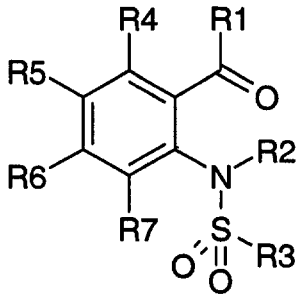
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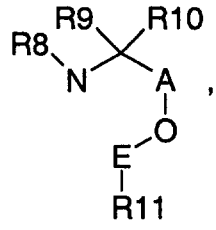
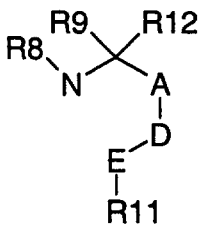
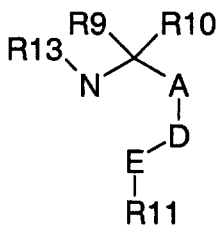
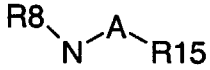
Anthranilamides with heteroarylsulfonyl side chain, process for their preparation, their use as medicament or diagnostic aid, and pharmaceutical preparations containing them

The invention relates to compounds of the formula I



I

in which R(1), R(2), R(3), R(4), R(5), R(6) and R(7) have the meanings stated below, and to the use thereof, especially in pharmaceuticals,

R(1)  ,  ,  or 

A $-C_nH_{2n}-$;

n = 0, 1, 2, 3, 4 or 5;

D a bond or -O-;

E $-C_mH_{2m}-$;

m = 0, 1, 2, 3, 4 or 5;

R(8) hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or C_pH_{2p}-R(14);

p 0, 1, 2, 3, 4 or 5;

R(14) phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

R(10) hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, phenyl, naphthyl or heteroaryl

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) alkyl having 1, 2, 3 or 4 carbon atoms, alkynyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(13) C_pH_{2p}-R(14);

p 0, 1, 2, 3, 4 or 5;

R(15) cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

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

R(3) heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

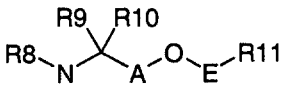
R(4), R(5), R(6) and R(7)

independently of one another, hydrogen, F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

Preference is given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0, 1, 2 or 3;

E is $-C_mH_{2m}-$;

m is 0, 1, 2 or 3;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0, 1, 2, or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having

1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

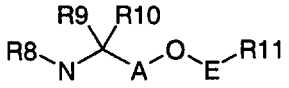
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

Particular preference is given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

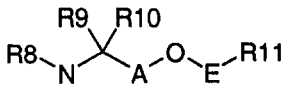
where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

Very particular preference is given to compounds I, in which:

R(1) is 

A is $-C_nH_{2n}-$;

n is 0 or 1;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN or OH;

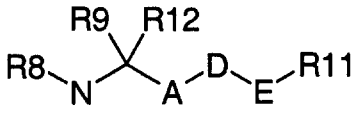
R(6) is hydrogen, F, Cl, CF_3, methyl, methoxy or OH;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

and the pharmaceutically acceptable salts thereof.

Preference is likewise given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0, 1, 2 or 3;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0, 1, 2 or 3;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14)

p is 0, 1, 2, or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) is alkyl having 1, 2 or 3 carbon atoms, alkynyl having 1, 2 or 3 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

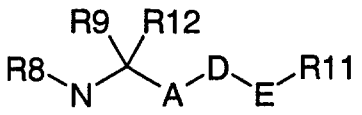
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmacologically acceptable salts thereof.

Particular preference is likewise given to compounds I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14)

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,
where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, methyl or ethyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,
where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) is alkyl having 1, 2 or 3 carbon atoms, ethynyl, cyclopropyl, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

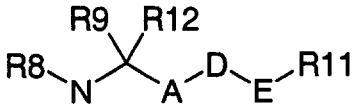
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmacologically acceptable salts thereof.

Very particular preference is likewise given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14)

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, ethyl or methyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(12) is alkyl having 1, 2 or 3 carbon atoms, ethynyl, cyclopropyl, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN or OH;

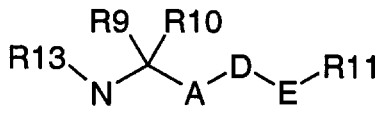
R(6) is hydrogen, F, Cl, CF_3, methyl or methoxy or OH;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

and the pharmacologically acceptable salts thereof.

Preference is equally given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$

n = 0, 1, 2 or 3;

D is a bond or -O-;

E is $-C_mH_{2m}-$

m is 0, 1, 2 or 3;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, thienyl, furanyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furanyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(13) is C_pH_{2p}-R(14);

p is 0, 1, 2 or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

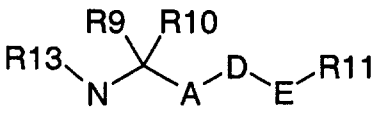
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

Particular preference is equally given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$

m is 0 or 1;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl and methylsulfonylamino;

R(13) is C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl or methylsulfonylamino;

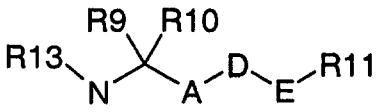
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

Very particular preference is equally given to compounds of the formula I in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(9) is hydrogen, ethyl or methyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group

consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl;

R(13) is C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl, methoxy;

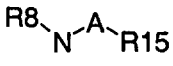
R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN, OH;

R(6) is hydrogen, F, Cl, CF_3, methyl, methoxy, OH;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy, OH;

and the pharmaceutically acceptable salts thereof.

Preference is equally given to compounds of the formula I in which:

R(1) is 

A is $-C_nH_{2n}-$;

n = 0, 1, 2 or 3

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0, 1, 2, or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

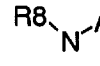
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

Particular preference is equally given to compounds of the formula I in which:

R(1) is ;

A is $-C_nH_{2n}-$;

n is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2,

3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

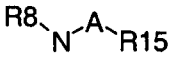
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

Very particular preference is equally given to compounds of the formula I in which:

R(1) is 

A is $-C_nH_{2n}-$;

n is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3; CN or OH;

R(6) is hydrogen, F, Cl, CF_3, methyl, methoxy or OH;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

Heteroaryl means in particular radicals which are derived from phenyl or naphthyl and in which one or more CH groups are replaced by N and/or in which at least two adjacent CH groups are replaced by S, NH or O (to form a five-membered aromatic ring). It is also possible for one or both atoms at the site of fusion of bicyclic radicals (as in indolizinyl) to be nitrogen atoms.

Heteroaryl means, in particular, furanyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl, cinnolinyl.

Alkyl radicals and alkylene radicals may be straight-chain or branched. This also applies to the alkylene radicals of the formulae C_mH_{2m}, C_nH_{2n}, and C_pH_{2p}. Alkyl radicals and alkylene radicals may also be straight-chain or branched if they are substituted or present in other radicals, e.g. in an alkoxy 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, 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, 1,1-butylene, 1,4-butylene, 1,5-pentylene, 2,2-dimethyl-1,3-propylene, 1,6-hexylene, etc. are examples of alkylene radicals.

If the compounds of the formula I contain one or more acidic or basic groups or one or more basic or acidic heterocycles, the invention also includes the corresponding physiologically or toxicologically acceptable salts, in particular the pharmaceutically

utilizable salts. Thus, the compounds of the formula I which have acidic groups, e.g. one or more COOH groups, can be used 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. Compounds of the formula I which have one or more basic, i.e. protonatable, 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 contain both acidic and basic groups in the molecule, the invention includes not only the salt forms described but also inner salts, called betaines. Salts can be obtained from the compounds of the formula I by conventional processes, for example by combining with an acid or base in a solvent or dispersant or else by anion exchange from other salts.

The compounds of the formula I may when appropriately substituted exist in stereoisomeric forms. If the compounds of the formula I contain one or more centers of asymmetry, these may have, independently of one another, the S configuration or the R configuration. The invention includes 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 includes, for example, enantiomers in enantiopure form, both as levorotatory and as dextrorotatory antipodes, and in the form of mixtures of the two enantiomers in various ratios or in the form of racemates. Individual stereoisomers can be prepared if required by fractionating a mixture by conventional methods or, for example, by stereoselective synthesis. If mobile hydrogen atoms are present, all tautomeric forms of the compounds of the formula I are also encompassed by the present invention.

The compounds of the invention of the formula I and their physiologically tolerated salts can thus be used on animals, preferably on mammals and, in particular, on humans as pharmaceuticals on their own or in mixtures with one another or in the form of pharmaceutical preparations. The present invention also relates to compounds of

the formula I and their physiologically tolerated salts for use as pharmaceuticals, to their use in the therapy and prophylaxis of the pathological states mentioned and to their use for producing medicaments therefor and medicaments with K^+ channel-blocking effect. The present invention further relates to pharmaceutical preparations which comprise as active ingredient an effective dose of at least one compound of the formula I and/or a physiologically tolerated salt thereof in addition to conventional pharmaceutically acceptable carriers and excipients. The pharmaceutical preparations normally contain from 0.1 to 90% by weight of the compounds of the formula I and/or their physiologically tolerated salts. The pharmaceutical preparations can be produced in a manner known per se. For this purpose, the compounds of the formula I and/or their physiologically tolerated salts are converted together with one or more solid or liquid pharmaceutical carriers and/or excipients and, if desired, in combination with other active pharmaceutical ingredients into a suitable administration form or dosage form which can then be used as pharmaceutical in human medicine or veterinary medicine.

Pharmaceuticals which comprise compounds of 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 individual case, e.g the particular manifestation of the disease to be treated.

The excipients suitable for the desired pharmaceutical formulation are familiar to the skilled worker on the basis of his expert knowledge. Besides solvents, gel formers, suppository bases, tablet excipients and other active ingredient carriers it is possible to use, for example, antioxidants, dispersants, emulsifiers, antifoams, flavor corrigents, preservatives, solubilizers, agents to achieve a depot effect, buffer substances or colorants.

The compounds of the formula I can also be combined with other active pharmaceutical ingredients to achieve an advantageous therapeutic effect. Thus, in the treatment of cardiovascular disorders, combinations with substances acting on the

cardiovascular system are possible and advantageous. Such combination partners advantageous for cardiovascular disorders are, for example, other antiarrhythmics, i.e. class I, class II or class III antiarrhythmics, such as, for example, IK_S or IK_r channel blockers, e.g. dofetilide, or, in addition, 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 blockers, phosphodiesterase inhibitors and other substances with a positive inotropic effect, such as, for example, digitalis glycosides, or diuretics.

For a form for oral use, the active compounds are mixed with the additives suitable for this purpose, such as carriers, stabilizers or inert diluents, and converted by conventional methods into the suitable administration forms such as tablets, coated tablets, hard gelatin capsules, aqueous, alcoholic or oily solutions. Examples of inert carriers which can be used are gum arabic, magnesia, magnesium carbonate, potassium phosphate, lactose, glucose or starch, especially corn starch. Preparation is possible in this connection both as dry and as wet granules. Suitable as oily carriers or as solvents are, for example, vegetable or animal oils, such as sunflower oil or fish liver oil. Examples of suitable solvents for aqueous or alcoholic solutions are water, ethanol or sugar solutions or mixtures thereof. Further examples of excipients, also for other administration forms, are polyethylene glycols and polypropylene glycols.

For subcutaneous or intravenous administration, the active compounds are converted into a solution, suspension or emulsion, if desired with the substances customary for this purpose, such as solubilizers, emulsifiers or other excipients. The compounds of the formula I and their physiologically tolerated salts can also be lyophilized and the resulting lyophilizates be used for example to produce products for injection or infusion. Examples of suitable solvents are water, physiological saline or alcohols, e.g. ethanol, propanol, glycerol, as well as sugar solutions such as glucose or mannitol solutions, or else mixtures of the various solvents mentioned.

Suitable as pharmaceutical formulation for administration in the form of aerosols or sprays are, for example, solutions, suspensions or emulsions of the active ingredients of the formula I or of their physiologically tolerated salts in a pharmaceutically acceptable solvent such as, in particular, ethanol or water, or a mixture of such solvents. The formulation can if required also contain other pharmaceutical excipients such as surfactants, emulsifiers and stabilizers, and a propellant gas. Such a preparation normally contains the active ingredient in a concentration of about 0.1 to 10, in particular of about 0.3 to 3, percent by weight.

The dosage of the active ingredient of the formula I to be administered or of the physiologically tolerated salts thereof depends on the individual case and should be adapted in a conventional way to the circumstances of the individual case for an optimal effect. Thus, of course, it depends on the frequency of administration and on the potency and duration of action of the compounds employed in each case for therapy or prophylaxis, but also on the nature and severity of the disease to be treated and on the sex, age, weight and individual response of the human or animal to be treated and on whether the therapy is acute or prophylactic. The daily dose of a compound of the formula I is normally, on administration to a patient weighing about 75 kg, from 0.001 mg/kg of bodyweight to 100 mg/kg of bodyweight, preferably 0.01 mg/kg of bodyweight to 20 mg/kg of bodyweight. The dose can be administered in the form of a single dose or else be divided into a plurality of, e.g. two, three or four single doses. Especially in the treatment of acute cases of cardiac arrhythmias, for example on an intensive care ward, parenteral administration by injection or infusion, e.g. by a continuous intravenous infusion, may also be advantageous.

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

Atrial fibrillation (AF) and atrial flutter are the commonest persistent cardiac arrhythmias. The occurrence increases with increasing age and frequently leads to fatal sequelae such as, for example, stroke. It affects about 1 million Americans each year and leads to more than 80 000 strokes annually in the USA. The class I and III antiarrhythmics in use at present reduce the rate of recurrence of AF but are used to only a limited extent because of their potential proarrhythmic side effects. There is thus a great medical need to develop 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 has been shown that most supraventricular arrhythmias are subject to so-called reentry waves. Such reentries occur when the cardiac tissue has a slow conductivity and, at the same time, very short refractory periods. Increasing the myocardial refractory period by prolonging the action potential is an acknowledged mechanism for terminating arrhythmias and preventing development thereof (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 through various K^+ channels. Particularly great importance is ascribed in this connection to a so-called delayed rectifier I_K which consists of 3 different components: IK_r, IK_s and IK_{ur}.

Most of the known class III antiarrhythmics (e.g. dofetilide, E4031 and d-sotalol) block predominantly or exclusively the rapidly activating potassium channel IK_r, which can be detected both in cells of the human ventricle and in the atrium. However, it has emerged that these compounds have an increased proarrhythmic risk at heart rates which are low or normal, and arrhythmias referred to as torsades de pointes have been observed in particular (D. M. Roden, Am. J. Cardiol. 72, 1993, 44B - 49B; "Current status of class III antiarrhythmic drug therapy"). Besides this high risk, which is fatal in some cases, when the rate is low, the activity of the I_{Kr} blockers has been found to decline under the conditions of tachycardia, which is just where the effect is required ("negative use-dependence").

Whereas some of these disadvantages can possibly be overcome by blockers of the slowly activating component (IK_S), their efficacy has not yet been proven because no clinical investigations with IK_S channel blockers are known.

