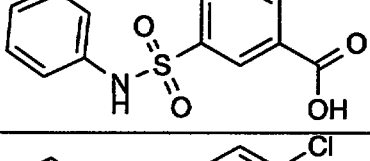
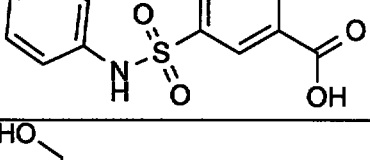
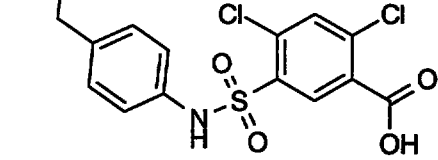
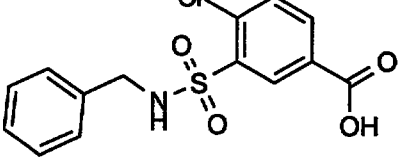
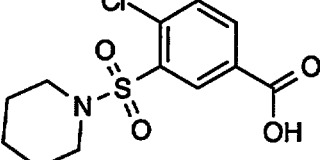
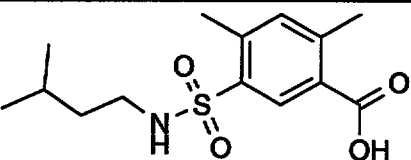
R(3)	R(4)	R(5)	R(6)	Yield	m.p. [°C]
H	Me	H	H	93%	174
H	H	H	Cl	91%	148
H	H	H	Me	95%	151
H	F	H	H	81%	140
H	Cl	H	H	86%	158
H	Cl	H	Cl	83%	185
H	F	H	Cl	82%	139
H	Cl	NO ₂	Cl	76%	235
H	H	NO ₂	Cl	42%	190
H	Cl	Cl	H	65%	207
H	OMe	H	H	75%	
H	H	H	OMe	80%	145
H	iPr	H	H	83%	192
H	H	Me	Me	82%	170
H	Me	H	Me	88%	190
H	Me	Me	H	81%	

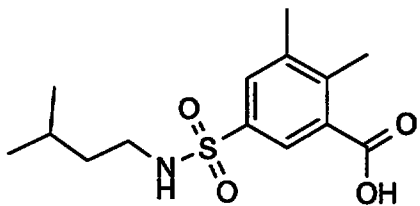
General method for the reaction of 3-chlorosulfonylbenzoic acids (Formula VI) with amines to give sulfonamides of the formula IV (Variant A):

- 5 10 mmol of the respective 3-chlorosulfonylbenzoic acid are added to a solution of 30 mmol of the corresponding amine in 20 ml of diethyl ether (or methylene chloride) and the reaction mixture is stirred overnight at RT. After the addition of 20 ml of ether (or methylene chloride) and 20 ml of water, the organic phase is extracted twice with dilute hydrochloric acid and then twice with saturated sodium bicarbonate solution. After acidification of
- 10 the bicarbonate extracts, the product of the formula IV is precipitated and is isolated either by filtration with suction or by extraction with EA.

Inter alia, the following sulfonamides of the formula IV were synthesized in this manner:

Structure	m.p. [°C]	Yield
	154	80%
	179	62%
	162	68%
	182	51%
	141	70%
	170	43%

	197	65%
	192	65%
	204	43%
	220	51%
	218	29% (in acetone as solvent)
	194	81% (in acetone as solvent)
	183	14% (in THF as solvent)
	201	
	209	36%
		76%

		87%
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General method for the synthesis of compounds, according to the invention, of the formula I from 3-chlorosulfonylbenzoic acids of the formula VI (Variant B):

5

3 mmol of an amine of the formula $\text{HNR}(1)\text{R}(2)$ are dissolved in 20 - 50 ml of diethyl ether, and 1 mmol of 3-chlorosulfonylbenzoic acid (formula VI) dissolved in ether is added. Stirring is carried out for 30 min at RT, the pH is adjusted to 1 with 2M hydrochloric acid and the phases are separated.

- 10 The organic phase is dried, filtered and evaporated down i. vac. The residue is refluxed with 5 ml of thionyl chloride for 40 min. Thereafter, the excess thionyl chloride is removed i vac., and coevaporation is effected several times with toluene. The product thus obtained is taken up in ether or dichloromethane and added to a solution of 1 mmol of aminoindane
- 15 (formula II or III) and 1 mmol of Hünig base in ether and stirred for 20 min at RT. Thereafter, the pH is adjusted to 1 with 2M HCl and the phases are separated. The organic phase is dried, filtered and evaporated down i. vac. The crude product is purified by flash chromatography.

- 20 General method for the synthesis of compounds, according to the invention, of the formula I from sulfonamides of the formula IV (Variant C):

- 1 mmol of a compound of the formula IV is refluxed with 5 ml of thionyl chloride for 40 min. Thereafter, the excess thionyl chloride is removed
- 25 i. vac. and coevaporation is effected several times with toluene. The product thus obtained is taken up in ether or dichloromethane and added to a solution of 10 mmol of aminoindane in ether and stirred at RT until the reaction is complete. After the reaction mixture has been evaporated down, the residue is purified by means of preparative HPLC.

30

General method for the synthesis of compounds, according to the invention, of the formula I from sulfonamides of the formula IV (Variant D):

From 1.15 to 1.40 mmol of carbonyldiimidazole are added to a solution or

suspension of 1 mmol of a compound of the formula IV in THF, and the reaction mixture is stirred for 3 h at RT. After the addition of from 1.1 to 1.5 mmol of a 1- or 2-aminoindane of the formula V a or V b, respectively, stirring is carried out overnight at RT and the reaction mixture is then
 5 evaporated down in vacuo. The residue is taken up in EA and washed with dilute hydrochloric acid and sodium bicarbonate solution. After the organic phase has been evaporated down in vacuo, the residue is dissolved in isopropanol and the product is precipitated by adding water. After filtration with suction and drying, the compounds of the formula I are obtained in a
 10 purity of > 90% (some of them are contaminated with up to 10% of the corresponding bisindanylurea).

General method for the synthesis of compounds, according to the invention, of the formula I from sulfonamides of the formula IV (Variant E):

15 1 mmol of a compound of the formula IV is reacted with 1 mmol of a 1- or 2-aminoindane of the formula Va or Vb, respectively, in DMF in the presence of 1 mmol of TOTU and 1 mmol of Hünig base. After stirring has been carried out for 2 h at RT, the solvent is removed in vacuo and the
 20 crude product is purified by chromatography over RP18 silica gel.

General method for the synthesis of compounds, according to the invention, of the formula I from sulfonamides of the formula IV (Variant F):

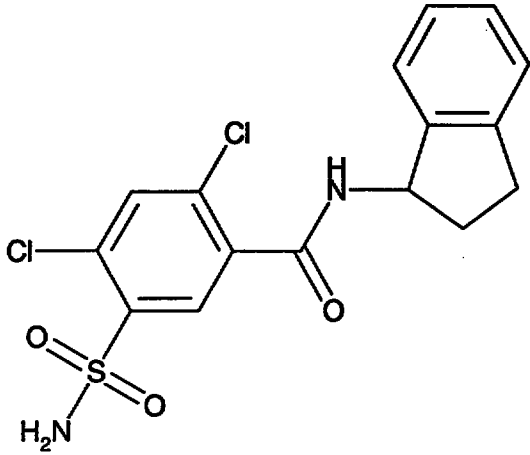
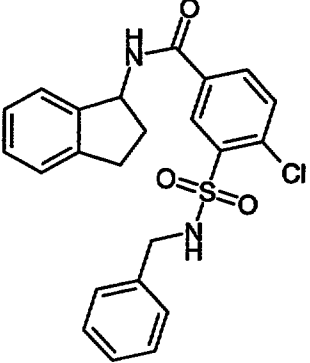
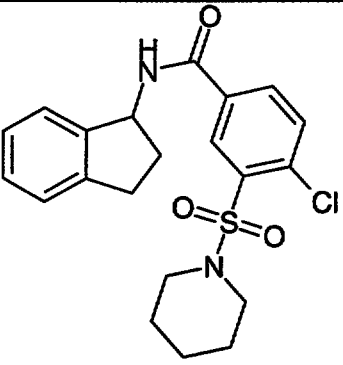
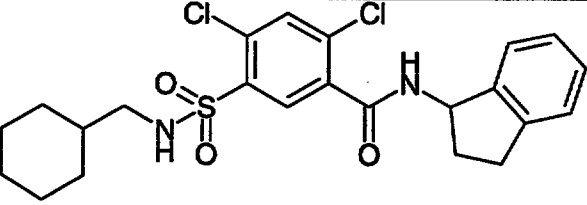
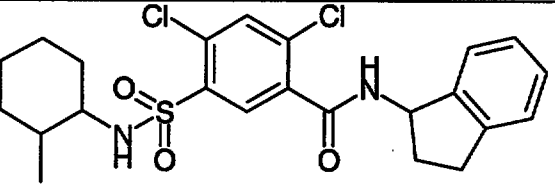
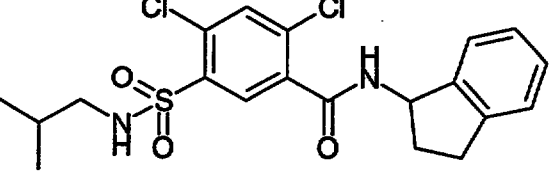
25 1.55 mmol of a 1- or 2-aminoindane of the formula V a or V b, respectively, are added to a solution of 1.4 mmol of a compound of the formula IV, 0.21 g (1.55 mmol) of HOBt and 0.19 g (1.55 mmol) of diisopropylcarbodiimide in 15 ml of THF at 0°C, and the reaction mixture is stirred overnight at RT. After the precipitate has been filtered off, the filtrate
 30 is evaporated down in vacuo and the residue is taken up in EA and is extracted with sodium bicarbonate solution.

