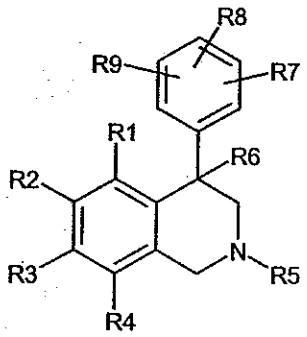
Description

Substituted 4-phenyltetrahydroisoquinolines, process for their preparation, their use as medicament, and medicament containing them

The invention relates to compounds of the formula I



I

in which the meanings are:

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, $C_{qq}H_{2qq-1}$, OC_bH_{2b+1}, COOR10, OCOR10, COR10 or O_x-$(CH_2)_y$-phenyl;

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

qq 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms,

x zero or 1;

y zero, 1, 2, 3 or 4;

where the phenyl ring in the group O_x-$(CH_2)_y$-phenyl is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CN, NO_2, OH, NH_2 or C_dH_{2d+1};

d 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms,

or

R1, R2, R3 and R4

independently of one another heteroaryl, it being possible for zero, 1, 2, 3 or 4 N atoms, zero or 1 oxygen atom or zero or 1 S atom to be present as ring atoms;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3, 4, 5, 6, 7 or 8,

rr 3, 4, 5, 6, 7, or 8,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR13;

R13 H or C_fH_{2f+1};

f 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R13 and a CH_2 group of R11 or R12 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R11 and R12

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R11 and R12

independently of one another COR14, CSR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms, and it being possible for one or more CH_2 groups to be replaced by O or NR13,

or

R1, R2, R3 and R4

independently of one another $-O_h-SO_j-R15$, with

h zero or 1;

j zero, 1 or 2;

R15 C_kH_{2k+1}, OH, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O, CO, CS or NR19;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R19 and a CH_2 group of R17 or R18 together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H,

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$, COR20 or SO_2R20;

p 1, 2, 3, 4, 5, 6, 7 or 8,

ss 3, 4, 5, 6, 7 or 8,

R20 C_qH_{2q+1};

q 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in the groups C_pH_{2p+1}, $C_{ss}H_{2ss-1}$ and C_qH_{2q+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR21;

R21 H or C_rH_{2r+1};

r 1, 2, 3 or 4;

it being possible for one or more H atoms in C_rH_{2r+1} to be replaced by F atoms;

R6 H, F, Cl, Br, I, C_sH_{2s+1}, $C_{dd}H_{2dd-1}$, OH, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

dd 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in C_sH_{2s+1}, $C_{dd}H_{2dd-1}$ and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another $-O_v-SO_w-R23$;

v zero or 1;

w zero, 1 or 2;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, OH, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8,

mm 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, $C_{zz}H_{2zz-1}$;

z 1, 2, 3, 4, 5, 6, 7 or 8;

zz 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms and,
in C_zH_{2z+1}, it being possible for one or more H atoms to be replaced by F atoms and it being possible for one or more CH_2 groups to be replaced by O, CO, CS or NR27;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;
it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_{bb}R30$;

R30 H, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

bb 2 or 3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6, 7 or 8;

h 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 forms together with a CH_2 group of R30 a 5-, 6- or 7-membered ring;

or

R30 a 5- or 6-membered heteroaryl with 1, 2, 3 or 4 N atoms, zero or 1 S atoms and zero or 1 O atoms,

which is unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71;

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ and COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

ww 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR44;

R44 H or $C_{gg}H_{2gg+1}$;

gg 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{gg}H_{2gg+1}$ to be replaced by F atoms, and it being possible for R44 together with a (CH_2) group of R40 or R41 and the N atom to which they are jointly bonded to form a 5- or 6-membered ring,

or

R40 and R41

with the N atom to which they are bonded a 5- or 6-membered ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

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

R1, R2, R3 and R4

independently of one another, H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1}, COOR10;

a and b

independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another 5- or 6-membered heteroaryl selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl and oxazolyl;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms

or

R11 and R12

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R11 and R12

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R_{15}, with

R15 C_kH_{2k+1}, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H, C_mH_{2m+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO and the second CH_2 group is replaced by NR19;