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 large part in the repolarization time in the human atrium. Inhibition of the IK_{ur} potassium outward current thus represents by comparison with inhibition of IK_r or IK_S a particularly effective method for prolonging the atrial action potential and thus for terminating or preventing atrial arrhythmias. Mathematical models of the human action potential suggest that the beneficial effect of blockade of the IK_{ur} ought to be particularly pronounced precisely under the pathological conditions of chronic atrial fibrillation (M. Courtemanche, R. J. Ramirez, S. Nattel, Cardiovascular Research 1999, 42, 477-489: "Ionic targets for drug therapy and atrial fibrillation-induced electrical remodeling: insights from a mathematical model").

In contrast to IK_r and IK_S, which also occur in the human ventricle, although IK_{ur} plays a significant part in the human atrium it does not in the ventricle. For this reason, when the IK_{ur} current is inhibited, in contrast to blockade of IK_r or IK_S, the risk of a proarrhythmic effect on the ventricle is precluded 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").

Antiarrhythmics which act via selective blockade of the IK_{ur} current or Kv1.5 channel have not to date been available on the market. Although numerous active pharmaceutical ingredients (e.g. tedisamil, bupivacaine or sertindole) have been described to have a blocking effect on the Kv1.5 channel, in each of these cases the

Kv1.5 blockade is only a side effect in addition to other principal effects of the substances.

WO 98 04 521 claims aminoindanes as potassium channel blockers which block the Kv1.5 channel. The use of various pyridazinones and phosphine oxides as antiarrhythmics which are said to act via IK_{ur} blockade is claimed in the applications WO 98 18 475 and WO 98 18 476. However, the same compounds were originally also described as immunosuppressants (WO 96 25 936). All the compounds described in the abovementioned applications have structures which are completely different from the compounds of the invention in this application.

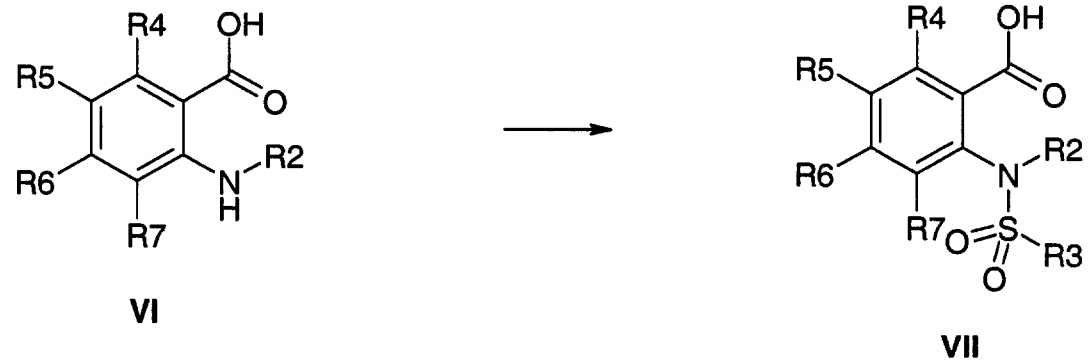
It has now been found, surprisingly, that the heteroarylsulfonylanthranilamides described herein are potent blockers of the human Kv1.5 channel. They can therefore be used as novel antiarrhythmics with a particularly advantageous safety profile. The compounds are particularly suitable for treating supraventricular arrhythmias, e.g. atrial fibrillation or atrial flutter.

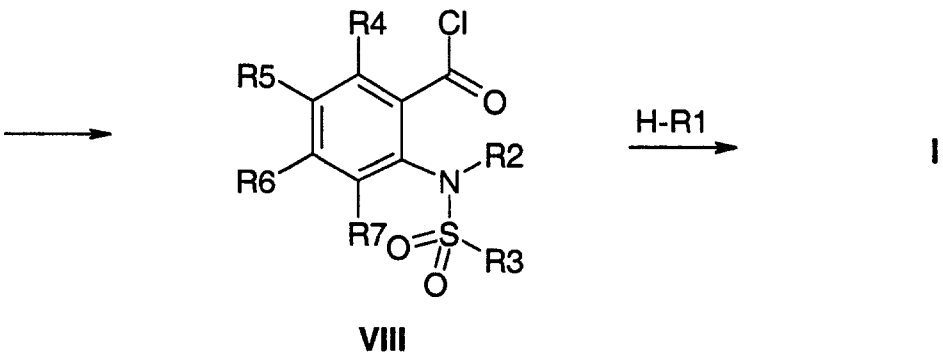
The compounds of the invention have not previously been disclosed. Some structurally related compounds are described in WO 0002851, EP 0 686 625 A1 and EP 0 947 500 A1. However, no potassium channel-blocking activity is disclosed for the anthranilic acid derivatives described therein.

Compounds of the invention can be prepared for example as shown in scheme 1 by initially reacting an amino carboxylic acid of the formula VI in a solvent such as water, pyridine or an ether in the presence of a base with a sulfonyl chloride of the formula R(3)-SO_2-Cl or with a sulfonic anhydride. Suitable as base are inorganic bases such as, for example, sodium carbonate or organic bases such as, for example, pyridine or triethylamine. The resulting sulfonylamino carboxylic acid of the formula VII can then be activated, for example by reaction with a chlorinating agent such as, for example, phosphorus pentachloride, phosphorus oxychloride or thionyl chloride, in an inert solvent to give an acid chloride of the formula VIII and then be reacted with an amine H-R(1) to give the title compounds of the formula I. However, activation of the carboxyl

group in the compound of the formula VII can also take place in a different way, for example by one of the numerous methods familiar to the skilled worker and used in peptide chemistry for forming amide bonds, for example by conversion into a mixed anhydride or an activated ester or with use of a carbodiimide such as dicyclohexylcarbodiimide.

Reaction of the activated sulfonylamino carboxylic acid with an amine H-R(1) is advantageously carried out in an inert solvent such as, for example, pyridine, tetrahydrofuran or toluene without addition or with addition of an inert base, for example a tertiary amine or pyridine.





Scheme 1

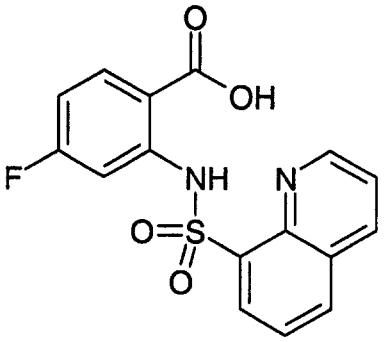
List of abbreviations

BuLi	Butyllithium
CDI	Carbonyldiimidazole
DIC	Diisopropylcarbodiimide
DIP	Diisopropyl ether
DIPEA	Diisopropylethylamine
DMAP	4-Dimethylaminopyridine
DMF	N,N-Dimethylformamide
EA	Ethyl acetate
EDAC	N-Ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride
HOBT	1-Hydroxy-1H-benzotriazole
Me	Methyl
M.p.	Melting point (unless otherwise indicated, the melting points of the unpurified crude products are stated; the melting points of the respective pure substances may very well be distinctly higher)
MTB	t-Butyl methyl ether
RT	Room temperature
THF	Tetrahydrofuran
TOTU	O-[(Cyano(ethoxycarbonyl)methylene)amino]-1,1,3,3-tetramethyluronium tetrafluoroborate

General method 1: Reaction of anthranilic acids with sulfonyl chlorides to give o-sulfonylaminobenzoic acids (analogous to Organic Syntheses 1952, 32, 8)

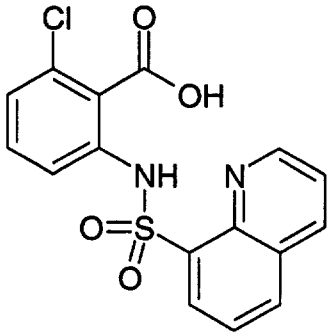
1.2 mol of the appropriate sulfonyl chloride are added in portions to a solution of 260 g (2.4 mol) of sodium carbonate and 1 mol of the appropriate anthranilic acid in 1.5 l of water at 60°C. The reaction mixture is heated at 60 - 80°C until reaction is complete (about 1 – 6 h), adding further sulfonyl chloride if necessary. After cooling, the reaction mixture is poured into 500 ml of 6 mol hydrochloric acid, and the precipitate is filtered off with suction and dried in an oven at 45°C in vacuo. If the product does not result as crystals, it is isolated by extraction with ethyl acetate.

Precursor 1 a: 4-Fluoro-2-(quinoline-8-sulfonylamino)benzoic acid



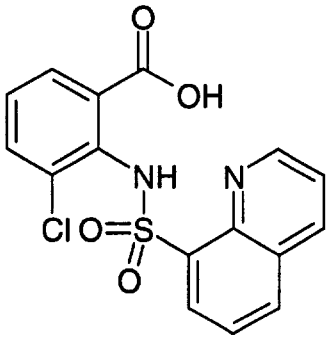
7.6 g of the title compound were obtained as a white solid by general method 1 from 5.0 g of 2-amino-4-fluorobenzoic acid and 8.8 g of 8-quinolinesulfonyl chloride.
M.p.: 248°C; MS (ES): 347 (M+1).

Precursor 1 b: 6-Chloro-2-(quinoline-8-sulfonylamino)benzoic acid



8.3 g of the title compound were obtained as a solid by general method 1 from 5.0 g of 2-amino-6-chlorobenzoic acid and 8.0 g of 8-quinolinesulfonyl chloride.
M.p.: 88°C; MS (ES): 363 (M+1).

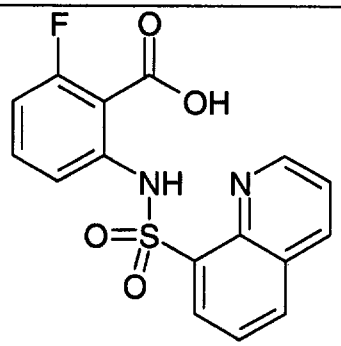
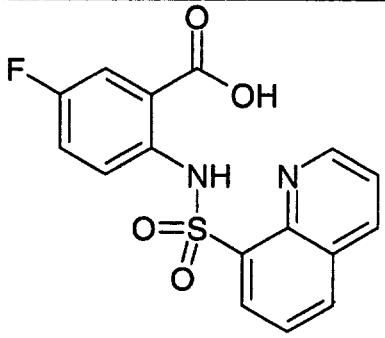
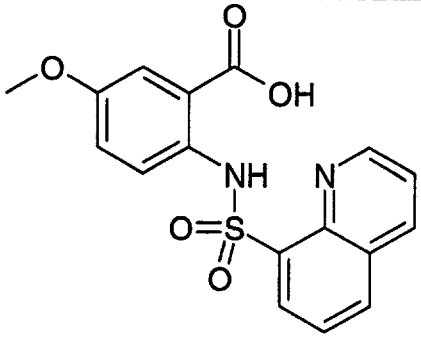
Precursor 1 c: 3-Chloro-2-(quinoline-8-sulfonylamino)benzoic acid



4.1 g of the title compound were obtained by general method 1 from 5.0 g of 2-amino-

6-chlorobenzoic acid and 8.0 g of 8-quinolinesulfonyl chloride.
MS (ES): 363 (M+1).

The following other precursors were synthesized inter alia by general method 1:

Precursor	Structure	Mass (ES)
1 d		347 (M+1)
1 e		347 (M+1)
1 f		359 (M+1)

General method 2: Conversion of sulfonylaminobenzoic acids into the corresponding acid chlorides

A) with phosphorus pentachloride

8 mmol of the sulfonylaminobenzoic acid are suspended in 15 ml of dry toluene and, at room temperature, 9.6 mmol of phosphorus pentachloride are slowly introduced. The

mixture is stirred at 50°C for 3 h and, after cooling to 0°C, the acid chloride is filtered off with suction, washed with a little toluene and dried in a vacuum oven at 45°C.

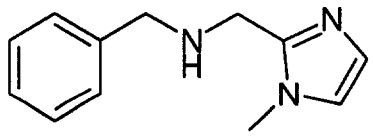
B) with thionyl chloride

8 mmol of the sulfonylaminobenzoic acid are heated in 6 ml of thionyl chloride at 60°C for 3 h and, after concentration, the residue is coevaporated twice with toluene.

General method 3 A: Preparation of secondary amines by reductive amination

0.18 mol of primary amine is dissolved in 200 ml of methanol and, after addition of 0.09 mol of aldehyde, 0.18 mmol of sodium cyanoborohydride and 0.18 mol of glacial acetic acid, stirred at room temperature for 6 h. The solution is concentrated, taken up in ethyl acetate and washed twice with $NaHCO_3$ solution. The organic phase is concentrated and the residue is distilled off under high vacuum. In the case of secondary amines of low volatility, volatile constituents are distilled out and the residue is dissolved in ether/THF and, after addition of an ethereal HCl solution, the precipitated hydrochloride is filtered off with suction, washed with ether and dried. The prepared secondary amines were employed without further purification for the reactions with the sulfonylaminobenzoyl chlorides or sulfonylaminobenzoic acids.

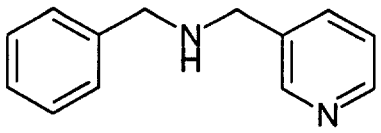
Precursor 3 a: Benzyl-(1-methyl-1H-imidazol-2-ylmethyl)-amine



The hydrochloride (20.5 g) was prepared by general method 3 A from 19.4 g of benzylamine and 10 g of 2-formyl-1-methylimidazole.

MS (ES+): m/z = 202 (M+1).

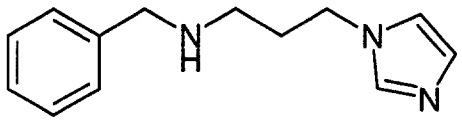
Precursor 3 b: Benzyl-pyridin-3-ylmethylamine



The secondary amine (2.8 g) was prepared by general method 3 A from 4.32 g of 3-pyridylmethylamine and 2.12 g of benzaldehyde after Kugelrohr distillation at 0.1 mbar and 130°C.

MS (ES+): m/z = 199 (M+1).

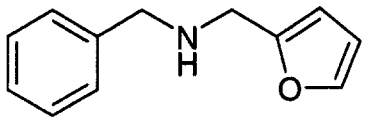
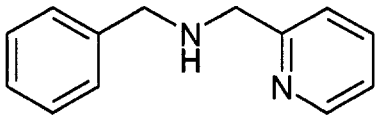
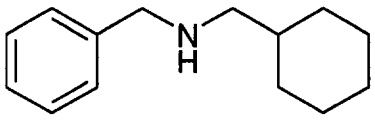
Precursor 3 c: Benzyl-(3-imidazol-1-yl-propyl)-amine

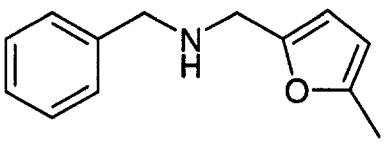
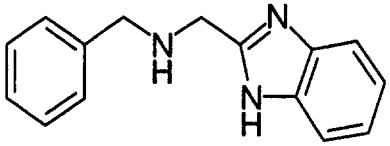
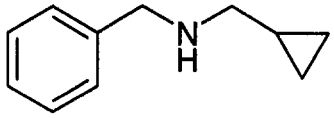
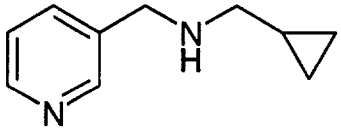
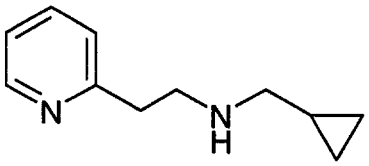


The secondary amine (3.5 g) was prepared by general method 3 A from 12.5 g of 3-imidazol-1-yl-propylamine and 5.3 g of benzaldehyde after Kugelrohr distillation at 0.1 mbar and 130°C.