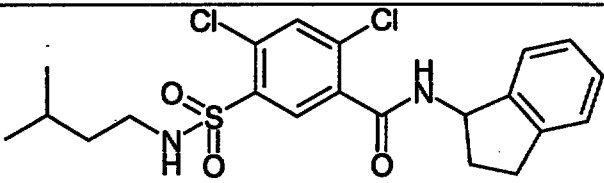
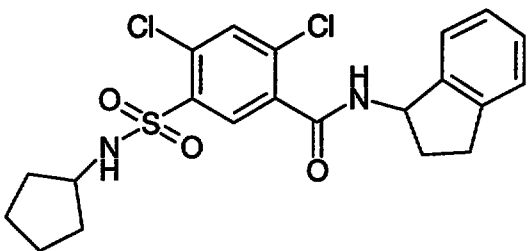
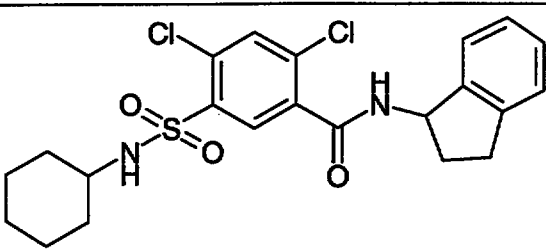
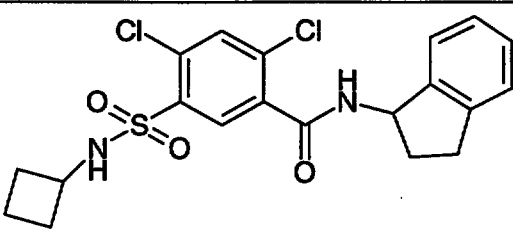
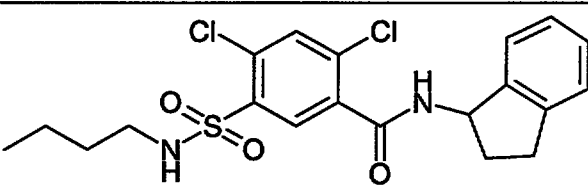
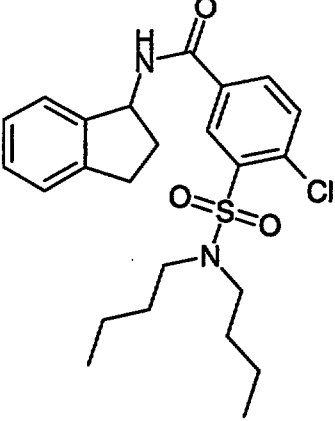
Inter alia, the following compounds of the formula I were synthesized according to the general methods (Variants B, C, D, E or F) and are shown
 35 in the table below.

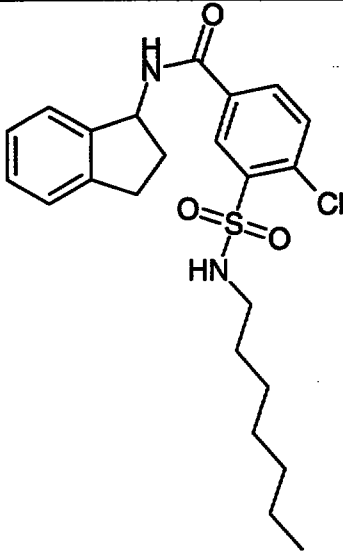
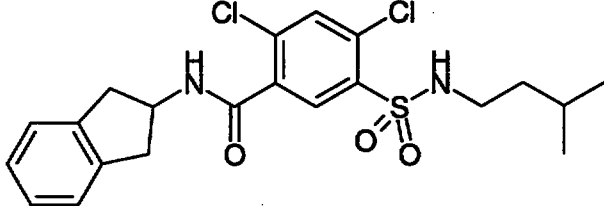
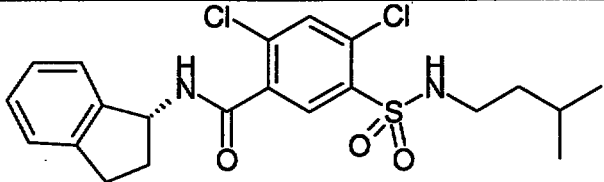
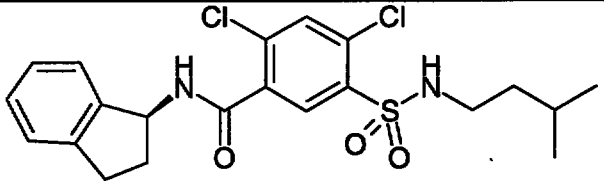
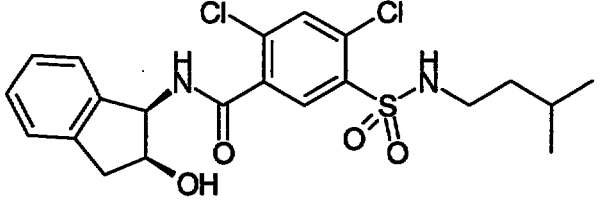
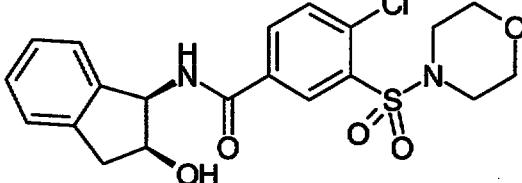
Compounds for which no melting point is given were isolated as oils or amorphous glassy products. Compounds for which no information on synthesis variant used is shown were obtained analogously to the methods described but with the use of slight variations, such as, for example,

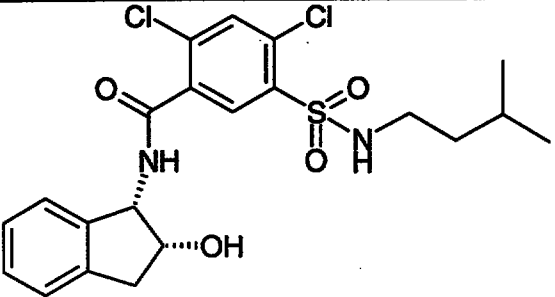
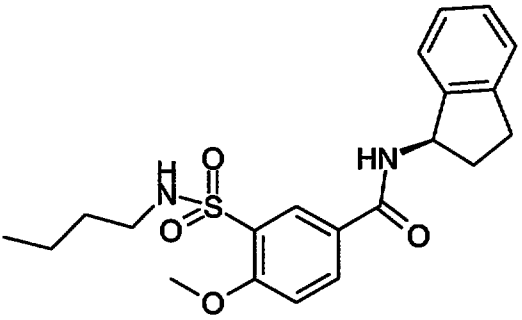
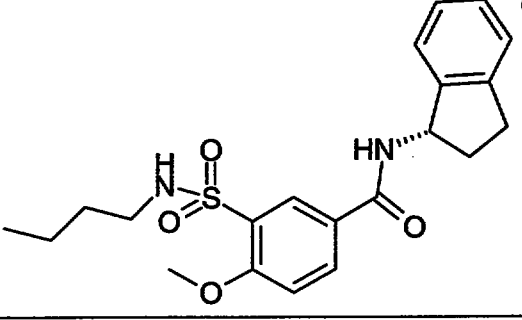
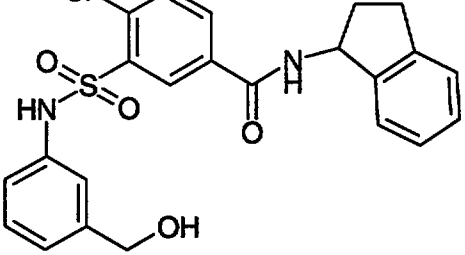
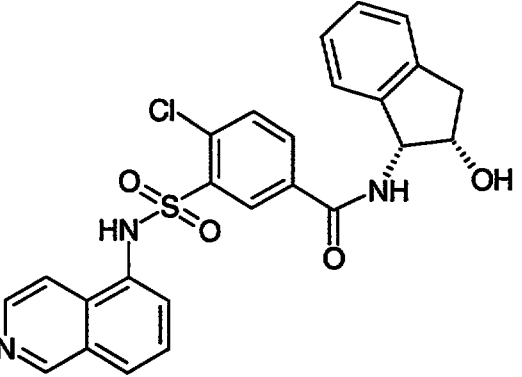
different solvents, different coupling reagent, etc. In no case is it absolutely essential to use a specific method, and as a rule all variants can be used.