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H,

R5 H, C_pH_{2p+1};

p 1, 2, 3 or 4;

it being possible for one or more H atoms in C_pH_{2p+1} to be replaced by F atoms;

R6 H, C_sH_{2s+1}, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in C_sH_{2s+1} and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4 or 5,

mm 3, 4, 5 or 6,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN, C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5 or 6;

h 1, 2, 3 or 4;

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups

$C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 a 5- or 6-membered heteroaromatic system selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thienyl, thiazolyl and oxazolyl,

which are unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71,

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ or COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42;

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

to be selected independently of one another hydroxyethyl, , N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methyl-piperazine, piperazine and morpholine;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_VSO_WR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

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

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H;

R5 methyl or trifluoromethyl;

R6 H;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or NR32SO_2R30;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, methyl or CF_3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5 or 6;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3 substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

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

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H;

R5 methyl or trifluoromethyl;

R6 H;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, methyl or CF_3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3 substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

Very particular specific preference is given to compounds

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N,N-dimethyl-benzenesulfonamide;
5) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
8) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
10) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
11) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-phenyl]-diethyl-amine

12) 6,8-dichloro-2-methyl-4-(4-piperidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
13) 6,8-dichloro-2-methyl-4-(4-pyrrolidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
14) 6,8-dichloro-2-methyl-4-[4-(4-methyl-piperazin-1-yl)-phenyl]-1,2,3,4-tetrahydro-isoquinoline;
15) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
16) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
17) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propylurea;
18) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;
19) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;
20) N-[4-(6-methanesulfonyl-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
21) N-[4-(2,6,8-trimethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
22) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
23) N-[4-(8-chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
24) N-[4-(8-chloro-2-methyl-6-morpholin-4-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
25) N-{4-[8-chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;
26) N-{4-[8-chloro-6-(cyclopropylmethyl-amino)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;
27) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;
28) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-N-methyl-benzamide;
29) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-ethyl-2-hydroxy-benzamide;

30) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;

31) N-[5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoyl]-guanidine;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

33) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

34) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

36) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]pentanamide;

38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

41) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

43) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

44) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

46) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

48) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

61) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

62) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

63) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

64) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

65) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

66) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

67) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

69) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-cyclobutanecarboxamide;

70) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

71) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

72) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

73) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

74) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

75) N',N'-dimethylamino-N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

78) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

80) N-{5-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

81) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

82) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

83) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

84) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

85) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

87) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

88) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

90) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoroethanesulfonamide;

91) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-ethanesulfonamide;

92) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

93) 2-chloro-5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

94) 2-methyl-4-phenyl-6,8-bis-trifluoromethyl-1,2,3,4-tetrahydro-isoquinoline;

95) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

96) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

97) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

98) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

99) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

100) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

101) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

102) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

103) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

104) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

105) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

106) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

107) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

108) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

109) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

110) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

111) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

112) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

113) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

114) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

115) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

116) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

117) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

118) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

119) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

120) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

121) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

122) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

123) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

124) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

125) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

126) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

127) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

128) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

129) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

130) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

131) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

132) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

133) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

134) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

135) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

136) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

137) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

138) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

139) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

140) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

141) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

142) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

143) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

144) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

145) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

146) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

147) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

148) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

149) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

150) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

151) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

152) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

153) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

154) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

155) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

156) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

157) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

158) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

159) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

160) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

161) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

162) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

163) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

164) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

165) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

166) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

167) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

168) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

169) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

170) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

171) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

172) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

173) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

174) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

175) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

176) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

177) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

178) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

179) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

180) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

181) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

182) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

183) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

184) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

185) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

186) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

187) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

188) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

189) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

190) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

191) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

192) ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

193) isopropyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

194) 2,2-dimethyl-propyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

195) methyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

196) isopropyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

197) 2,2-dimethyl-propyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

198) ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

199) (R)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

200) (S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

201) (R)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

202) (S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

203) N-[3-(6,8-difluoro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

204) 4-(3-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline;

205) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

206) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;

207) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.

and the pharmaceutically acceptable salts thereof.