MS (ES+): m/z = 216 (M+1).

The following other precursors were prepared inter alia by general method 3 A:

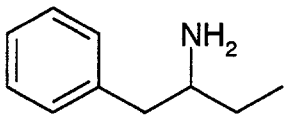
Precursor	Structure	Mass
3 d		188 (M+1)
3 e		199 (M+1)
3 f		204 (M+1)

3 g		202 (M+1)
3 h		238 (M+1)
3 i		162 (M+1)
3 j		163 (M+1)
3 k		177 (M+1)

General method 3 B: Preparation of α-branched amines from ketones

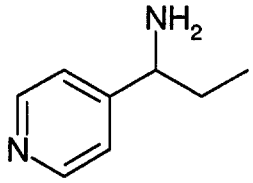
A solution of 67 mmol of the appropriate ketone in 120 ml of ethanol is added dropwise to a solution of 200 mmol of hydroxylammonium chloride and 200 ml of sodium acetate in 120 ml of water at 30°C, and the mixture is heated at 60°C until reaction is complete (1 – 3 h). After cooling, the reaction mixture is diluted with water, and the precipitated oxime is filtered off with suction or, if necessary, isolated by extraction. The resulting product is dissolved in 100 ml of methanol, 100 ml of THF and 10 ml of concentrated ammonia solution and hydrogenated in the presence of Raney nickel at RT and atmospheric pressure until hydrogen uptake ceases. Removal of the catalyst by filtration and concentration of the reaction mixture result in the corresponding amine which is purified by chromatography if necessary.

Precursor 3 l: 1-Benzylpropylamine



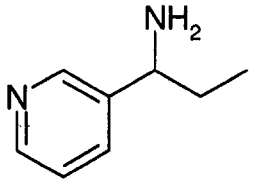
4.5 g of the title compound were obtained by general method 3 B from 10 g of 1-phenyl-2-butanone.

Precursor 3 m: 1-Pyridin-4-yl-propylamine



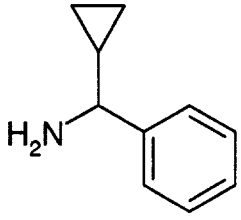
10.2 g of the title compound were obtained by general method 3 B from 10 g of 4-propionylpyridine.

Precursor 3 n : 1-Pyridin-3-yl-propylamine



0.9 g of the title compound was obtained by general method 3 B from 1 g of 1-pyridin-3-yl-propan-1-one.

Precursor 3o: 1-Cyclopropyl-1-phenylmethylamine hydrochloride



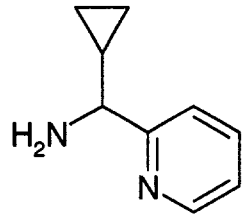
a) N-(Cyclopropylphenylmethyl)-formamide

14.8 g (0.1 mol) of cyclopropyl phenyl ketone, 11.4 ml (0.3 mol) of formic acid and 20 ml (0.5 mol) of formamide were heated at 160°C for 18 h. Cooling and addition of 100 ml of water were followed by extraction 2x with 50 ml of ether each time. The ethereal phase was washed with 50 ml of 10% Na_2CO_3 solution, dried over Na_2SO_4 and concentrated. 13.6 g (77.4 mmol) of a yellow oil were obtained.

b) 1-Cyclopropyl-1-phenylmethylamine hydrochloride

13.6 g (77.4 mmol) of N-(cyclopropylphenylmethyl)-formamide (see a) were heated to reflux in 100 ml of 2N HCl for 18 h. After cooling and extraction 2x with 50 ml of dichloromethane each time, the aqueous phase was concentrated. The residue was taken up in 30 ml of 2-propanol, heated to boiling and cooled in a refrigerator overnight. The crystals of 1-cyclopropyl-1-phenylmethylamine hydrochloride (3.85 g, 21 mmol) which had separated out were filtered off with suction and dried in a vacuum oven.

Precursor 3p: Cyclopropylpyridin-2-yl-methylamine hydrochloride



a) Cyclopropylpyridin-2-yl-methyleneamine

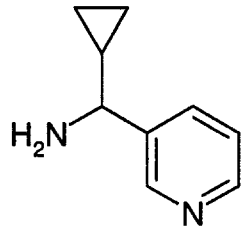
25 g (157.5 mmol) of 2-bromopyridine in 100 ml of diethyl ether were added dropwise over the course of 20 min to 100 ml (160 mmol) of n-BuLi solution in 300 ml of diethyl ether at –70°C. The dark red solution was stirred for 5 h and then 8.8 g (131 mmol) of cyclopropanecarbonitrile in 100 ml of ether were added. The mixture was stirred at -70°C for 30 min, warmed to room temperature and stirred for a further 30 min. Then 15 g of Na_2SO_4 x 10 H_20 were added and stirring was continued for 1 h. Addition of Na_2SO_4 to the red solution was followed by filtration and concentration. The product

was distilled in a Kugelrohr apparatus at 75°C – 120°C /0.3 mbar as a pale yellow oil (18.6 g, 127 mmol) and was stored at –18°C.

b) Cyclopropylpyridin-2-yl-methylamine hydrochloride

2.72 g (18.6 mmol) of cyclopropylpyridin-2-yl-methyleneamine (see a) were dissolved in 35 ml of dry methanol. 0.69 g (18.6 mmol) of $NaBH_4$ was added in portions at 0°C. After 30 min at 0°C, the mixture was stirred at room temperature for 2 h, the pH was adjusted to 3 with 1M HCl, the methanol was stripped off in a rotary evaporator, and the residue was freeze dried. 8.8 g of cyclopropylpyridin-2-ylmethylamine hydrochloride mixed with inorganic salts and boric acid were obtained.

Precursor 3 q: Cyclopropylpyridin-3-yl-methylamine hydrochloride



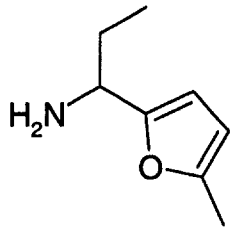
a) Cyclopropylpyridin-3-yl-methyleneamine

7.5 g (51 mmol) of the imine were isolated as a yellow oil in accordance with the method for precursor 3p from 8.8 g (131 mmol) of cyclopropanecarbonitrile, 25 g (157.5 mmol) of 3-bromopyridine and 173 mmol of n-BuLi solution and after Kugelrohr distillation (130°C/0.2 mbar).

b) Cyclopropylpyridin-3-yl-methylamine hydrochloride

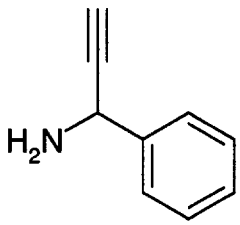
16.6 g of cyclopropylpyridin-3-ylmethylamine hydrochloride mixed with inorganic salts and boric acid were obtained in accordance with the method for precursor 3p from 7.5 g (51.5 mmol) of imine (see a) and 1.9 g (51.4 mmol) of $NaBH_4$.

Precursor 3 r: 1-(5-Methyl-furan-2-yl)-propylamine



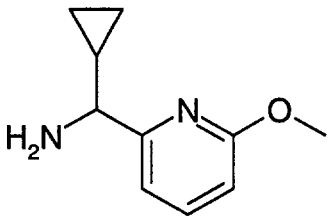
11.35 g (180 mmol) of sodium cyanoborohydride were introduced in portions into 5 g (36 mmol) of 2-methyl-5-propionylfuran and 28.2 g (366 mmol) of ammonium acetate in 300 ml of methanol with stirring, and reaction was allowed to take place at RT for 18 h. The mixture was substantially concentrated and, after addition of 200 ml of dichloromethane, the organic phase was washed 3x with 50 ml of $NaHCO_3$ solution each time, dried over Na_2SO_4 and concentrated. 3.9 g (28 mmol) of the amine were obtained in the form of a pale yellow oil.

Precursor 3s: 1-Phenyl-prop-2-ynylamine hydrochloride



The compound was prepared by a Ritter reaction starting from 1-phenyl-2-propynyl alcohol and subsequent hydrolysis with hydrochloric acid by the method of Bjorn M. Nilsson et al. J. Heterocycl. Chem. (1989), 26(2), 269-75.

Precursor 3t: C-Cyclopropyl-C-(6-methoxy-pyridin-2-yl)-methylamine



a) Cyclopropanecarbaldehyde O-benzyloxime

6.7 g (95.6 mmol) of cyclopropanecarbaldehyde were stirred together with 15.3 g (95.6 mmol) of O-benzylhydroxylamine and 15.7 g (191.2 mmol) of sodium acetate in 250 ml of ethanol at room temperature for 18 h and, after concentration, Na_2SO_4 was added. The residue was extracted 3x with 50 ml of dichloromethane each time, the organic phase was concentrated, and the crude product was purified by chromatography on silica gel. 5 g (28.6 mmol) of a colorless liquid were obtained.

b) O-Benzyl-N-[cyclopropyl-(6-methoxypyridin-2-yl)-methyl]-hydroxylamine

8.8 ml (22 mmol) of n-BuLi (2.5 M in toluene) were added to 3.76 g (20 mmol) of 2-bromo-6-methoxypyridine in 20 ml of THF at –78°C. After 30 min, this dark red solution was added to a solution of 1.4 g (8 mmol) of cyclopropanecarbaldehyde O-benzyloxime (see a) and 2.52 ml (20 mmol) of BF_3-etherate in 40 ml of toluene, which was stirred at –78°C for 15 min. The mixture was stirred at –78°C for 4 h, slowly warmed to RT and, after addition of water, made alkaline with saturated Na_2CO_3 solution.

The organic phase was separated off, the aqueous phase was extracted with toluene, and the combined organic phases were dried over Na_2SO_4 and concentrated. The crude product was taken up in 12 ml of acetonitrile, insoluble constituents were removed, and the product was isolated by preparative HPLC (650 mg, red oil).

c) C-Cyclopropyl-C-(6-methoxy-pyridin-2-yl)-methylamine

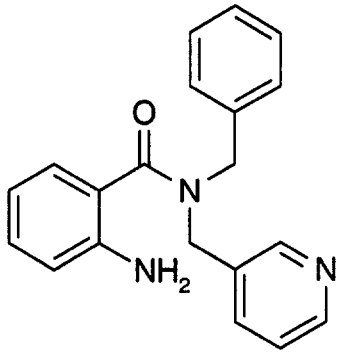
650 mg (2.3 mmol) of O-benzyl-N-[cyclopropyl-(6-methoxypyridin-2-yl)-methyl]-hydroxylamine (see a) were dissolved in 18 ml of glacial acetic acid and diluted with 18 ml of water. 3.3 g of zinc dust were added, and the suspension was reacted in an ultrasonic bath for 24 h. The mixture was filtered through kieselguhr and washed with half-concentrated acetic acid, and the filtrate was partially evaporated and adjusted to pH 11 with saturated Na_2CO_3 solution. This was followed by extracting 3x with 100 ml

of dichloromethane each time, drying over Na_2SO_4 and concentrating. 0.4 g (2.2 mmol) of the product was obtained in the form of a dark red oil.

General method 4 A: Preparation of 2-aminobenzamides from 2-nitrobenzoic acids

The appropriate 2-nitrobenzoic acid is initially reacted in analogy to general methods 2 and 5 with the particular amine to give a 2-nitrobenzamide. Subsequently, 4 mmol of the 2-nitrobenzamide are hydrogenated in 50 ml of THF and 50 ml of methanol in the presence of a spatula tip of 10% palladium on carbon at RT under atmospheric pressure. The catalyst is filtered off with suction, the reaction mixture is concentrated, and the appropriate 2-aminobenzamide is obtained.

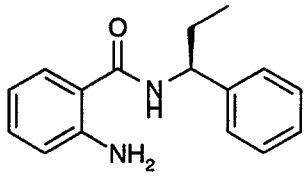
The following precursor was synthesized inter alia in this way:

Precursor	Structure	Mass
4 a		318 (M+1)

General method 4 B: Preparation of 2-aminobenzamides from isatoic anhydride

A solution of 20 mmol of isatoic anhydride and 22 mmol of the appropriate amine in 75 ml of DMF is heated at 60°C until reaction is complete. 100 ml of water are added to the reaction mixture, and the product is filtered off with suction or isolated by extraction.

Precursor 4 b: (S)-2-Amino-N-(1-phenyl-propyl)-benzamide



3.4 g of the title compound were obtained by general method 4 B from 3 g of (S)-1-phenylpropylamine and 3.2 g of isatoic anhydride after 2 h at 60°C.

General method 5: Reaction of sulfonylaminobenzoyl chlorides with amines

0.6 mmol of the particular sulfonylaminobenzoyl chloride is added to a solution of 0.66 mmol of the particular amine and 0.9 mmol of triethylamine in 3 ml of methylene chloride, and the mixture is stirred at room temperature overnight. The reaction mixture is diluted with 5 ml of water and 10 ml of methylene chloride, and the organic phase is washed successively with 1 M hydrochloric acid solution and saturated sodium bicarbonate solution. After drying over magnesium sulfate, the solution is concentrated in vacuo, and the product is purified if necessary by preparative HPLC or column chromatography.

General method 6: Reaction of sulfonylaminobenzoic acids with amines

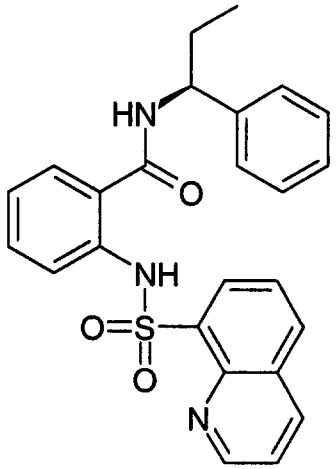
0.44 mmol of the particular amine is added dropwise to a solution of 0.42 mmol of the appropriate sulfonylaminobenzoic acid, 0.44 mmol of HOBT and 0.44 mmol of EDAC in 5 ml of THF at 0°C, and the mixture is stirred at RT for 4 to 12 h. The reaction mixture is diluted with EA and washed with dilute hydrochloric acid and sodium bicarbonate solution. Drying over magnesium sulfate and concentration in vacuo result in the appropriate amide which is purified if necessary by preparative HPLC.