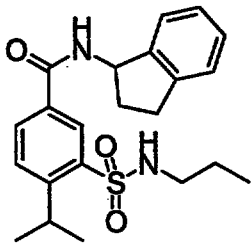
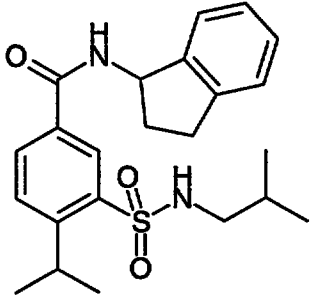
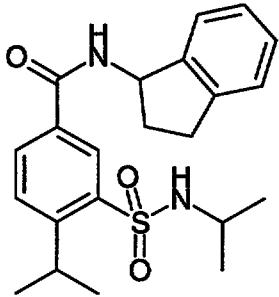
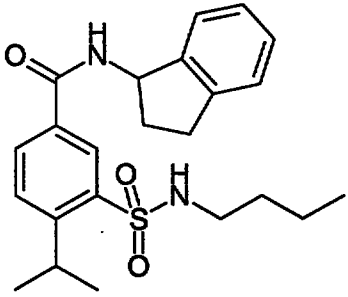
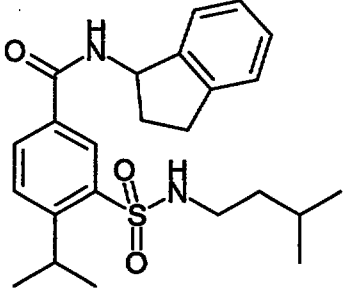
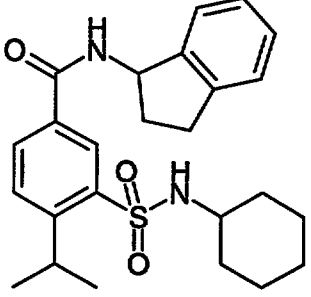
Example	Structure	m.p. [°C]	Method	Yield
1		210		
2		217		
3		139		
4		239		

5		248		
6		177		45%
7				
8			B	
9			B	
10			B	

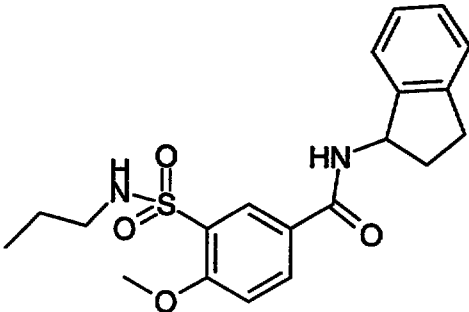
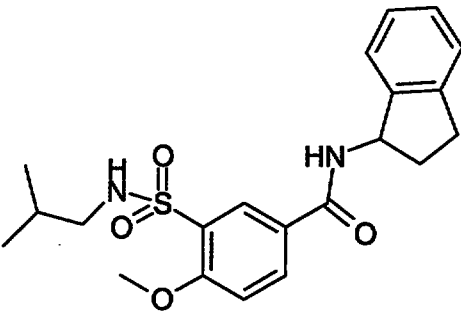
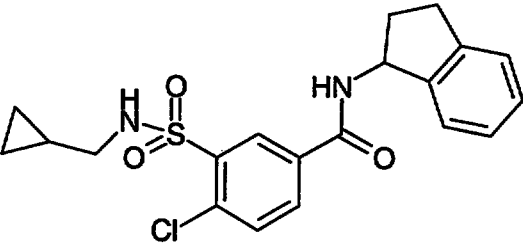
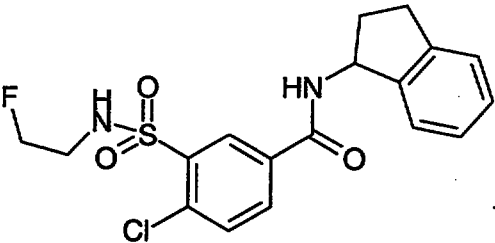
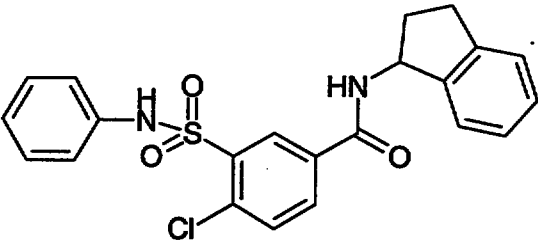
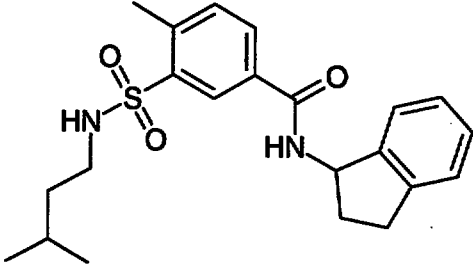
11			B	
12		82	C	54%
13		71	B	66%
14		86	C	14%
15		71	C	74%
16				

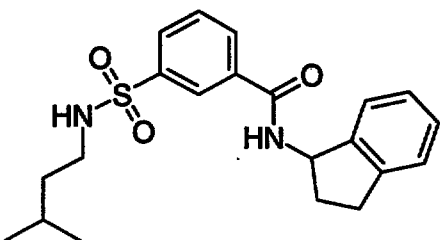
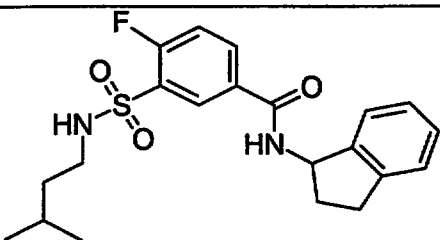
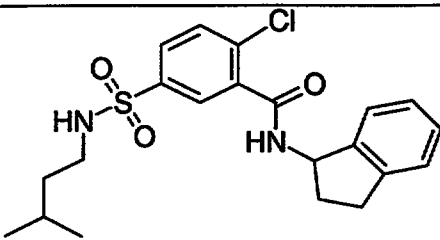
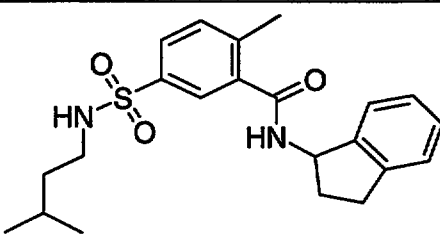
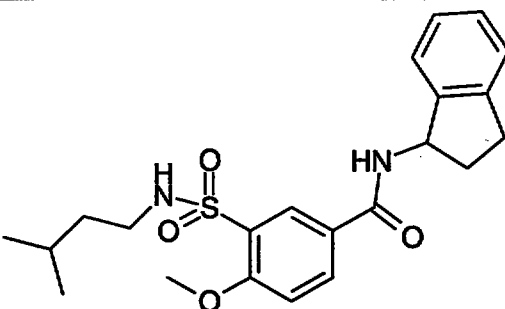
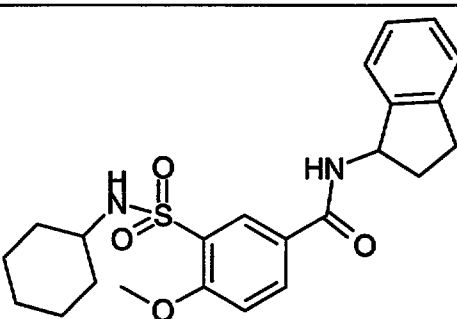
17	 <chem>CCCCCCCCNS(=O)(=O)c1ccc(cc1Cl)C(=O)Nc2c3ccccc3c2</chem>			
18	 <chem>CC(C)CN(S(=O)(=O)c1cc(Cl)cc(Cl)c1C(=O)Nc2c3ccccc3c2)</chem>			
19	 <chem>CC(C)CN(S(=O)(=O)c1cc(Cl)cc(Cl)c1C(=O)N[C@H]2c3ccccc3c2)</chem> Chiral			
20	 <chem>CC(C)CN(S(=O)(=O)c1cc(Cl)cc(Cl)c1C(=O)N[C@@H]2c3ccccc3c2)</chem> Chiral			
21	 <chem>CC(C)CN(S(=O)(=O)c1cc(Cl)cc(Cl)c1C(=O)N[C@@H]2c3ccccc3[C@@H]2O)</chem>			
22	 <chem>C1CCN(C1)S(=O)(=O)c2ccc(cc2Cl)C(=O)N[C@@H]3c4ccccc4[C@@H]3O</chem>			