Exceptionally particular preference is given to compounds from the group of

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;
5) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;
6) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
7) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
8) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
9) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;
10) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;
11) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;
12) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;
13) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
14) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;
15) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;
16) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

17) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

18) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

19) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

20) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

21) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

22) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;

23) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

24) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

25) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

26) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

27) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

28) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

29) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

30) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

31) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

32) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

33) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

34) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

36) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-carboxamide;

41) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

42) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

43) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

44) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

45) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

46) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

47) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

48) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-carboxamide;

51) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

56) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

57) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

58) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

59) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

60) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

61) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

62) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

63) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

64) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-diethylamino-propyl)-urea;

65) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

66) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl)-urea;

67) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

69) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

70) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

71) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

72) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

73) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

74) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

75) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

76) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

77) N-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

78) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

79) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

80) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

81) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

82) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

83) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

84) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

85) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

86) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

87) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

88) (R or S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

89) (R or S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

90) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

and the pharmaceutically acceptable salts thereof.

The invention further encompasses the use of the compounds of the formula I for producing a medicament for the treatment of disorders which can be influenced by inhibition of the sodium-proton exchanger of subtype III (NHE3), in which the meanings are:

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, $C_{qq}H_{2qq-1}$, OC_bH_{2b+1}, COOR10, OCOR10, COR10 or O_x-$(CH_2)_y$-phenyl;

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

qq 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms,

x zero or 1;

y zero, 1, 2, 3 or 4;

where the phenyl ring in the group O_x-$(CH_2)_y$-phenyl is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CN, NO_2, OH, NH_2 or C_dH_{2d+1};

d 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms,

or

R1, R2, R3 and R4

independently of one another heteroaryl, it being possible for zero, 1, 2, 3 or 4 N atoms, zero or 1 oxygen atom or zero or 1 S atom to be present as ring atoms;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3, 4, 5, 6, 7 or 8,

rr 3, 4, 5, 6, 7, or 8,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR13;

R13 H or C_fH_{2f+1};

f 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R13 and a CH_2 group of R11 or R12 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R11 and R12

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R11 and R12

independently of one another COR14, CSR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms, and it being possible for one or more CH_2 groups to be replaced by O or NR13,

or

R1, R2, R3 and R4

independently of one another $-O_h-SO_j-R15$, with

h zero or 1;

j zero, 1 or 2;

R15 C_kH_{2k+1}, OH, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O, CO, CS or NR19;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R19 and a CH_2 group of R17 or R18 together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$, COR20 or SO_2R20;

p 1, 2, 3, 4, 5, 6, 7 or 8,

ss 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms

R20 C_qH_{2q+1};

q 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_qH_{2q+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR21;

R21 H or C_rH_{2r+1};

r 1, 2, 3 or 4;

it being possible for one or more H atoms in C_rH_{2r+1} to be replaced by F atoms;

R6 H, F, Cl, Br, I, C_sH_{2s+1}, $C_{dd}H_{2dd-1}$, OH, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

dd 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in C_sH_{2s+1}, $C_{dd}H_{2dd-1}$ and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another $-O_v-SO_w-R23$;

v zero or 1;

w zero, 1 or 2;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, OH, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8,

mm 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, $C_{zz}H_{2zz-1}$;

z 1, 2, 3, 4, 5, 6, 7 or 8;

zz 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms and,

in C_zH_{2z+1}, it being possible for one or more H atoms to be replaced by F atoms and it being possible for one or more CH_2 groups to be replaced by O, CO, CS or NR27;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_{bb}R30$;

R30 H, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

bb 2 or 3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6, 7 or 8;

h 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more (CH_2) groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 forms together with a CH_2 group of R30 a 5-, 6- or 7-membered ring;

or

R30 a 5- or 6-membered heteroaryl with 1, 2, 3 or 4 N atoms, zero or 1 S atoms and zero or 1 O atoms,

which is unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71;

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ and COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

ww 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR44;

R44 H or $C_{gg}H_{2gg+1}$;

gg 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{gg}H_{2gg+1}$ to be replaced by F atoms,

or

R40 and R41

with the N atom to which they are bonded a 5- or 6-membered ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

and the pharmaceutically acceptable salts thereof.