General method 7: Reaction of 2-aminobenzamides with sulfonyl chlorides
A solution of 0.3 mmol of the appropriate sulfonyl chloride in 2 ml of methylene chloride is added dropwise to a solution of 0.2 mmol of the appropriate 2-aminobenzamide (precursor 4) and 0.6 mmol of pyridine in 5 ml of methylene chloride at 0°C, and the mixture is stirred at RT overnight. The organic phase is washed with water, dilute hydrochloric acid and sodium bicarbonate solution, and the resulting crude product is

purified if necessary by preparative HPLC.

Example 1: (S)-N-(1-Phenyl-propyl)-2-(quinoline-8-sulfonylamino)-benzamide

a) 2-(Quinoline-8-sulfonylamino)-benzoic acid



690 mg of anthranilic acid were added in portions to a solution of 1.32 g of Na_2CO_3 in 10 ml of water at 60°C. After stirring at this temperature for 10 minutes, 1.25 g of 8-quinolinesulfonyl chloride were added in portions at 70°C. After stirring at 70°C for 5 hours, a further 230 mg of 8-quinolinesulfonyl chloride were added. After stirring at 70°C for 2 hours, the reaction mixture was allowed to cool to RT. The pH was adjusted to 1 with a 2N aqueous HCl solution, and the suspension was stirred at RT for a further hour. The precipitate was then filtered off and dried under medium vacuum at 60°C to result in 1.57 g of a colorless amorphous solid.

MS (ESI): 329 $(M+H)^+$

b) 2-(Quinoline-8-sulfonylamino)-benzoyl chloride

100 mg of 2-(quinoline-8-sulfonylamino)-benzoic acid were dissolved in 1 ml of $SOCl_2$ and boiled under reflux for 4½ hours. The volatile constituents were subsequently removed in vacuo, the residue was taken up in 10 ml of toluene and subsequently the volatile constituents were again removed in vacuo. 120 mg of the acid chloride were obtained and were reacted further without purification.

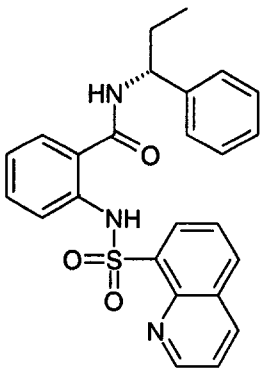
c) (S)-N-(1-Phenylpropyl)-2-(quinoline-8-sulfonylamino)-benzamide

120 mg of 2-(quinoline-8-sulfonylamino)-benzoyl chloride were suspended in 4 ml of CH_2Cl_2 and, at RT, 85 µl of triethylamine were added. A solution of 41 mg of (S)-1-phenylpropylamine in 2 ml of CH_2Cl_2 was then added, and the mixture was stirred at RT for 18 hours. The reaction mixture was diluted with 50 ml of CH_2Cl_2 and washed twice with 20 ml of a saturated aqueous Na_2CO_3 solution each time. The aqueous phase was then extracted with a further 20 ml of CH_2Cl_2, the combined organic phases were dried over Na_2SO_4, and the solvent was removed in vacuo. Chromatography of the residue on silica gel with MTB/DIP 1:1 afforded 77 mg of an amorphous solid.

R_f (MTB/DIP 1:1) = 0.31 MS (ES) : 446 $(M+H)^+$

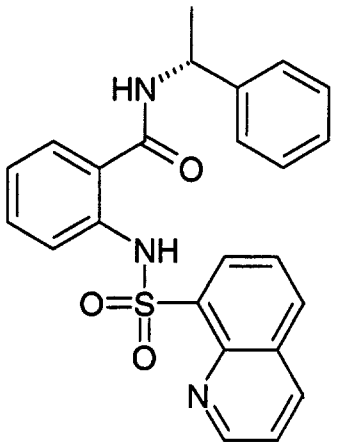
The title compounds of examples 2-11 were synthesized in analogy to example 1:

Example 2: (R)-N-(1-Phenylpropyl)-2-(quinoline-8-sulfonylamino)-benzamide



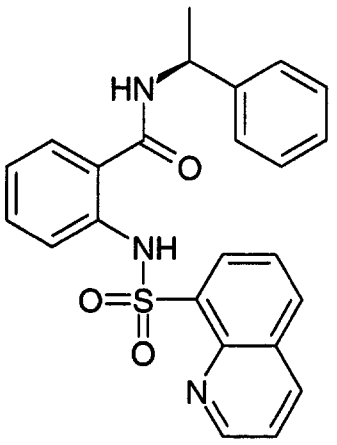
R_f (MTB/DIP 1:1) = 0.31 MS (ES) : 446 $(M+H)^+$

Example 3: (R)-N-(1-Phenylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



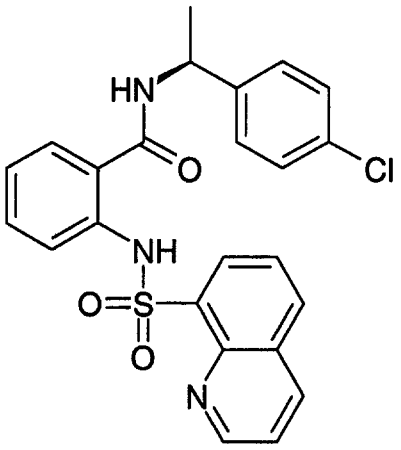
R_f (MTB/DIP 1:1) = 0.25 MS (ES) : 432 $(M+H)^+$

Example 4: (S)-N-(1-Phenylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



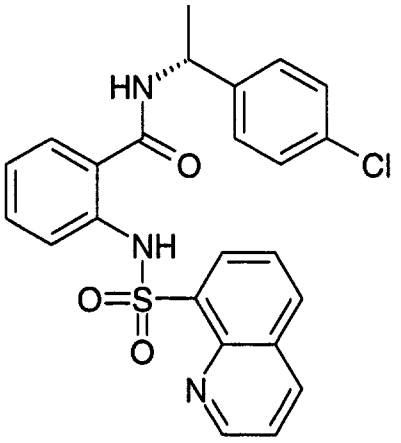
R_f (MTB/DIP 1:1) = 0.25 MS (ES) : 432 $(M+H)^+$

Example 5: (S)-N-[1-(4-Chlorophenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



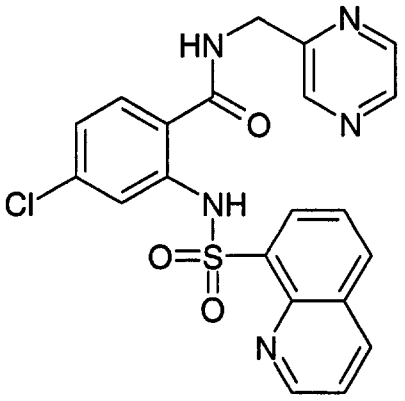
R_f (MTB/DIP 1:1)= 0.23 MS (ES): 466 $(M+H)^+$

Example 6: (R)-N-[1-(4-Chlorophenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



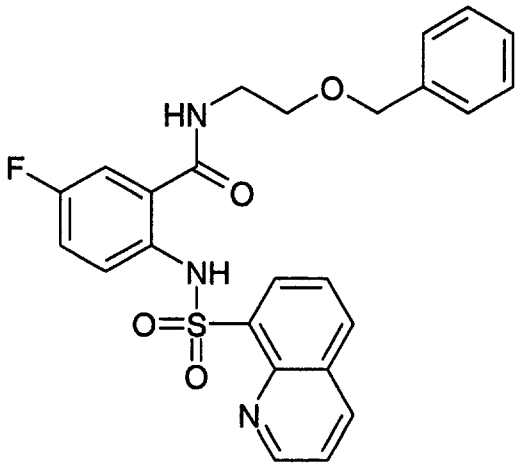
R_f (MTB/DIP 1:1) 0.23 MS (ES): 466 $(M+H)^+$

Example 7: 4-Chloro-N-pyrazin-2-ylmethyl-2-(quinoline-8-sulfonylamino)-benzamide



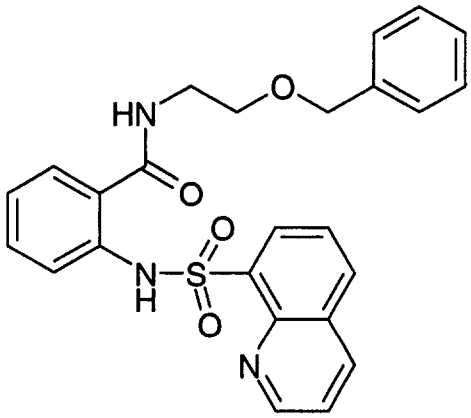
R_f (EA)= 0.10 MS (ES): 454 $(M+H)^+$

Example 8: N-(2-Benzyloxyethyl)-5-fluoro-2-(quinoline-8-sulfonylamino)-benzamide



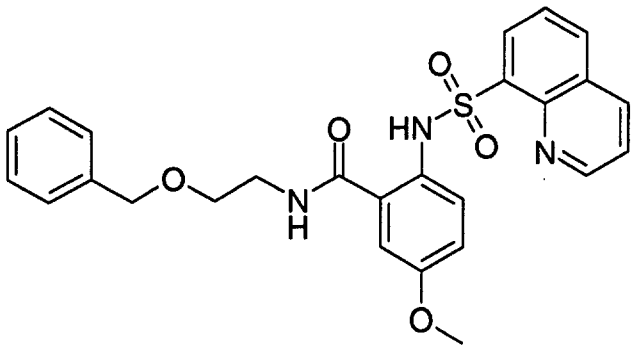
R_f (MTB/DIP 1:1) = 0.24 MS (ES) : 480 $(M+H)^+$

Example 9: N-(2-Benzyloxyethyl)-2-(quinoline-8-sulfonylamino)-benzamide



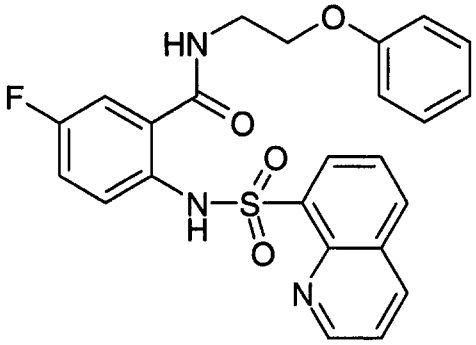
R_f (MTB) = 0.36 MS (ES) : 462 $(M+H)^+$

Example 10: N-(2-Benzyloxyethyl)-5-methoxy-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 492 $(M+H)^+$

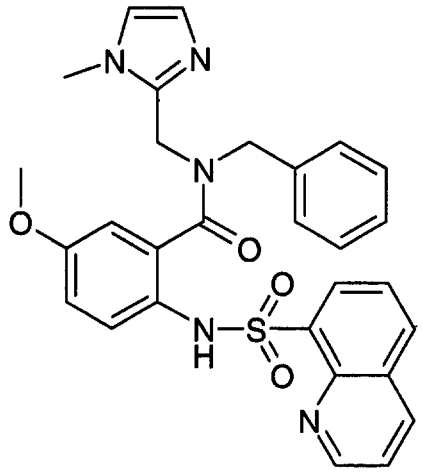
Example 11: 5-Fluoro-N-(2-phenoxyethyl)-2-(quinoline-8-sulfonylamino)-benzamide



R_f (MTB/DIP 1:1) = 0.29

MS (ES) : 466 $(M+H)^+$

Example 12: N-Benzyl-5-methoxy-N-(1-methyl-1H-imidazol-2-ylmethyl)-2-(quinoline-8-sulfonylamino)-benzamide



a) Benzyl-(1-methyl-1H-imidazol-2-ylmethyl)-amine

19.4 g (0.18 mol) of benzylamine were dissolved in 200 ml of methanol and, after addition of 10 g (0.09 mol) of 2-formyl-1-methylimidazole, 11.4 g of sodium cyanoborohydride (0.18 mol) and 10.9 g (0.18 mol) of glacial acetic acid, stirred at RT for 16 h. The solution was concentrated, taken up in EA and washed twice with $NaHCO_3$ solution. The organic phase was dried, concentrated and distilled under medium vacuum to remove benzylamine which was still present. The residue was dissolved in diethyl ether/THF 1:1, and a saturated solution of HCl in diethyl ether was added. The precipitated hydrochloride (20.5 g) was filtered off with suction, washed with diethyl ether and dried in vacuo.

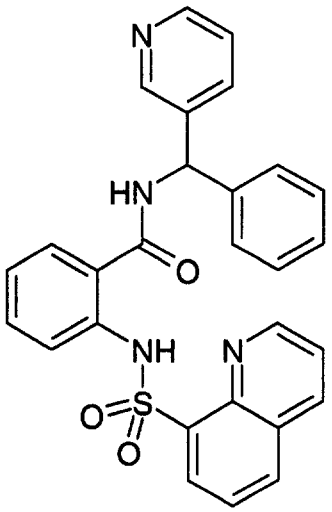
MS (ES) : 202 $(M+H)^+$

b) N-Benzyl-5-methoxy-N-(1-methyl-1H-imidazol-2-ylmethyl)-2-(quinoline-8-sulfonylamino)-benzamide

66 mg of benzyl-(1-methyl-1H-imidazol-2-ylmethyl)-amine were reacted as described under 1c) to result in 78 mg of the title compound as an amorphous solid.

R_f (EA) = 0.09 MS (ES) : 542 $(M+H)^+$

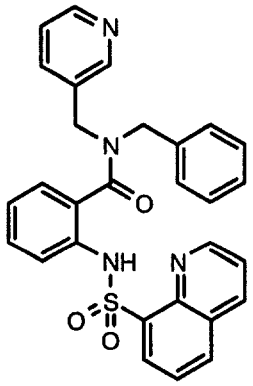
Example 13: N-(Phenylpyridin-3-ylmethyl)-2-(quinoline-8-sulfonylamino)-benzamide



120 mg of phenylpyridin-3-ylmethylamine (Synthesis 1976, 593) were reacted with 450 mg of 2-(quinoline-8-sulfonylamino)-benzoyl chloride in analogy to example 1 to result in 130 mg of an amorphous solid.

R_f (EA) = 0.29 MS (ES) : 495 $(M+H)^+$

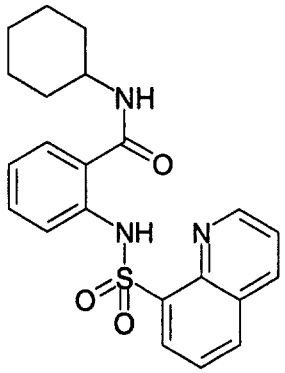
Example 14: N-Benzyl-N-pyridin-3-ylmethyl-2-(quinoline-8-sulfonylamino)-benzamide



99 mg of N-benzyl-N-(3-pyridylmethyl)amine (precursor 3b) were reacted with 87 mg of 2-(quinoline-8-sulfonylamino)-benzoyl chloride in analogy to example 1 to result in 66 mg of an amorphous white solid.