23	 Chiral			
24	 Chiral	173	D	99%
25	 Chiral	174	D	99%
26		89	E	38%
27			E	28%

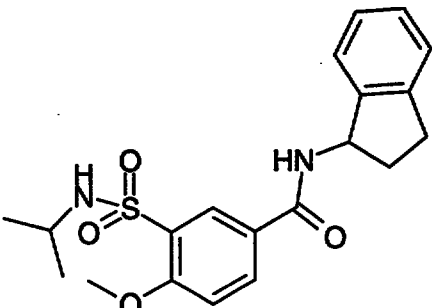
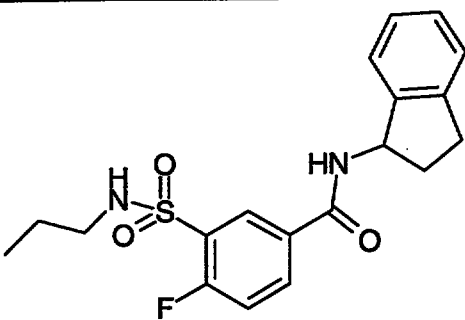
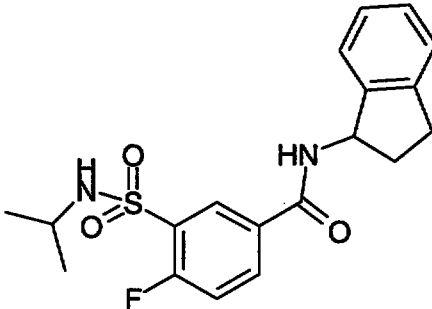
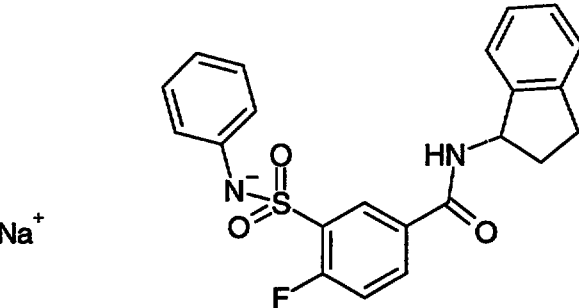
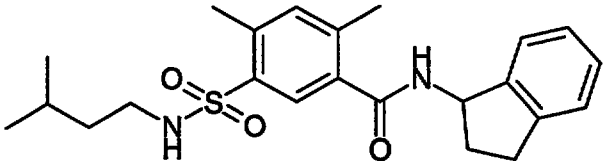
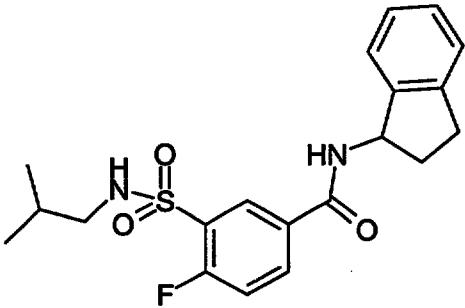
28			D	99%
29			D	99%
30			D	99%
31			D	99%
32			D	99%
33			D	99%

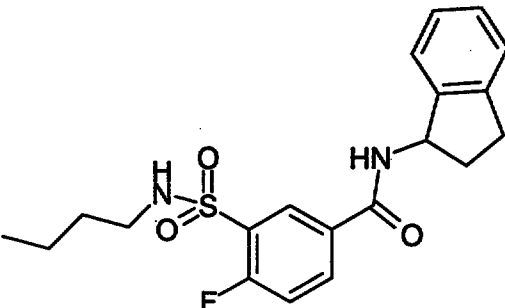
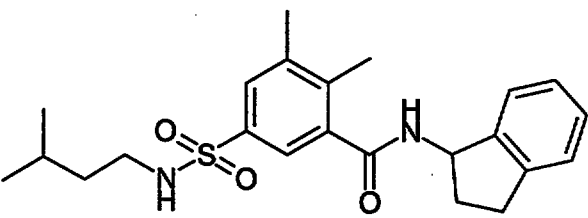
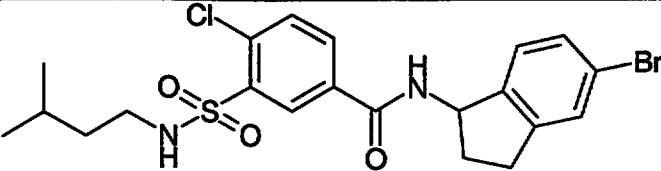
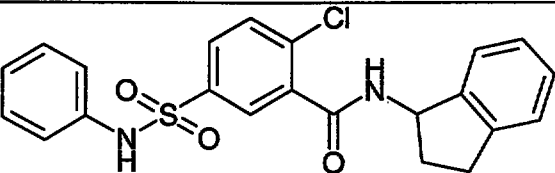
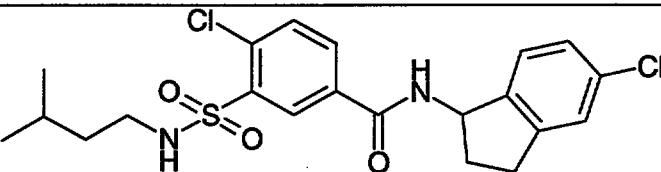
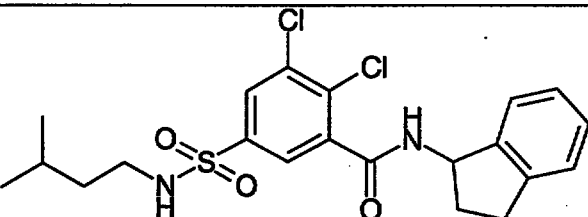
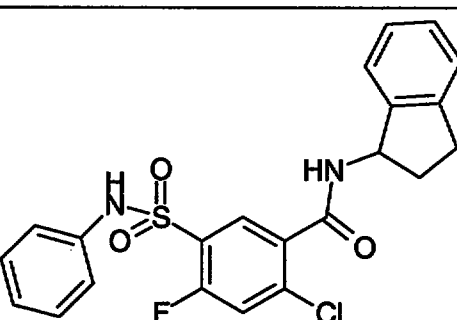
33

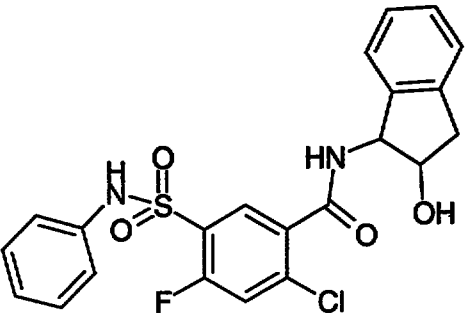
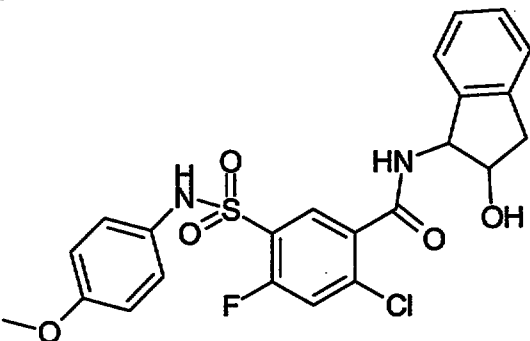
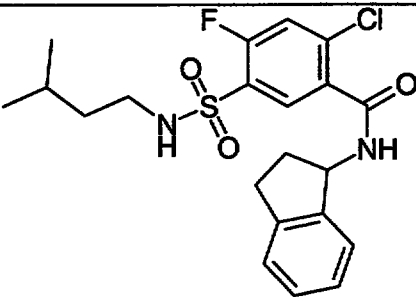
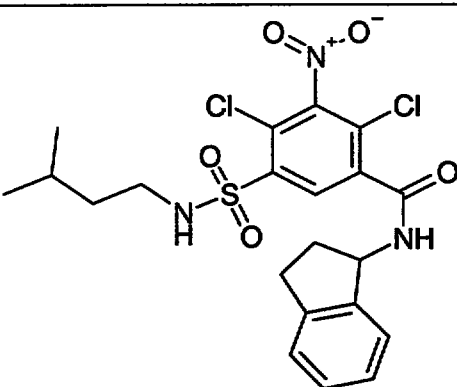
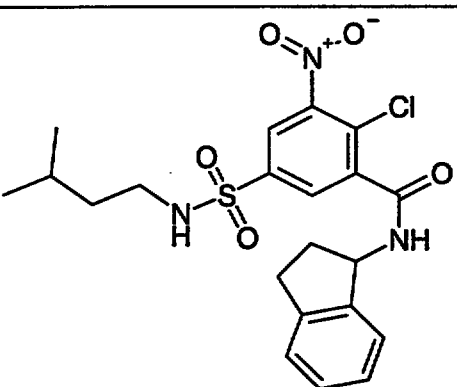
34		168	D	99%
35		186	D	99%
36				
37				
38				
39		139	D	84%