Preference is given to the use of compounds of the formula I, in which the meanings are:

R1, R2, R3 and R4

independently of one another, H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1}, COOR10;

a and b

independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another 5- or 6-membered heteroaryl selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl and oxazolyl;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms

or

R11 and R12

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R11 and R12

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R_{15}, or

R15 C_kH_{2k+1}, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H, C_mH_{2m+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO and the second CH_2 group is replaced by NR19;

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$;

p 1, 2, 3 or 4;

ss 3, 4, 5 or 6, it being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms;

R6 H, C_sH_{2s+1}, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in C_sH_{2s+1} and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4 or 5,

mm 3, 4, 5 or 6,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN, C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5 or 6;

h 1, 2, 3 or 4;

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more (CH_2) groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 together with a CH_2 group or R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 a 5- or 6-membered heteroaromatic system selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thienyl, thiazolyl and oxazolyl,

which are unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71,

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ or COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv independently of one another 1, 2, 3 or 4;
it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42;

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

to be selected independently of one another hydroxyethyl, , N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methyl-piperazine, piperazine and morpholine;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

and the pharmaceutically acceptable salts thereof.

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

R1, R2, R3 and R3

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$;

p 1, 2, 3 or 4;

ss 3, 4, 5 or 6, it being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms;

R6 H, CH_3;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, CH_3 or CF_3;

cc 1, 2, 3, 4, 5 , 6, 7 or 8;

yy 3, 4, 5 or 6;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more (CH_2) groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3 substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

and the pharmaceutically acceptable salts thereof.

Very particular preference is given to the use of compounds selected from the group consisting of

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N,N-dimethyl-benzenesulfonamide;
5) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
8) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
10) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
11) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-phenyl]-diethyl-amine
12) 6,8-dichloro-2-methyl-4-(4-piperidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
13) 6,8-dichloro-2-methyl-4-(4-pyrrolidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;

14) 6,8-dichloro-2-methyl-4-[4-(4-methyl-piperazin-1-yl)-phenyl]-1,2,3,4-tetrahydro-isoquinoline;

15) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;

16) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

17) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propylurea;

18) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

19) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

20) N-[4-(6-methanesulfonyl-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

21) N-[4-(2,6,8-trimethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

22) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

23) N-[4-(8-chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

24) N-[4-(8-chloro-2-methyl-6-morpholin-4-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

25) N-{4-[8-chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

26) N-{4-[8-chloro-6-(cyclopropylmethyl-amino)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

27) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;

28) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-N-methyl-benzamide;

29) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-ethyl-2-hydroxy-benzamide;

30) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;

31) N-[5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoyl]-guanidine;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

33) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

34) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

36) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]pentanamide;

38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

41) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

43) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

44) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

46) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

48) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

61) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

62) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

63) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

64) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

65) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

66) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

67) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

69) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-cyclobutanecarboxamide;

70) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

71) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

72) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

73) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

74) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

75) N',N'-dimethylamino-N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

78) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

80) N-{5-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

81) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

82) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

83) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

84) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

85) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

87) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

88) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

90) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoroethanesulfonamide;

91) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-ethanesulfonamide;

92) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

93) 2-chloro-5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

94) 2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;

95) 6,8-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

96) 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;