MS (ES) : 509 $(M+H)^+$

Example 15: N-Cyclohexyl-2-(quinoline-8-sulfonylamino)-benzamide

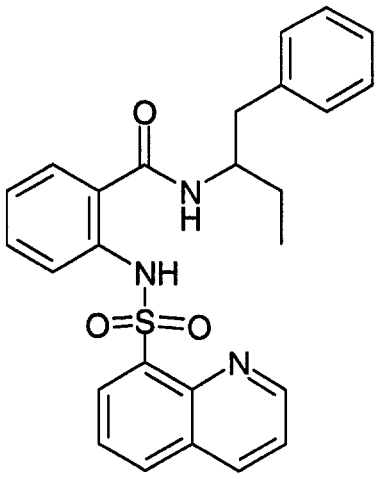


50 mg of cyclohexylamine were reacted with 87 mg of 2-(quinoline-8-sulfonylamino)-benzoyl chloride in analogy to example 1 to result in 59 mg of an amorphous white solid.

MS (ES) : 410 $(M+H)^+$

The title compounds of examples 16 - 44 were synthesized in analogy to example 1:

Example 16: N-(1-Benzylpropyl)-2-(quinoline-8-sulfonylamino)-benzamide

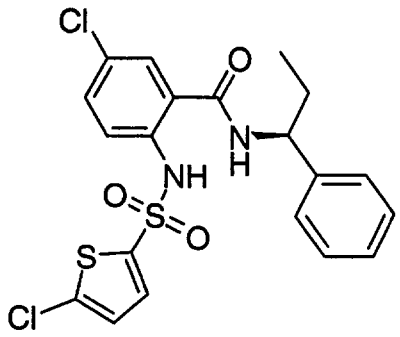


The title compound was obtained from 2-(quinoline-8-sulfonylamino)-benzoyl chloride (example 1b) and 1-benzylpropylamine (precursor 3l).

MS (ES) : 460 $(M+H)^+$

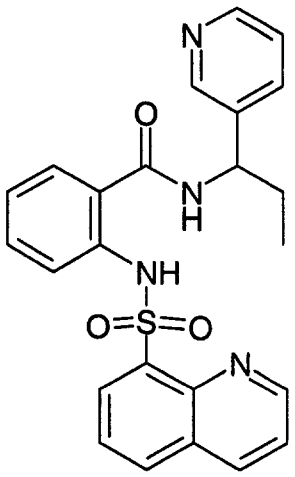
Example 17: (S)-5-Chloro-2-(5-chlorothiophene-2-sulfonylamino)-N-(1-phenylpropyl)-

benzamide



MS (ES) : 469 $(M+H)^+$

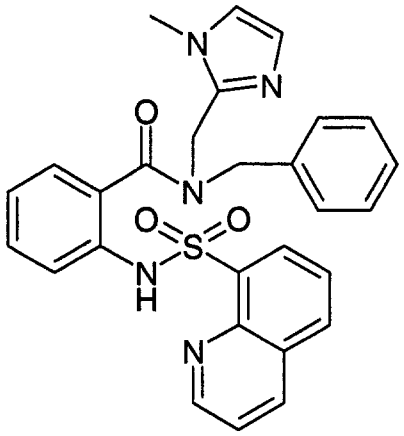
Example 18: N-(1-Pyridin-3-yl-propyl)-2-(quinoline-8-sulfonylamino)-benzamide



The title compound was obtained from 2-(quinoline-8-sulfonylamino)-benzoyl chloride (example 1b) and 1-pyridin-3-ylpropylamine (precursor 3n).

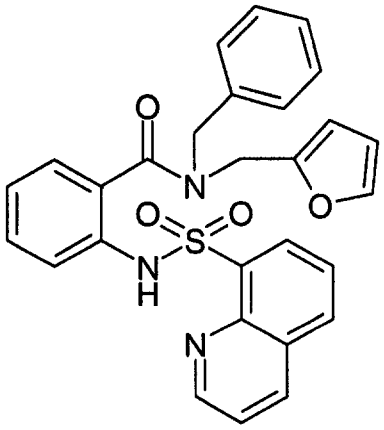
MS (ES) : 447 $(M+H)^+$

Example 19: N-Benzyl-N-(1-methyl-1H-imidazol-2-ylmethyl)-2-(quinoline-8-sulfonylamino)-benzamide



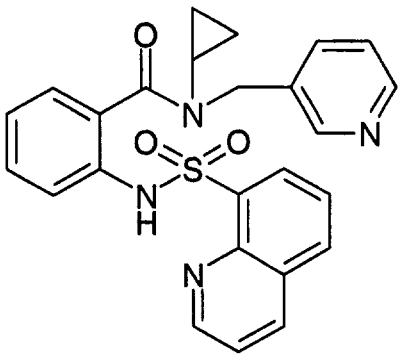
MS (ES) : 512 $(M+H)^+$

Example 20: N-Benzyl-N-furan-2-ylmethyl-2-(quinoline-8-sulfonylamino)-benzamide



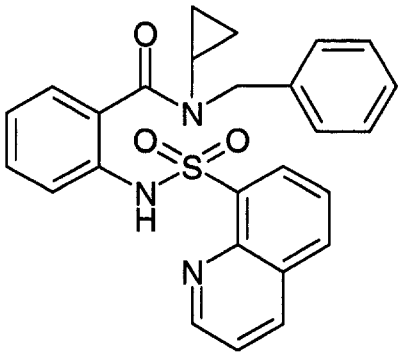
MS (ES) : 498 $(M+H)^+$

Example 21: N-Cyclopropyl-N-pyridin-3-ylmethyl-2-(quinoline-8-sulfonylamino)-benzamide



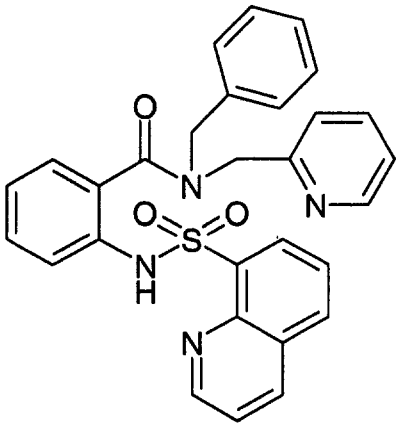
MS (ES) : 459 $(M+H)^+$

Example 22: N-Benzyl-N-cyclopropyl-2-(quinoline-8-sulfonylamino)-benzamide



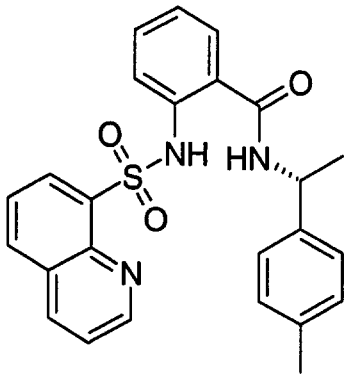
MS (ES) : 458 $(M+H)^+$

Example 23: N-Benzyl-N-pyridin-2-ylmethyl-2-(quinoline-8-sulfonylamino)-benzamide



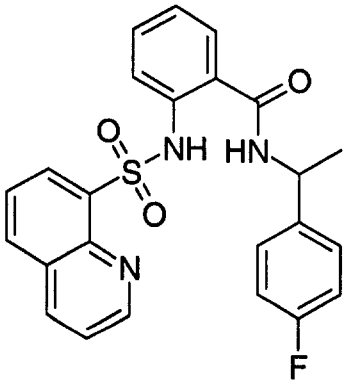
MS (ES) : 509 $(M+H)^+$

Example 24: (R)-2-(Quinoline-8-sulfonylamino)-N-(1-p-tolyl-ethyl)-benzamide



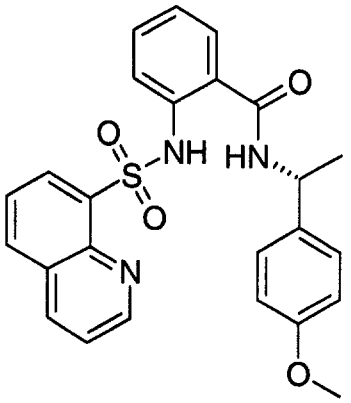
MS (ES) : 446 $(M+H)^+$

Example 25: N-[1-(4-Fluorophenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



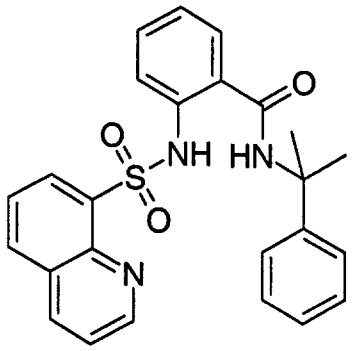
MS (ES) : 450 $(M+H)^+$

Example 26: (R)-N-[1-(4-Methoxyphenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



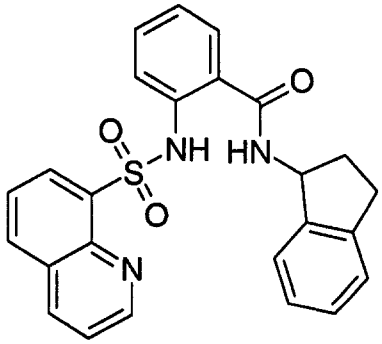
MS (ES) : 462 $(M+H)^+$

Example 27: N-(1-Methyl-1-phenylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



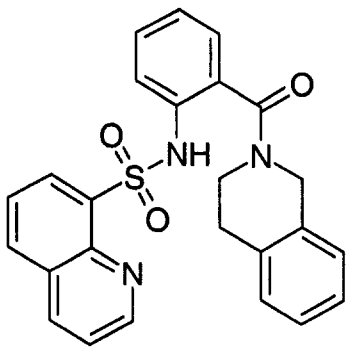
MS (ES) : 446 $(M+H)^+$

Example 28: N-Indan-1-yl-2-(quinoline-8-sulfonylamino)-benzamide



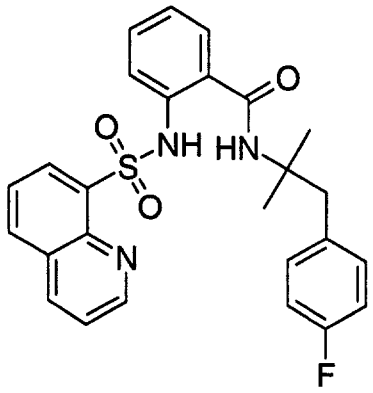
MS (ES) : 444 $(M+H)^+$

Example 29: N-[2-(3,4-dihydro-1H-isoquinoline-2-carbonyl)-phenyl]-quinoline-8-sulfonamide



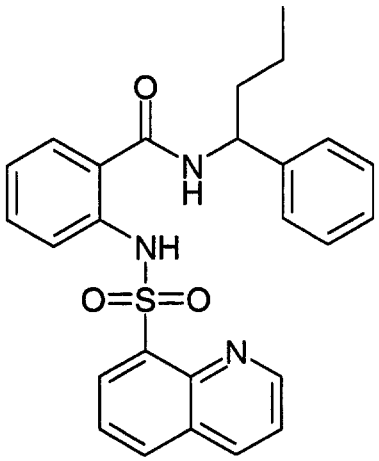
MS (ES) : 444 $(M+H)^+$

Example 30: N-[2-(4-Fluorophenyl)-1,1-dimethylethyl]-2-(quinoline-8-sulfonylamino)-benzamide



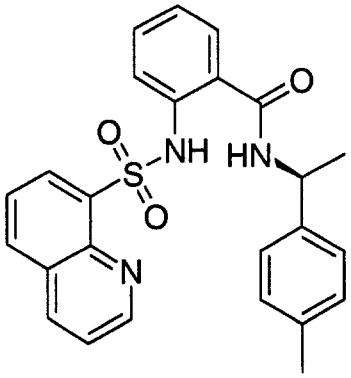
MS (ES) : 478 $(M+H)^+$

Example 31: N-(1-Phenylbutyl)-2-(quinoline-8-sulfonylamino)-benzamide



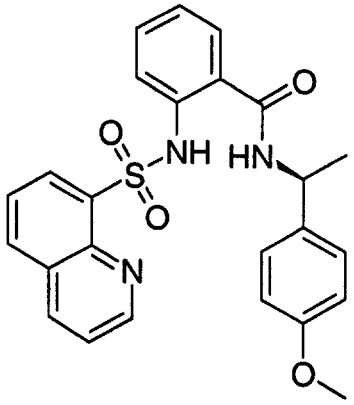
MS (ES) : 460 $(M+H)^+$

Example 32: (S)-2-(Quinoline-8-sulfonylamino)-N-(1-p-tolylethyl)-benzamide



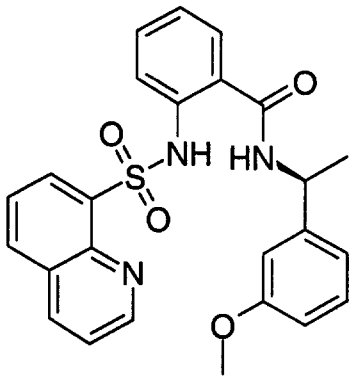
MS (ES) : 446 $(M+H)^+$

Example 33 (S)-N-[1-(4-Methoxyphenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



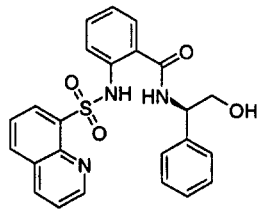
MS (ES) : 462 $(M+H)^+$

Example 34: (S)-N-[1-(3-Methoxyphenyl)-ethyl]-2-(quinoline-8-sulfonylamino)-benzamide



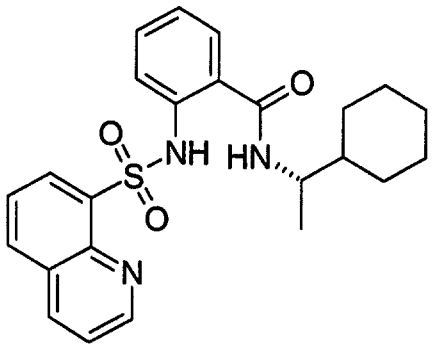
MS (ES) : 462 $(M+H)^+$

Example 35 (R)-N-(2-Hydroxy-1-phenylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



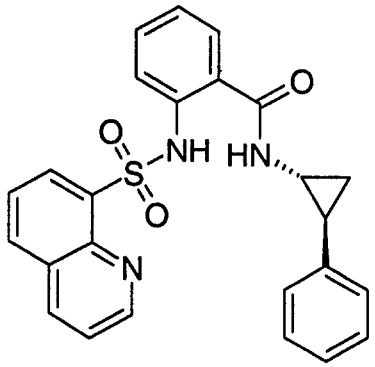
MS (ES) : 448 $(M+H)^+$

Example 36: (S)-N-(1-Cyclohexylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