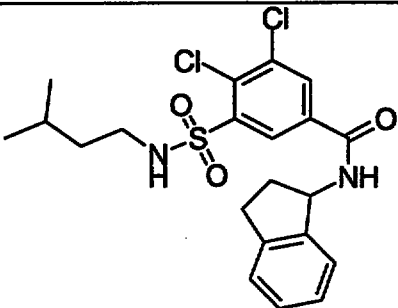
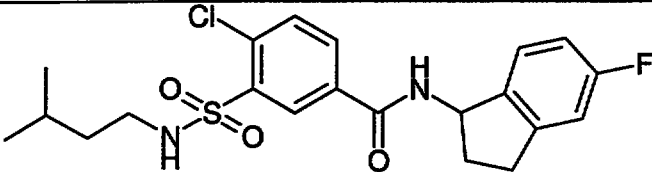
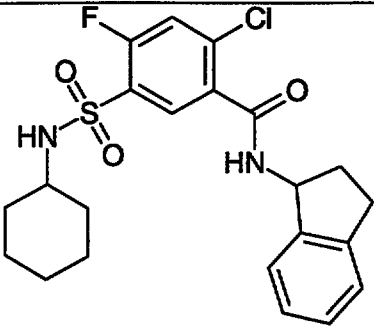
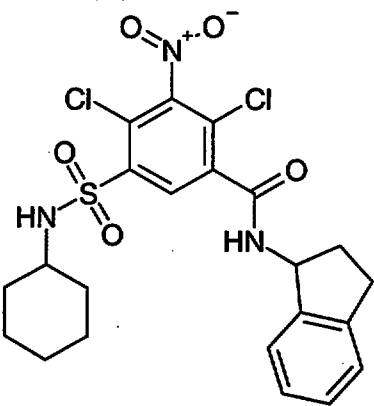
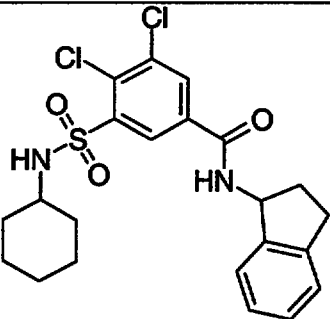
40		136	D	75%
41		145	D	80%
42		110	D	79%
43		114	D	70%
44		70-80	D	72%
45		193-197	D	99%

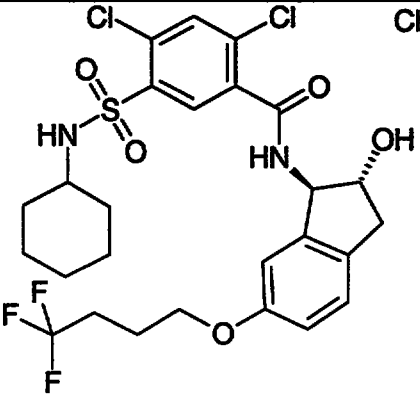
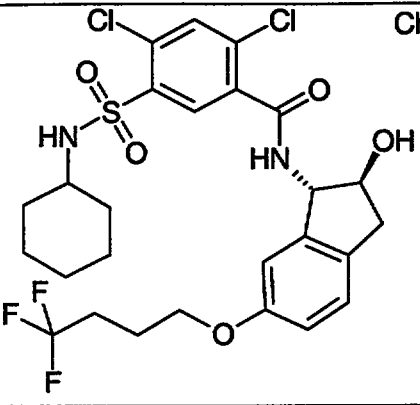
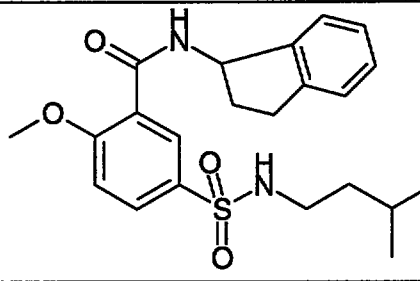
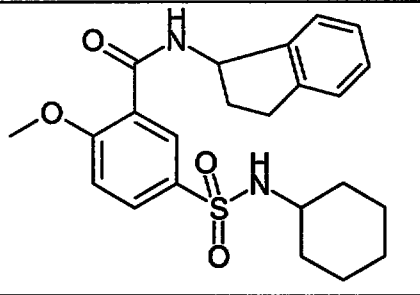
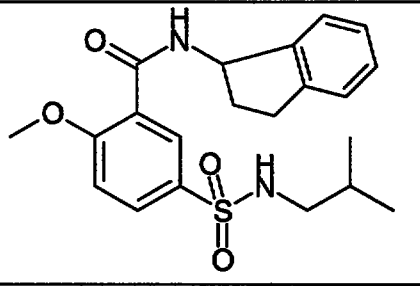
46		196	E	34%
47		154	D	26%
48		185	D	45%
49		176	D	75%
50		(glassy)	D	51%
51		(glassy)	D	89%
52		141	E	44%

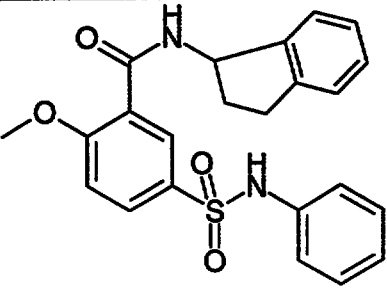
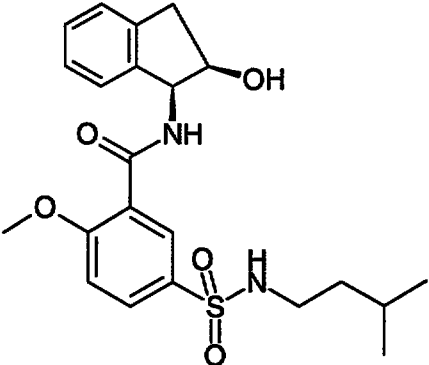
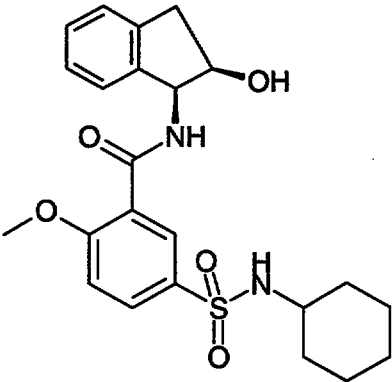
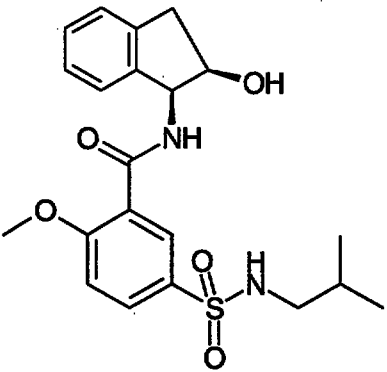
53		183	D	85%
54			D	90%
55			D	98%
56		225- 229	D	99%
57			E	61%
58			D	62%

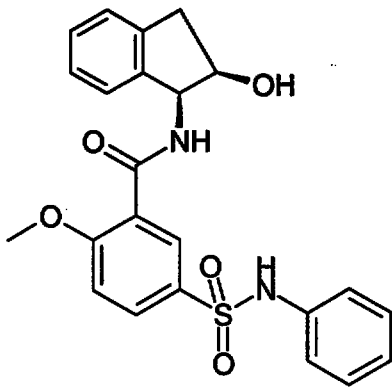
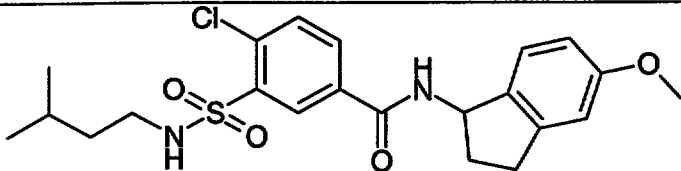
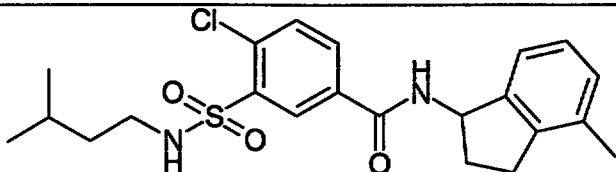
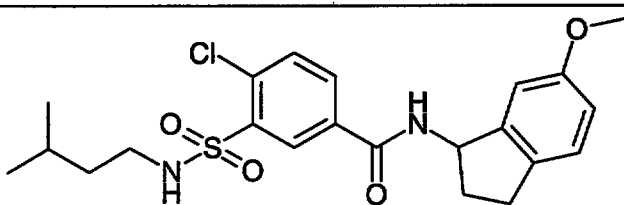
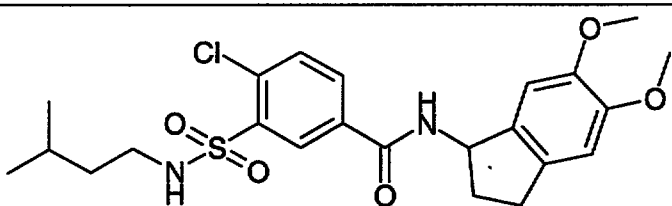
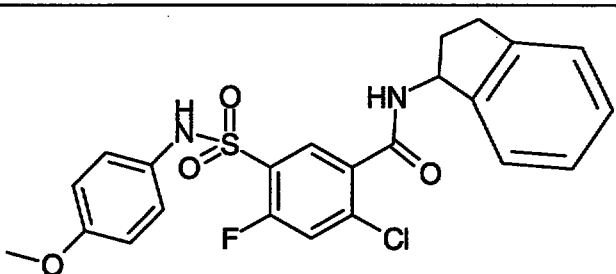
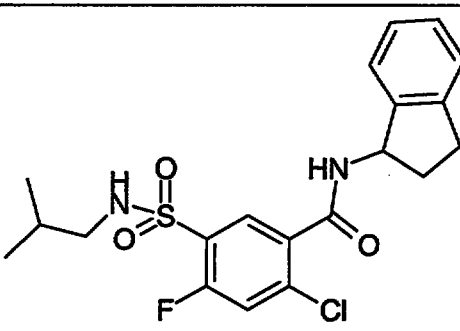
59		133	D	90%
60		144	E	79%
61		108	E	49%
62		140	F	54%
63		69	E	24%
64			E	
65			D	