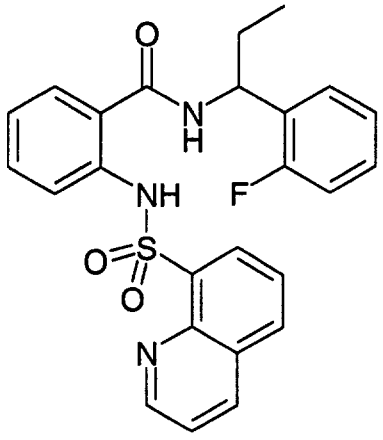
MS (ES) : 438 $(M+H)^+$

Example 37: N-(2-Phenylcyclopropyl)-2-(quinoline-8-sulfonylamino)-benzamide



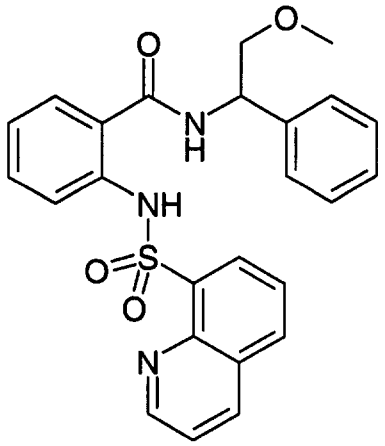
MS (ES) : 444 $(M+H)^+$

Example 38: N-[1-(2-Fluorophenyl)-propyl]-2-(quinoline-8-sulfonylamino)-benzamide



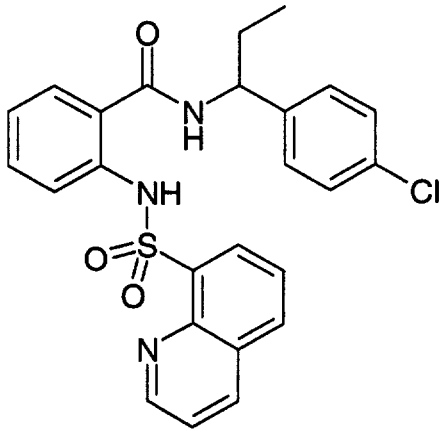
MS (ES) : 464 $(M+H)^+$

Example 39: N-(2-Methoxy-1-phenylethyl)-2-(quinoline-8-sulfonylamino)-benzamide



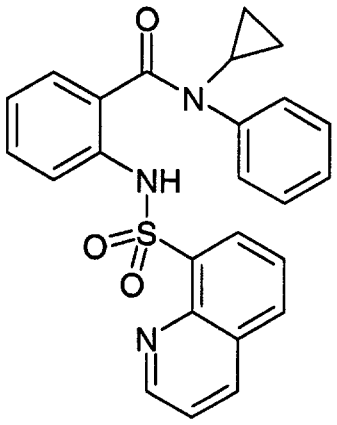
MS (ES) : 462 $(M+H)^+$

Example 40: N-[1-(4-Chlorophenyl)-propyl]-2-(quinoline-8-sulfonylamino)-benzamide



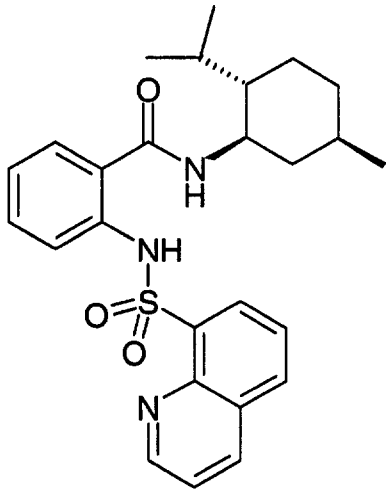
MS (ES) : 480 $(M+H)^+$

Example 41: N-Cyclopropyl-N-phenyl-2-(quinoline-8-sulfonylamino)-benzamide



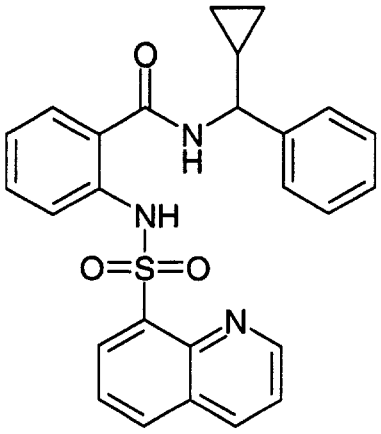
MS (ES) : 444 $(M+H)^+$

Example 42: N-(2-Isopropyl-5-methylcyclohexyl)-2-(quinoline-8-sulfonylamino)-benzamide



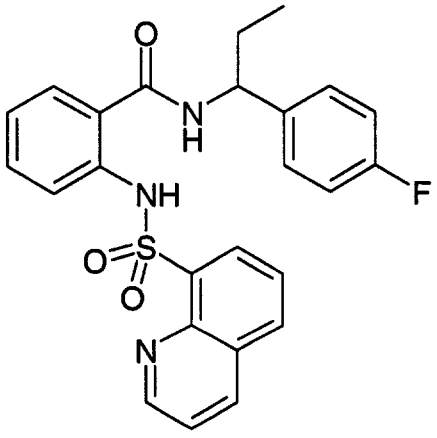
MS (ES) : 466 $(M+H)^+$

Example 43: N-(Cyclopropylphenylmethyl)-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 458 $(M+H)^+$

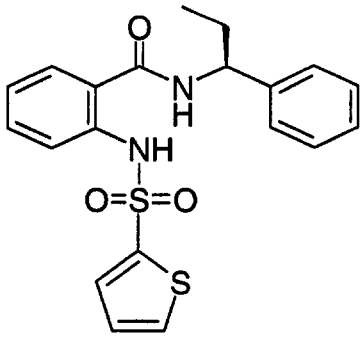
Example 44: N-[1-(4-Fluorophenyl)-propyl]-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 464 $(M+H)^+$

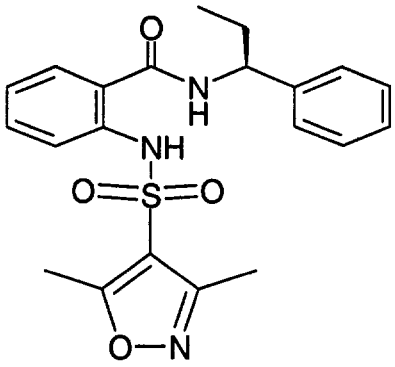
The title compounds of examples 45 - 51 were prepared from (S)-2-amino-N-(1-phenylpropyl)-benzamide (precursor 4b) by general method 7:

Example 45: (S)-N-(1-Phenylpropyl)-2-(thiophene-2-sulfonylamino)-benzamide



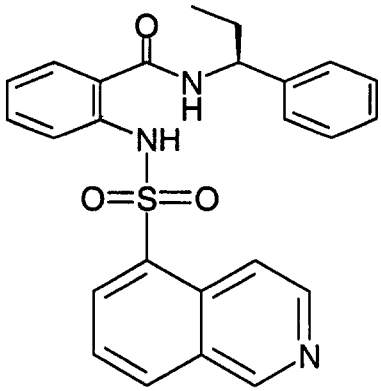
MS (ES) : 401 $(M+H)^+$

Example 46: 2-(3,5-Dimethylisoxazole-4-sulfonylamino)-N-(1-phenylpropyl)-benzamide



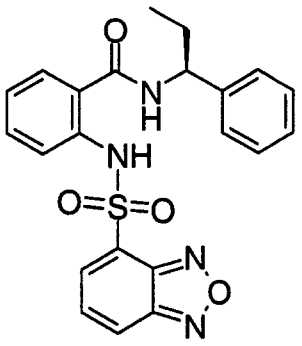
MS (ES) : 414 $(M+H)^+$

Example 47: (S)-2-(Isoquinoline-5-sulfonylamino)-N-(1-phenylpropyl)-benzamide



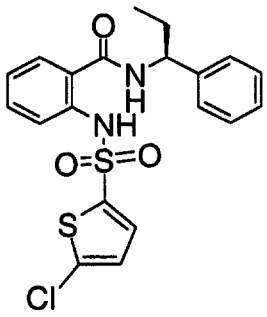
MS (ES) : 446 $(M+H)^+$

Example 48: 2-(Benzo[1,2,5]oxadiazole-4-sulfonylamino)-N-(1-phenylpropyl)-benzamide



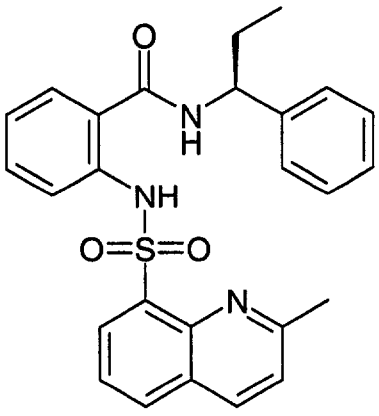
MS (ES) : 437 $(M+H)^+$

Example 49: 2-(5-Chlorothiophene-2-sulfonylamino)-N-(1-phenylpropyl)-benzamide



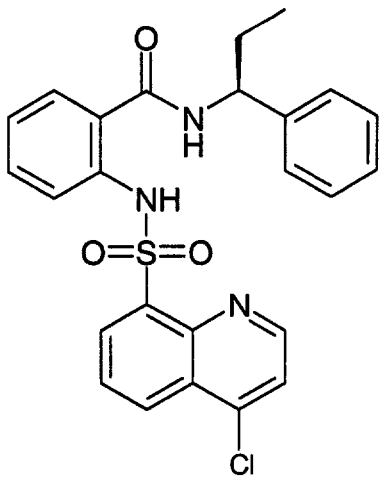
MS (ES) : 435 $(M+H)^+$

Example 50: 2-(2-Methylquinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



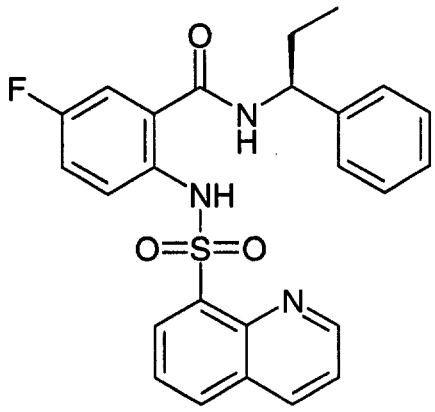
MS (ES) : 460 $(M+H)^+$

Example 51: (S)-2-(4-Chloroquinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



MS (ES) : 480 $(M+H)^+$

Example 52: (S)-5-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



a) 5-Fluoro-2-(quinoline-8-sulfonylamino)-benzoic acid

A reaction mixture composed of 10.0 g (64 mmol) of 5-fluoro-2-aminobenzoic acid, 16.3 g (193 mmol) of sodium bicarbonate and 16.3 g of 8-quinolinesulfonyl chloride in 325 ml of water and 325 ml of ethyl acetate was stirred at RT overnight. The aqueous phase was separated off and extracted once with 50 ml of ethyl acetate. The aqueous phase was then acidified with concentrated hydrochloric acid and stirred for 2 h. The precipitate was filtered off with suction and dried in vacuo to result in 19.5 g of 5-fluoro-2-(quinoline-8-sulfonylamino)-benzoic acid.

b) 5-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide

5.7 g of the title compound were obtained from 5.5 g (15.9 mmol) of 5-fluoro-2-(quinoline-8-sulfonylamino)-benzoic acid and 2.3 g (16.7 mmol) of (S)-

phenylpropylamine by general method 6.

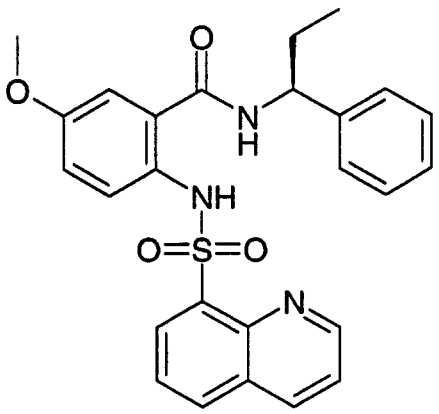
M.p.: 163°C; MS (ES) : 464 $(M+H)^+$

(S)-5-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide sodium salt

2 ml of a 30 percent strength sodium methanolate solution were added to a solution of 5 g of the compound of example 52 in 120 ml of ethyl acetate. The precipitated sodium salt was filtered off with suction and recrystallized from 25 ml of ethanol to result in 3.3 g of the title compound.

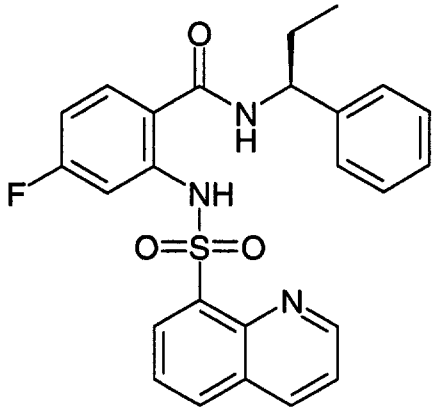
The title compounds of examples 53 - 58 were prepared from the corresponding precursors 1 and (S)-phenylpropylamine by general method 6:

Example 53: (S)-5-Methoxy-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



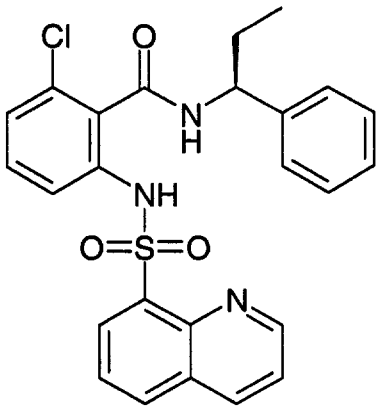
MS (ES) : 476 $(M+H)^+$

Example 54: (S)-4-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



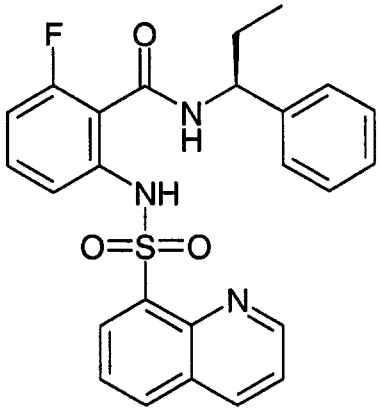
MS (ES) : 464 $(M+H)^+$

Example 55: (S)-6-Chloro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



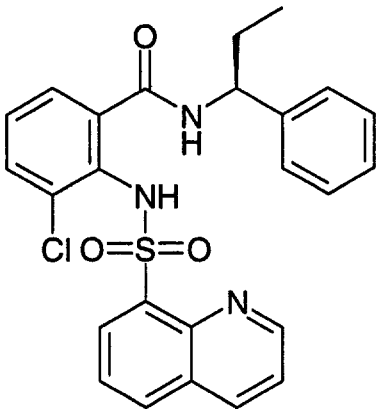
MS (ES) : 480 $(M+H)^+$

Example 56: (S)-6-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



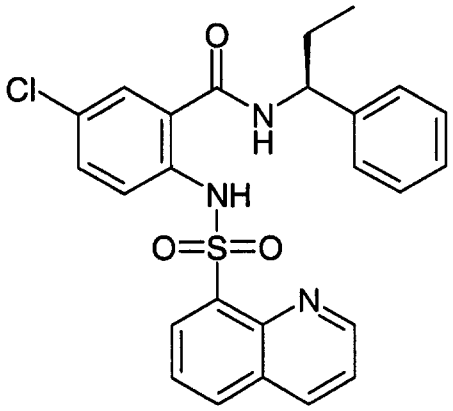
MS (ES) : 464 $(M+H)^+$

Example 57: (S)-3-Chloro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



MS (ES) : 480 $(M+H)^+$

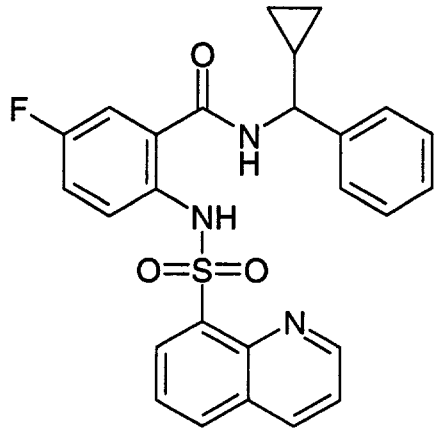
Example 58: (S)-5-Chloro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide



MS (ES) : 480 $(M+H)^+$

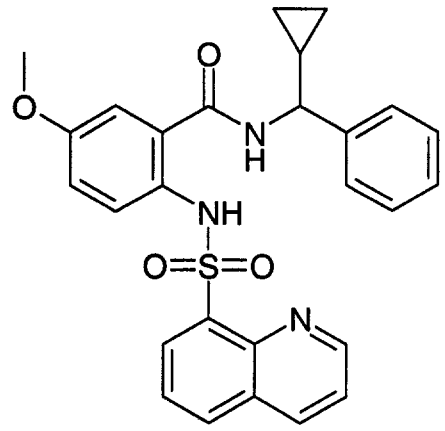
The title compounds of examples 59 - 60 were prepared from the corresponding precursors 1 and α-cyclopropylbenzylamine (precursor 3o) by general method 6:

Example 59: N-(Cyclopropylphenylmethyl)-5-fluoro-2-(quinoline-8-sulfonylamino)-benzamide



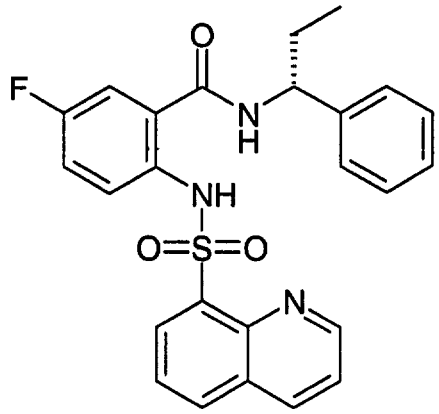
MS (ES) : 476 $(M+H)^+$

Example 60: N-(Cyclopropylphenylmethyl)-5-methoxy-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 488 $(M+H)^+$

Example 61: (R)-5-Fluoro-2-(quinoline-8-sulfonylamino)-N-(1-phenylpropyl)-benzamide

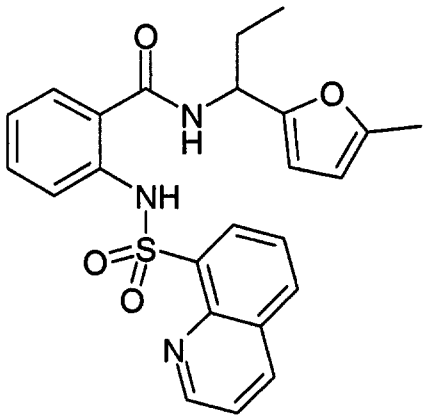


The title compound was obtained in analogy to example 52 from (R)-phenylpropylamine.

MS (ES) : 464 $(M+H)^+$

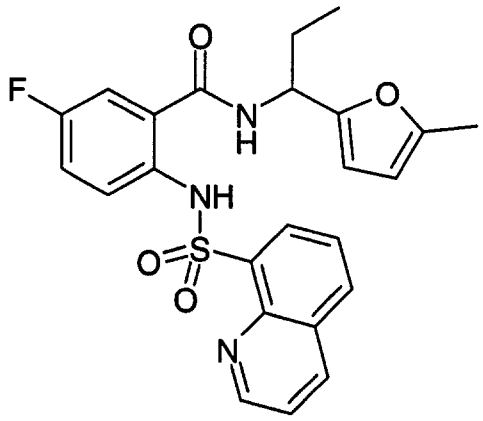
The title compounds of examples 62 - 63 were prepared from the corresponding precursors 1 and 1-(5-methylfuran-2-yl)-propylamine (precursor 3r) by general method 5:

Example 62: N-[1-(5-Methylfuran-2-yl)-propyl]-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 450 $(M+H)^+$

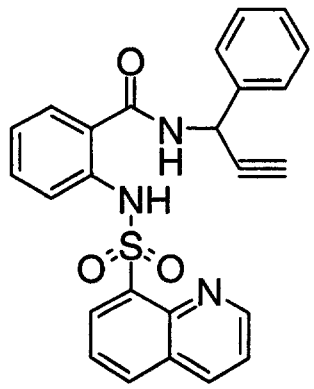
Example 63: 5-Fluoro-N-[1-(5-methylfuran-2-yl)-propyl]-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 468 $(M+H)^+$

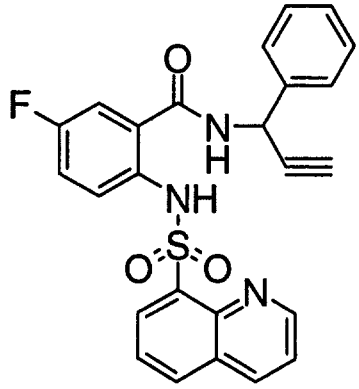
The title compounds of examples 64 - 66 were prepared from the corresponding precursors 1 and 1-phenylprop-2-ynylamine (precursor 3s) by general method 5:

Example 64: N-(1-Phenylprop-2-ynyl)-2-(quinoline-8-sulfonylamino)-benzamide



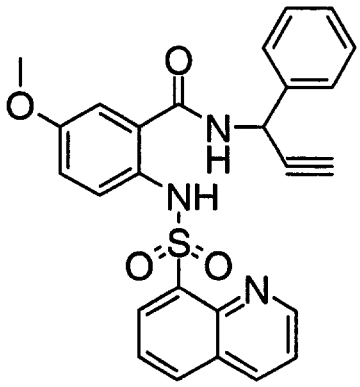
MS (ES) : 442 $(M+H)^+$

Example 65: 5-Fluoro-N-(1-phenylprop-2-ynyl)-2-(quinoline-8-sulfonylamino)-benzamide



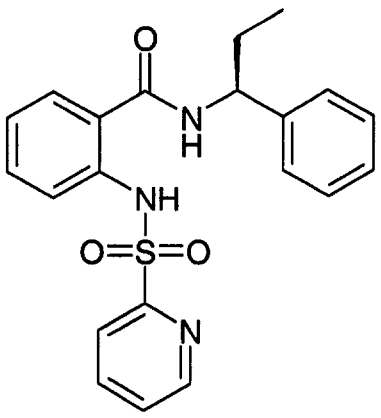
MS (ES) : 460 $(M+H)^+$

Example 66: 5-Methoxy-N-(1-phenylprop-2-ynyl)-2-(quinoline-8-sulfonylamino)-benzamide



MS (ES) : 472 $(M+H)^+$

Example 67: N-(1-Phenylpropyl)-2-(pyridine-2-sulfonylamino)-benzamide

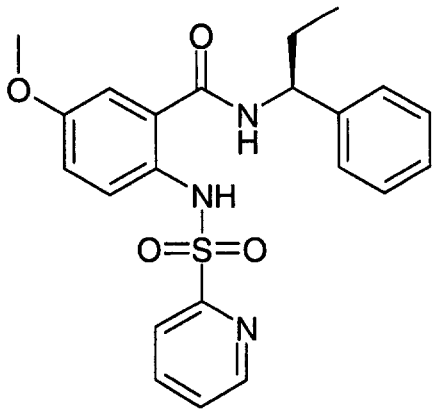


a) Pyridine-2-sulfonyl chloride (analogous to J. Org. Chem. 54, 2, 1989, 389-393). 60.4 mmol of 2-mercaptopyridine are dissolved in 100 mL of hydrochloric acid (20%) and cooled to 2 – 5°C. Chlorine gas is then passed through the solution for 30 min in such a way that the temperature does not exceed 5°C. Then a further 50 mL of water are added. The aqueous phase is extracted with ether (3 × 100 mL), washed with saturated sodium bicarbonate solution, dried (Na_2SO_4) and concentrated. Yield: 4.52 g (42%).

b) 11 mg of N-(1-phenylpropyl)-2-(pyridine-2-sulfonylamino)-benzamide were obtained as a white solid by general method 7 from 100 mg of (S)-2-amino-N-(1-phenylpropyl)-benzamide and 70 mg of pyridine-2-sulfonyl chloride.

MS (ES) : 396 $(M+H)^+$

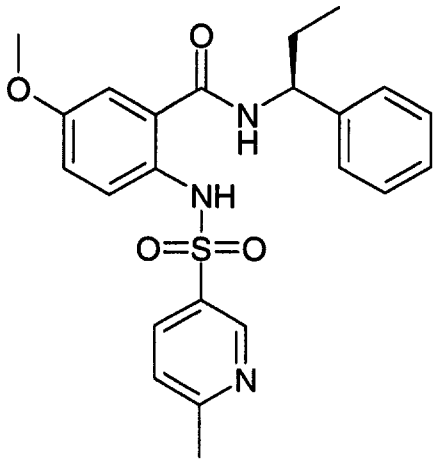
Example 68: 5-Methoxy-N-(1-phenylpropyl)-2-(pyridine-2-sulfonylamino)-benzamide



30 mg of the title compound were obtained as a white solid by general method 7 from 100 mg of (S)-2-amino-5-methoxy-N-(1-phenylpropyl)-benzamide and 62 mg of pyridine-2-sulfonyl chloride.

MS (ES) : 426 $(M+H)^+$

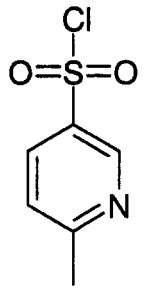
Example 69: 5-Methoxy-2-(6-methylpyridine-3-sulfonylamino)-N-(1-phenylpropyl)-benzamide



a) 6-Methylpyridine-3-sulfonic acid (analogous to J. Amer. Chem. Soc. 65, 1943, 2233-2236).

0.1 mol of 2-picoline is added dropwise over the course of 10 min. to 0.408 mol of oleum (20% free sulfur trioxide) while cooling in ice. Then 0.843 mmol of mercury sulfate is added, and the mixture is stirred at 230°C for 24 h. The sulfuric acid is then removed by distillation in vacuo. The product is precipitated by adding 200 mL of acetonitrile. It is filtered off with suction, washed with a little acetonitrile and dried at 100°C. Yield: 8.16 g (48%).

b) 6-Methylpyridine-3-sulfonyl chloride (analogous to J. Org. Chem. 54, 2, 1989, 389-393).

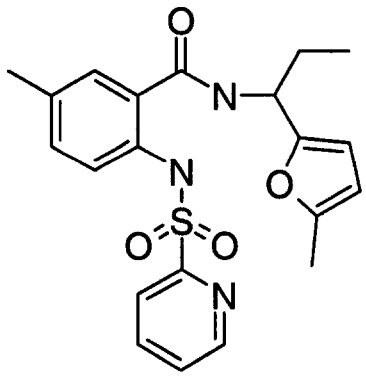


A mixture of 47.1 mmol of 6-methylpyridine-3-sulfonic acid and 56.5 mmol of phosphorus pentachloride is suspended in 80 mL of phosphorus oxychloride and stirred at 120°C for 24 h. The solution is concentrated in vacuo and, while cooling, water is cautiously added. The aqueous phase is then extracted with ether (3 × 100 mL), dried (Na_2SO_4) and concentrated. Yield: 0.6 g (7%).

c) 67 mg of 5-methoxy-2-(6-methylpyridine-3-sulfonylamino)-N-(1-phenylpropyl)-benzamide were obtained as a white solid by general method 7 from 445 mg of (S)-2-amino-5-methoxy-N-(1-phenylpropyl)-benzamide and 300 mg of 6-methylpyridine-3-sulfonyl chloride.

MS (ES) : 440 $(M+H)^+$

Example 70: 5-Methyl-N-[1-(5-methylfuran-2-yl)-propyl]-2-(pyridine-2-sulfonylamino)-benzamide



a) 5-Methyl-N-[1-(5-methylfuran-2-yl)-propyl]-2-nitrobenzamide

2 g (10 mmol) of 2-nitro-5-methylbenzoyl chloride and 1.39 g (10 mmol) of 1-(5-methyl-furan-2-yl)-propylamine (= precursor 3r) were reacted together with 1.3 ml of DIPEA in 20 ml of dichloromethane at room temperature for 18 h. The mixture was diluted with

dichloromethane, washed, dried over Na_2SO_4 and purified by chromatography on silica gel. 1.14 g (3.8 mmol) of a pale yellow solid were obtained.

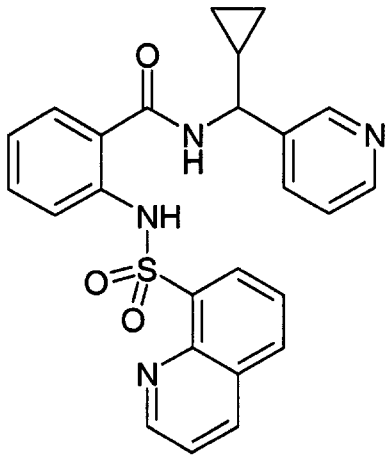
b) 2-Amino-5-methyl-N-[1-(5-methylfuran-2-yl)-propyl]-benzamide

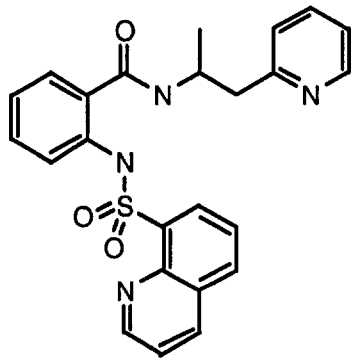
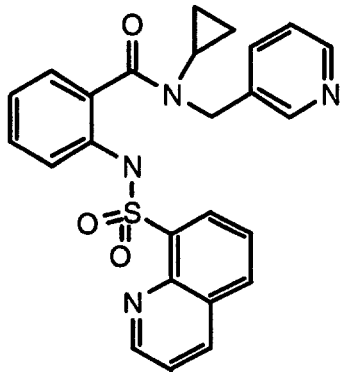
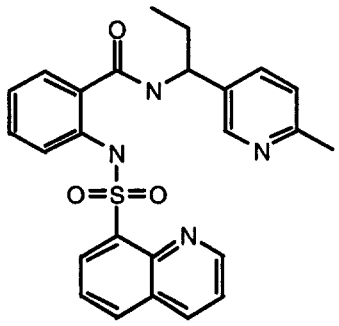
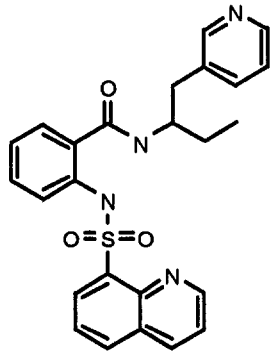
1.14 g (3.8 mmol) of 5-methyl-N-[1-(5-methylfuran-2-yl)-propyl]-2-nitrobenzamide (see a) were dissolved in 20 ml of methanol and hydrogenated with 1 g of palladium on carbon (10%) under atmospheric pressure at room temperature. Filtration and concentration resulted in 0.9 g (3.3 mmol) of solid.