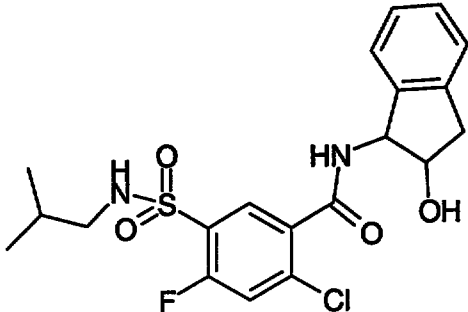
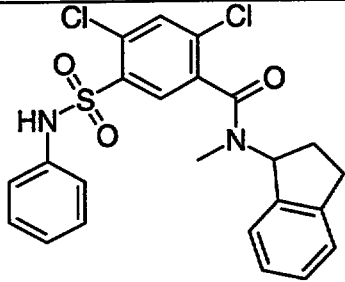
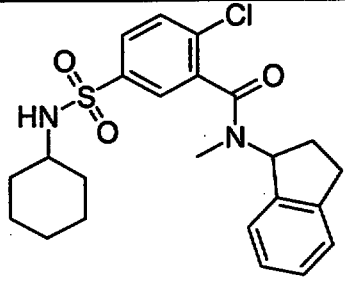
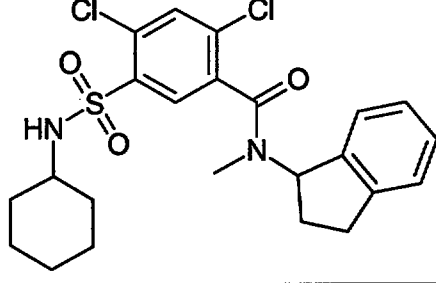
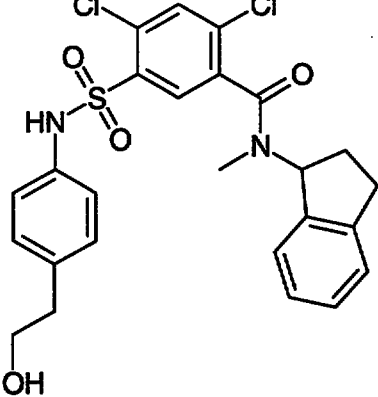
66			D	
67			D	
68		145	F	88
69		165	F	84
70		168	F	86

71		127	F	81
72			E	
73		164	F	63
74		201	F	28
75			F	63

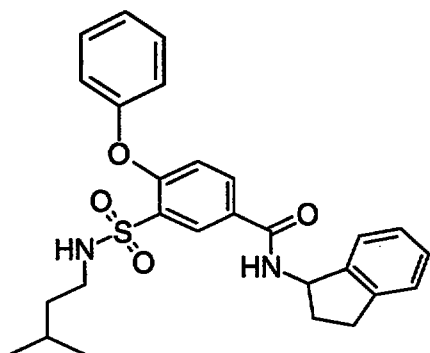
76	 Chiral		F	42
77	 Chiral		F	25
78			D	
79			D	
80			D	

81			D	
82			D	
83			D	
84			D	

85			D	
86			E	
87			E	
88			E	
89			E	
90		155	D	
91		153	D	

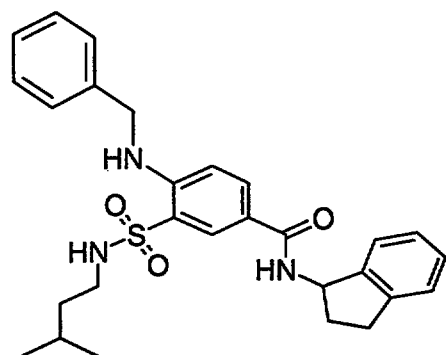
92		182	D	
93		114	F	37
94			F	50
95		183	F	37%
96			F	6%

Example 97:



5 A solution of 100 mg of 4-fluoro-N-indan-1-yl-3-(3-methyl-butylsulfamoyl)-benzamide (Example 41), 26 mg of phenol and 100 mg of potassium carbonate in 4 ml of N,N-dimethylacetamide was heated to 100°C for 6 h. After water had been added and the precipitated product filtered off with suction, 82 mg of 4-phenoxy-N-indan-1-yl-3-(3-methyl-butylsulfamoyl)-benzamide were obtained; m.p. 73°C.

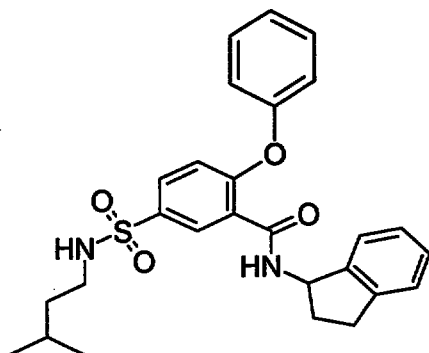
Example 98:



10 A solution of 100 mg of 4-fluoro-N-indan-1-yl-3-(3-methylbutylsulfamoyl)-benzamide (Example 41), 29 mg of benzylamine and 100 mg of potassium carbonate in 4 ml of N,N-dimethylacetamide was heated to 100°C for 6 h. After the addition of water, extraction with EA and chromatographic separation, 33 mg of 4-benzylamino-N-indan-1-yl-3-(3-methylbutylsulfamoyl)benzamide were obtained.

15

Example 99:



75 mg of of 2-phenoxy-N-indan-1-yl-5-(3-methylbutylsulfamoyl)benzamide
 were obtained from 100 mg of 2-chloro-N-indan-1-yl-5-(3-
 5 methylbutylsulfamoyl)benzamide (Example 42) analogously to Example 97.

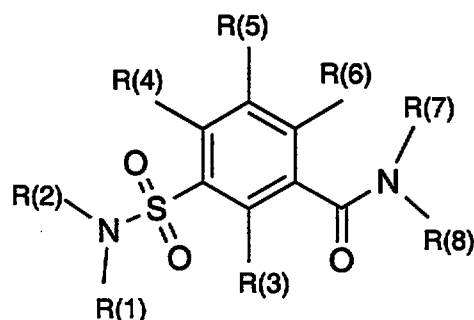
Pharmacological Investigations

- 10 Human Kv1.5 channels were expressed in *Xenopus* oocytes. For this
 purpose, oocytes were first isolated from *Xenopus laevis* and were
 defolliculated. Kv1.5-coding RNA synthesized in vitro was then injected into
 these oocytes. After Kv1.5 protein expression for 1-7 days, kv1.5 currents
 were measured on the oocytes by the two microelectrode voltage clamp
 15 technique. Here, the Kv1.5 channels were activated as a rule with voltage
 jumps to 0 mV and 40 mV lasting for 500 ms. The bath was flushed with a
 solution of the following composition: 96 mM NaCl, 2 mM KCl, 1.8 mM
 CaCl₂, 1 mM MgCl₂ and 5 mM HEPES (tritrated with NaOH to pH 7.4).
 These experiments were carried out at room temperature. The following
 20 were used for data acquisition and analysis: Geneclamp amplifier (Axon
 Instruments, Foster City, USA) and MacLab D/A converter and software
 (ADInstruments, Castle Hill, Australia). The substances according to the
 invention were tested by adding them in different concentrations to the bath
 solution. The effects of the substances were calculated as percentage
 25 inhibition of the Kv1.5 control current obtained when no substance was
 added to the solution. The data were then extrapolated using the Hill
 equation, in order to determine the inhibitory concentration IC₅₀ for the
 respective substances.
- 30 In this way, the following IC₅₀ values were determined for the compounds
 listed below:

Compound	IC ₅₀ [μ M]
Example 1	>> 10
Example 3	7.7
Example 10	4.8
Example 11	2.8
Example 13	3.9
Example 14	4.2
Example 19	~ 3
Example 20	~3
Example 43	5.3
Example 51	7.1
Example 57	8.8
Example 60	6.9
Example 62	6.3
Example 73	6.2
Example 88	8.7
Example 89	5.6
Example 90	2.8
Example 94	2.2

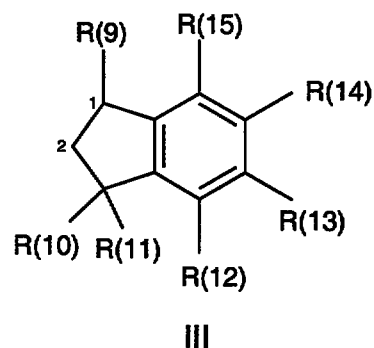
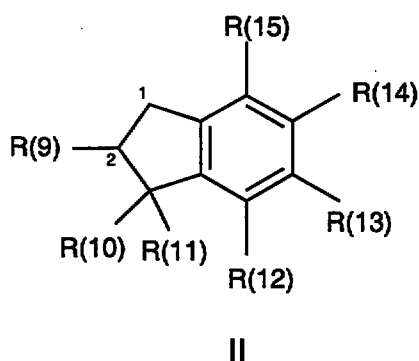
Patent claims

1. A compound of the formula I



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in which R(8) is either a 1-indanyl radical of the formula II or a 2-indanyl radical of the formula III



10

and in which:

R(1) and R(2),

independently of one another, are $R(20)-C_rH_{2r}$,

15

where a CH_2 group of the group C_rH_{2r} may be replaced by -O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -NR(21)- or -CONR(21);

R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

R(20) is H, CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23), -CONR(22)R(23), -OR(24), -COOR(24), phenyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

20

where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents,

25



- selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, hydroxymethyl, hydroxyethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 5 R(22) and R(23),
independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- or
R(22) and R(23)
- 10 together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)- ;
R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
r is zero, 1, 2, 3, 4, 5, 6, 7 or 8;
- 15 or
R(1) and R(2)
together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)- ;
- 20 R(3), R(4), R(5) and R(6),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂, OR(25) or NR(26)R(27);
R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a
25 fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or phenyl,
which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl,
30 methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- x is 0, 1, 2 or 3;
y is 1, 2 or 3;
- R(26) and R(27),
- 35 independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- or
R(26) and R(27)



* C L H S *

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)- ;

- R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- 5 R(9) is hydrogen, OR(28) or OCOR(28);
R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- R(10) and R(11),
independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- 10 R(12), R(13), R(14) and R(15),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CN, -CF₃, -C₂F₅, -C₃F₇, -N₃, -NO₂, -Y-C₈H₂S-R(29), phenyl, thienyl, furyl or an N-containing heterocycle having
- 15 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where phenyl, thienyl, furyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 20 Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-, -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left;
- 25 R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
- s is zero, 1, 2, 3, 4, 5 or 6;
- R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31), -NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing
- 30 heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents, selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 35 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(32) and R(33),
independently of one another, are hydrogen or



alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(32) and R(33)

together form a chain of 4 or 5 methylene groups,
of which one CH₂ group can be replaced by -O-,
-S-, -NH-, -N(CH₃)- or -N(benzyl)-;

5

and its physiologically tolerated salts.

2. A compound of the formula I as claimed in claim 1, but where at least
10 one of the radicals R(1) and R(2) is other than hydrogen.

3. A compound of the formula I as claimed in claim 1 or 2, in which R(8) is
either a 1-indanyl radical of the formula II or a 2-indanyl radical of the
formula III and in which:

15 R(1) is hydrogen;

R(2) is R(20)-C_rH_{2r},

where one CH₂ group of the group C_rH_{2r} may be replaced
by -O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-,
-SO₂-, -NR(21)- or -CONR(21);

20

R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(20) is CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl having
3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23),
-CONR(22)R(23), -OR(24), -COOR(24), phenyl or an
N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9
25 carbon atoms,

25

where phenyl and the N-containing heterocycle are
unsubstituted or substituted by 1 or 2 substituents
selected from the group consisting of F, Cl, Br, I,
CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, hydroxy-
methyl, hydroxyethyl, methoxy, dimethylamino,
sulfamoyl, methylsulfonyl and methylsulfonylamino;

30

R(22) and R(23),

independently of one another, are hydrogen or
alkyl having 1, 2, 3 or 4 carbon atoms;

35

or

R(22) and R(23)

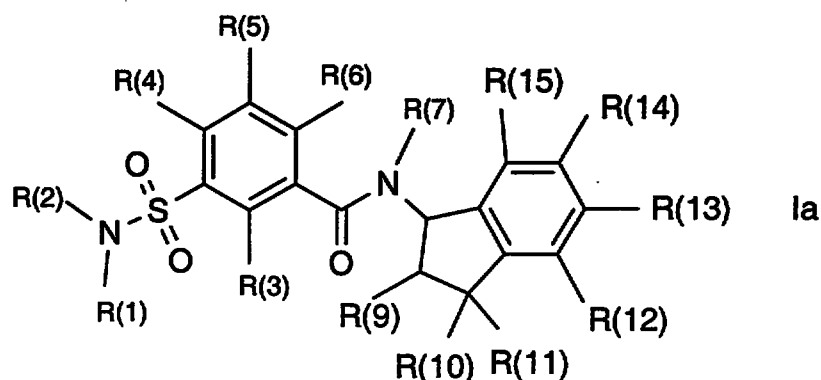
together form a chain of 4 or 5 methylene groups,
of which one CH₂ group can be replaced by -O-,
-S-, -NH-, -N(methyl)- or -N(benzyl)-;



- R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
r is zero, 1, 2, 3, 4, 5, 6, 7 or 8;
- R(3), R(4), R(5) and R(6),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl
having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7
or 8 carbon atoms, CN, CF₃, NO₂, OR(25) or NR(26)R(27);
- R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a
fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or
phenyl,
which is unsubstituted or substituted by 1 or 2
substituents selected from the group consisting of
F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl,
methoxy, dimethylamino, sulfamoyl, methylsulfonyl
and methylsulfonylamino;
- x is 0, 1, 2 or 3;
y is 1, 2 or 3;
- R(26) and R(27),
independently of one another, are hydrogen or alkyl having
1, 2, 3 or 4 carbon atoms;
- or
R(26) and R(27)
together form a chain of 4 or 5 methylene groups, of which
one CH₂ group can be replaced by -O-, -S-, -NH-,
-N(methyl)- or -N(benzyl)-;
- R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
R(9) is hydrogen, OR(28) or OCOR(28);
R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;
- R(10) and R(11),
independently of one another, are hydrogen or alkyl having 1, 2, 3
or 4 carbon atoms;
- R(12), R(13), R(14) and R(15),
independently of one another, are hydrogen, F, Cl, Br, I, alkyl
having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7
or 8 carbon atoms, -CN, -CF₃, -C₂F₅, -C₃F₇, -N₃, -NO₂, -Y-C₆H₄-
R(29), phenyl, thienyl, furyl or an N-containing heterocycle having
1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
where phenyl, thienyl, furyl and the N-containing
heterocycle are unsubstituted or substituted by 1 or 2
substituents selected from the group consisting of F, Cl, Br,



- I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- 5 Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-,
 -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link
 to the backbone is in each case via the atom on the left;
 R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 s is zero, 1, 2, 3, 4, 5 or 6;
 R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3,
 10 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31),
 -NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing
 heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,
 where phenyl and the N-containing heterocycle are
 unsubstituted or substituted by 1 or 2 substituents
 15 selected from the group consisting of F, Cl, Br, I,
 CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy,
 dimethylamino, sulfamoyl, methylsulfonyl and
 methylsulfonylamino;
 R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
 20 R(32) and R(33),
 independently of one another, are hydrogen or
 alkyl having 1, 2, 3 or 4 carbon atoms;
 or
 R(32) and R(33)
 25 together form a chain of 4 or 5 methylene groups,
 of which one CH₂ group can be replaced by -O-,
 -S-, -NH-, -N(CH₃)- or -N(benzyl)-;
- and its physiologically tolerated salts.
- 30 4. A compound of the formula I as claimed in one or more of claims 1 to 3,
 in which R(8) is a 1-indanyl radical of the formula II, i.e. compounds of the
 formula Ia



in which:

R(1) is hydrogen;

5 R(2) is R(20)-C_rH_{2r},

where one CH₂ group of the group C_rH_{2r} may be replaced by -O-, -CH=CH-, -C≡C-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -NR(21)- or -CONR(21);