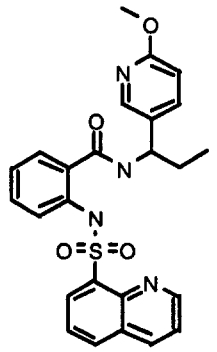
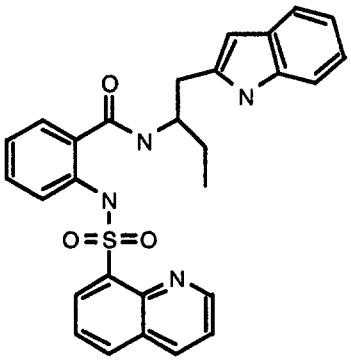
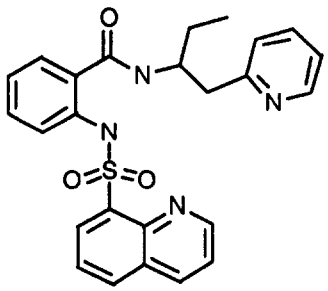
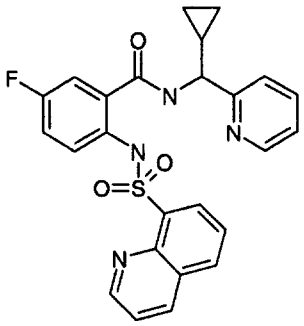
c) 5-Methyl-N-[1-(5-methylfuran-2-yl)-propyl]-2-(pyridine-2-sulfonylamino)-benzamide

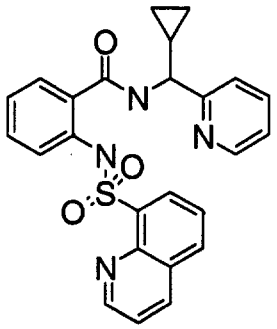
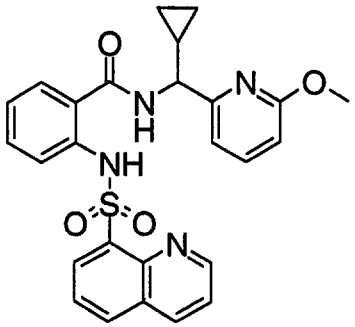
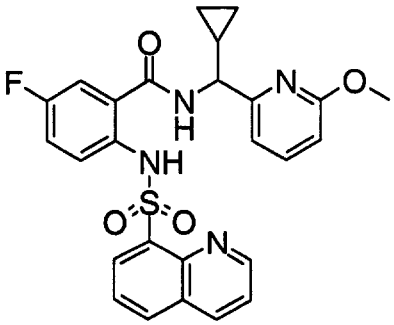
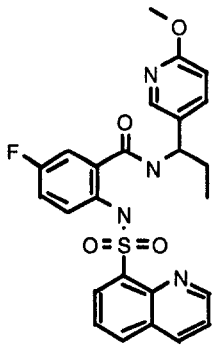
100 mg (0.37 mmol) of 2-amino-5-methyl-N-[1-(5-methylfuran-2-yl)-propyl]-benzamide (see b) and 117 mg (0.66 mmol) of 2-pyridinesulfonyl chloride hydrochloride were dissolved in 1 ml of pyridine and reacted at room temperature for 18 h. The reaction mixture was concentrated and the compound of example 70 (61 mg, 0.12 mmol) was isolated by means of preparative HPLC as trifluoroacetate after freeze drying.

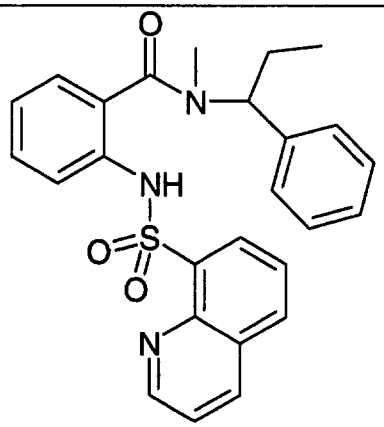
The following compounds were also obtained in analogy to the examples described above:

Example	Structure	Mass (ES)
71		459 (M+1)

72		447 (M+1)
73		459 (M+1)
74		461 (M+1)
75		461 (M+1)

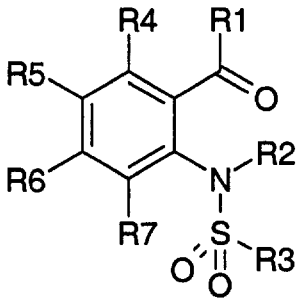
76		477(M+1)
77		499 (M+1)
78		461 (M+1)
79		477 (M+1)

80		459 (M+1)
81		489 (M+1)
82		507 (M+1)
83		495 (M+1)

84		460 (M+1)

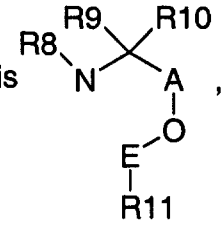
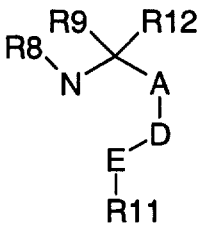
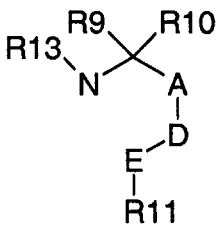
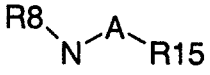
Patent claims

1. A compound of the formula I



I

in which:

R(1) is  ,  ,  or 

A is $-C_nH_{2n}-$;

n = 0, 1, 2, 3, 4 or 5;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m = 0, 1, 2, 3, 4 or 5;

R(8) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or C_pH_{2p}-R(14);

p is 0, 1, 2, 3, 4 or 5;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having

1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms;

R(10) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) is alkyl having 1, 2, 3 or 4 carbon atoms, alkynyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon

atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(13) is C_pH_{2p}-R(14);

p is 0, 1, 2, 3, 4 or 5;

R(15) is cycloalkyl having 3, 4, 5, 6, 7 or 8 carbon atoms;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

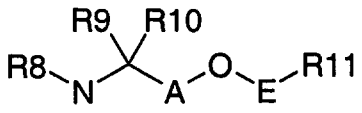
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, Br, I, CF_3, OCF_3, NO_2, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

2. A compound of the formula I as claimed in claim 1, in which:

R(1) is



A is -C_nH_{2n}-;

n is 0, 1, 2 or 3;

E is -C_mH_{2m}-;

m is 0, 1, 2 or 3;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0, 1, 2 or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl, naphthyl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4

carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

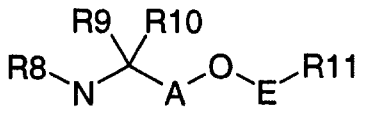
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

3. A compound of the formula I as claimed in claim 1 or 2, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2,

3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

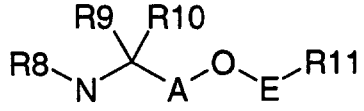
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

4. A compound I as claimed in claims 1 to 3, in which

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN or OH;

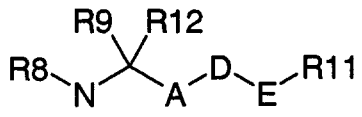
R(6) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

and the pharmaceutically acceptable salts thereof.

5. A compound of the formula I as claimed in claim 1, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0, 1, 2 or 3;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0, 1, 2 or 3;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14)

p is 0, 1, 2, or 3;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group

consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) is alkyl having 1, 2 or 3 carbon atoms, alkynyl having 1, 2 or 3 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

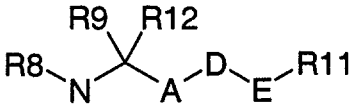
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmacologically acceptable salts thereof.

6. A compound I as claimed in claims 1 and/or 5, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14)

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, methyl or ethyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(12) is alkyl having 1, 2 or 3 carbon atoms, ethynyl, cyclopropyl, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

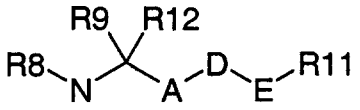
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmacologically acceptable salts thereof.

7. A compound of the formula I as claimed in claims 1, 5 and/or 6, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$;

m is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(9) is hydrogen, ethyl or methyl;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(12) is alkyl having 1, 2 or 3 carbon atoms, ethynyl, cyclopropyl, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN or OH;

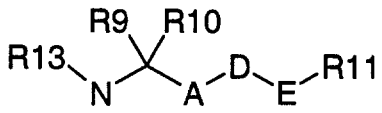
R(6) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(7) is hydrogen, F, Cl, CF_3, methyl, methoxy or OH;

and the pharmacologically acceptable salts thereof.

8. A compound of the formula I as claimed in claim 1, in which:

R(1) is



in which:

A is $-C_nH_{2n}-$

n = 0, 1, 2 or 3;

D is a bond or -O-;

E is $-C_mH_{2m}-$

m is 0, 1, 2 or 3;

R(9) is hydrogen or alkyl having 1, 2, 3 or 4 carbon atoms;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, thienyl, furanyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, thienyl, furanyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(13) is C_pH_{2p}-R(14);

p is 0, 1, 2 or 3;

R(14) is phenyl, naphthyl or heteroaryl,
where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

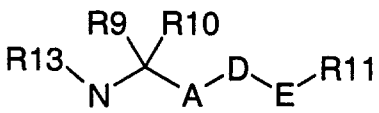
R(3) is heteroaryl,
where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4), R(5), R(6) and R(7)
are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

9. A compound of the formula I as claimed in claims 1 and /or 8, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$

m is 0 or 1;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(13) is C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe,

alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

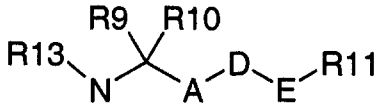
R(4), R(5), R(6) and R(7)

are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

and the pharmaceutically acceptable salts thereof.

10. A compound of the formula I as claimed in claims 1, 8 and/or 9, in which

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

D is a bond or -O-;

E is $-C_mH_{2m}-$

m is 0 or 1;

R(9) is hydrogen, methyl or ethyl;

R(10) is hydrogen, alkyl having 1, 2 or 3 carbon atoms, phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(11) is phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl,

where phenyl, naphthyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, quinolyl, isoquinolyl, phthalazinyl, quinoxalinyl, quinazolinyl or cinnolinyl are unsubstituted or

substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(13) is C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3, CN or OH;

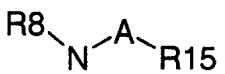
R(6) is hydrogen, F, Cl, CF_3, methyl, methoxy or OH

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

and the pharmaceutically acceptable salts thereof.

11. A compound of the formula I as claimed in claim 1, in which:

R(1) is



A is -C_nH_{2n}-;

n = 0, 1, 2 or 3

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0, 1, 2, or 3;

R(14) is phenyl, naphthyl or heteroaryl,
where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

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

R(3) is heteroaryl,
where heteroaryl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COOMe, $CONH_2$, COMe, NH_2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

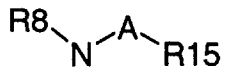
R(4), R(5), R(6) and R(7)
are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

12. A compound of the formula I as claimed in claims 1 and/or 11, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,
where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group

consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen, methyl or ethyl;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4), R(5), R(6) and R(7)

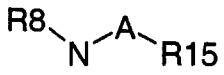
are, independently of one another, hydrogen, F, Cl, CF_3, OCF_3, CN, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, methoxy, ethoxy, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

13. A compound of the formula I as claimed in claims 1, 11 and/or 12, in which:

R(1) is



A is $-C_nH_{2n}-$;

n is 0 or 1;

R(8) is hydrogen, alkyl having 1, 2 or 3 carbon atoms or C_pH_{2p}-R(14);

p is 0 or 1;

R(14) is phenyl, naphthyl or heteroaryl,

where phenyl, naphthyl and heteroaryl are unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl and methylsulfonyl;

R(2) is hydrogen;

R(3) is heteroaryl,

where heteroaryl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF_3, OCF_3, CN, COMe, methyl, methoxy, ethoxy, dimethylamino, sulfamoyl or methylsulfonyl;

R(4) is hydrogen, F, Cl, CF_3, methyl or methoxy;

R(5) is hydrogen, F, Cl, CF_3, methyl, methoxy, COMe, OCF_3; CN or OH;

R(6) is hydrogen, F, Cl, CF_3, methyl, methoxy or OH;

R(7) is hydrogen, F, Cl, CF_3, methyl, ethyl, methoxy or OH;

R(15) is cycloalkyl having 3, 4, 5, 6 or 7 carbon atoms;

and the pharmaceutically acceptable salts thereof.

14. A compound of the formula I as claimed in one or more of claims 1 to 13 and the physiologically tolerated salts thereof for use as pharmaceutical.

15. A pharmaceutical preparation comprising an effective amount of at least one compound of the formula I as claimed in one or more of claims 1 to 13 and/or a physiologically tolerated salt thereof as active ingredient together with pharmaceutically acceptable carriers and additives and, where appropriate, also one or more other pharmacological active ingredients.

16. The use of a compound of the formula I as claimed in one or more of claims 1 to 13 and/or of a physiologically tolerated salt thereof for producing a medicament with a K^+ channel-blocking action for the therapy and prophylaxis of K^+ channel-mediated diseases.

17. The use of a compound of the formula I as claimed in one or more of claims 1 to 13 and/or of a physiologically tolerated salt thereof for producing a medicament for the therapy or prophylaxis of cardiac arrhythmias which can be abolished by prolongation of the action potential.

18. The use of a compound of the formula I as claimed in one or more of claims 1 to 13 and/or of a physiologically tolerated salt thereof for producing a medicament for the

therapy and prophylaxis of reentry arrhythmias.

19. The use of a compound of the formula I as claimed in one or more of claims 1 to 13 and/or of a physiologically tolerated salt thereof for producing a medicament for the therapy and prophylaxis of supraventricular arrhythmias.

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

21. A pharmaceutical preparation comprising an effective amount of at least one compound of the formula I as claimed in one or more of claims 1 to 13 and/or of a physiologically tolerated salt thereof plus a beta-blocker as active ingredients, together with pharmaceutically acceptable carriers and additives.