10 R(21) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(20) is CH₃, CH₂F, CHF₂, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, NR(22)R(23), -CONR(22)R(23), -OR(24), -COOR(24), phenyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

15 where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, hydroxymethyl, hydroxyethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

20 R(22) and R(23),
independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

25 R(22) and R(23)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(methyl)- or -N(benzyl)-;

30 R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
r is zero, 1, 2, 3, 4, or 5;

R(3), R(4), R(5) and R(6),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl



having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂ or OR(25);

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a fluorinated alkyl radical of the formula

5

-C_xH_{2x}CF_yH_{3-y} or phenyl,

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

10

x is 0, 1, 2 or 3;

y is 1, 2 or 3;

R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

15 R(9) is hydrogen, OR(28) or OCOR(28);

R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) and R(11),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

20 R(12), R(13), R(14) and R(15),

independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CN, -CF₃, -C₂F₅, -C₃F₇, -NO₂, -Y-C₅H_{2s}-R(29), phenyl, thienyl, furyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms,

25

where phenyl, thienyl, furyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

30

Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-, -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left;

35

R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

s is zero, 1, 2, 3, 4, 5 or 6;

R(29) is hydrogen, methyl, CF₃, C₂F₅, C₃F₇, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -OR(31), -COOR(31),

-NR(32)R(33), -CONR(32)R(33), phenyl or an N-containing heterocycle having 1, 2, 3, 4, 5, 6, 7, 8 or 9 carbon atoms, where phenyl and the N-containing heterocycle are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, NH₂, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(32) and R(33), independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(32) and R(33)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-, -S-, -NH-, -N(CH₃)- or -N(benzyl)-;

and its physiologically tolerated salts.

5. A compound of the formula Ia as claimed in one or more of claims 1 to 4, in which:

R(1) is hydrogen;

R(2) is R(20)-C_rH_{2r};

R(20) is CH₃, CH₂F, CHF₂, CF₃, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, -CONR(22)R(23), -OR(24), -COOR(24) or phenyl,

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl, hydroxymethyl, hydroxyethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(22) and R(23),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

or

R(22) and R(23)

together form a chain of 4 or 5 methylene groups, of which one CH₂ group can be replaced by -O-,

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-S-, -NH-, -N(methyl)- or -N(benzyl)-;

R(24) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

r is zero, 1, 2, 3, 4, or 5;

R(3), R(4), R(5) and R(6),

5 independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, NO₂ or OR(25);

R(25) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, a fluorinated alkyl radical of the formula -C_xH_{2x}CF_yH_{3-y} or phenyl,

10



which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

15

x is 0, 1, 2 or 3;

y is 1, 2 or 3;

R(7) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(9) is hydrogen or OR(28);

20 R(28) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) and R(11),

independently of one another, are hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(12), R(13), R(14) and R(15),

25 independently of one another, are hydrogen, F, Cl, Br, I, alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms, CN, CF₃, -NO₂ or -Y-C₅H_{2s}-R(29);

Y is -O-, -CO-, -CO-O-, -O-CO-, -S-, -SO-, -SO₂-, -O-SO₂-, -SO₂NR(30)-, -CONR(30)- or -NR(30)CO-, where the link to the backbone is in each case via the atom on the left;

30

R(30) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;

s is zero, 1, 2, 3, 4 or 5;

R(29) is hydrogen, methyl, CF₃, -OR(31), -COOR(31), -NR(32)R(33), -CONR(32)R(33) or phenyl,

35

which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, OH, methyl, ethyl, methoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;



R(31) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
R(32) and R(33),

independently of one another, are hydrogen or
alkyl having 1, 2, 3 or 4 carbon atoms;

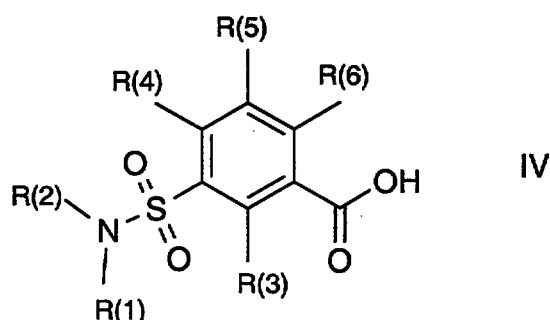
or

R(32) and R(33)

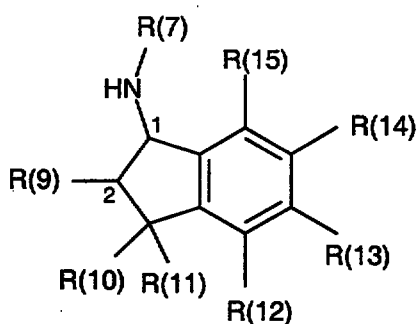
together form a chain of 4 or 5 methylene groups,
of which one CH₂ group can be replaced by -O-,
-S-, -NH-, -N(CH₃)- or -N(benzyl)-;

and its physiologically tolerated salts.

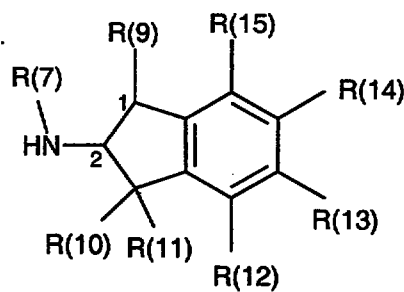
6. A process for the preparation of compounds of the formula I as claimed
in one or more of claims 1 to 5, which comprises reacting a carboxylic acid
of the formula IV



in which R(1), R(2), R(3), R(4), R(5) and R(6) have the meanings stated in
claims 1 to 5, with an amine of the formula V a or V b



Va



Vb

in which R(7), R(9), R(10), R(11), R(12), R(13), R(14) and R(15) have the
meanings stated in claims 1 to 6, in an amidation reaction.

7. A compound of the formula I as claimed in one or more of claims 1 to 5
and its physiologically tolerated salts for use as medicaments.



8. A pharmaceutical formulation containing an effective amount of at least one compound of the formula I as claimed in one or more of claims 1 to 5 and/or one physiologically tolerated salt thereof as an active substance, together with pharmaceutically acceptable carriers and additives and, if
5 required, also one or more other pharmacological active substances.

9. The use of a compound of the formula I as claimed in one or more of claims 1 to 5 and/or a physiologically tolerated salt thereof for the preparation of a medicament having a K^+ -channel-blocking effect for the
10 therapy and prophylaxis of K^+ -channel mediated diseases.

10. The use of a compound of the formula I as claimed in one or more of claims 1 to 5 and/or a physiologically tolerated salt thereof for the preparation of a medicament for the therapy or prophylaxis of cardiac
15 arrhythmias which can be eliminated by lengthening the action potential.

11. The use of a compound of the formula I as claimed in one or more of claims 1 to 5 and/or a physiologically tolerated salt thereof for the preparation of a medicament for the therapy or prophylaxis of re-entry
20 arrhythmias.

12. The use of a compound of the formula I as claimed in one or more of claims 1 to 5 and/or a physiologically tolerated salt thereof for the preparation of a medicament for the therapy or prophylaxis of
25 supraventricular arrhythmias.

13. The use of a compound of the formula I as claimed in one or more of claims 1 to 5 and/or a physiologically tolerated salt thereof for the preparation of a medicament for the therapy or prophylaxis of atrial
30 fibrillation or atrial flutter.

14. A pharmaceutical formulation containing an effective amount of at least one compound of the formula I as claimed in one or more of claims 1 to 5 and/or of one physiologically tolerated salt thereof and of a beta-blocker as
35 active substances, together with pharmaceutically acceptable carriers and additives.

15. A pharmaceutical formulation containing an effective amount of at least one compound of the formula I as claimed in one or more of claims 1 to 5

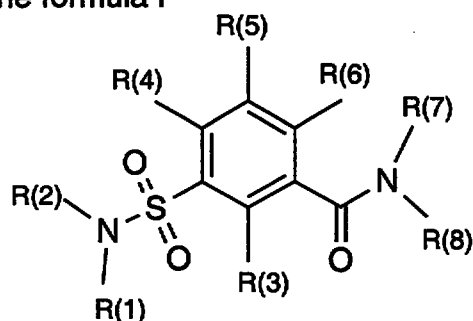
and/or of a physiologically tolerated salt thereof and of an IK_s -channel blocker as active substances, together with pharmaceutically acceptable carriers and additives. _____



Indanyl-substituted benzenecarboxamides, processes for their preparation, their use as a medicament and pharmaceutical formulations containing them



Compounds of the formula I



I,

in which R(1) to R(8) have the meanings stated in the claims, act on the Kv1.5 potassium channel and inhibit a potassium current I, referred to as "ultra-rapidly activating delayed rectifier", in the human atrium. They are therefore very particularly suitable as novel antiarrhythmic active substances, in particular for the treatment and prophylaxis of atrial arrhythmias, e.g. atrial fibrillation (AF) or atrial flutter.