97) 8-methoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

98) 2-(8-amino-2-ethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;
99) 2-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;
100) 5-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-methoxy-phenol;
101) 2-methyl-8-nitro-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
102) 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-1,2-diol;
103) 2,8-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
104) 4-(3,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
105) 4-(3,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
106) 4-(2,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
107) 4-(3-chloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
108) 2,4-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
109) 2-butyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
110) N-(2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-yl)-acetamide;
111) 7-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
112) 8-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
113) 2,6-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
114) 6-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
115) 6-methoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
116) 2-ethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
117) 2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
118) 6,8-dichloro-2-ethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
119) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
120) 2-methyl-4-phenyl-6,8-bis-trifluoromethyl-1,2,3,4-tetrahydro-isoquinoline;
121) 6,8-dichloro-2-isopropyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
122) 5,8-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
123) 6,8-dichloro-4-(4-fluoro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
124) 6,8-dichloro-2-methyl-4-p-tolyl-1,2,3,4-tetrahydro-isoquinoline;
125) 5,6-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
126) 6,7-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
127) 8-bromo-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
128) 6,8-dichloro-4-(4-chloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
129) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

130) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

131) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

132) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

133) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

134) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

135) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

136) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

137) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

138) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

139) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

140) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

141) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

142) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

143) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

144) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

145) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

146) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

147) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

148) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

149) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

150) N[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

151) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

152) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

153) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

154) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

155) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

156) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

157) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

158) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

159) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

160) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

161) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

162) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

163) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

164) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

165) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

166) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

167) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

168) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

169) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

170) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

171) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

172) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

173) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

174) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

175) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

176) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

177) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

178) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

179) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

180) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

181) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

182) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

183) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

184) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

185) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

186) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

187) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

188) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

189) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

190) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

191) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

192) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

193) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

194) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

195) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

196) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

197) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

198) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

199) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

200) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

201) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

202) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

203) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

204) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

205) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

206) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

207) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

208) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

209) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl morpholine-4-carboxamide;

210) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

211) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

212) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

213) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

214) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

215) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

216) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

217) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

218) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

219) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

220) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

221) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

222) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

223) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

224) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

225) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

226) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

227) ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

228) isopropyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

229) 2,2-dimethyl-propyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

230) methyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

231) isopropyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

232) 2,2-dimethyl-propyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

233) ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

234) (R)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

235) (S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

236) (R)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

237) (S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

238) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

239) 4-(3-bromo-phenyl)-6,8-dichloro-methyl-1,2,3,4-tetrahydro-isoquinoline;

240) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

241) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;

242) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.

and the pharmaceutically acceptable salts thereof.

Exceptionally particular preference is given to the use of compounds selected from the group consisting of

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
5) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
8) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
10) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;
11) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;
12) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
13) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;
14) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;
15) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
16) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
17) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
18) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

19) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

20) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

21) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;

22) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

23) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

24) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

25) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

26) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

27) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

28) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

29) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

30) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

31) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;

33) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

34) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

35) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

36) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

37) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

38) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

39) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

40) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

41) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

43) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

44) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

46) 2,6-diamino N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

48) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

49) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

50) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyazole-4-carboxamide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

53) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

54) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

55) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

61) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

62) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

63) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

64) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

65) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

66) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

67) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

68) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

69) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

70) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

71) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

72) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

73) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

74) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

75) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

78) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

80) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

81) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

82) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

83) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

84) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

85) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

87) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

88) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

90) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

91) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

92) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

93) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

94) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

95) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

96) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

97) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

98) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

99) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

100) (R or S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

101) (R or S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

102) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

103) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;

104) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.

and the pharmaceutically acceptable salts thereof.

If the compounds of the formula I contain one or more centers of asymmetry, these may have both the S and the R configuration. The compounds may be in the form of optical isomers, of diastereomers, of racemates or of mixtures thereof.

The invention also relates to the use of the compounds of formula I for producing a medicament for the treatment or prophylaxis of disorders of respiratory drive; respiratory disorders, in particular sleep-related respiratory disorders such as sleep apneas; snoring; acute and chronic renal disorders, particularly of acute renal failure and of chronic renal failure; disorders of intestinal function; disorders of biliary function; ischemic states of the peripheral and central nervous system and of stroke; ischemic states of peripheral organs and limbs; or states of shock.

The invention further relates to the use of the compound of formula I for producing a medicament for use in surgical operations and organ transplants.

The invention also relates to the use of the compound of formula I for producing a medicament for the treatment of disorders in which cell proliferation represents a primary or secondary cause.

The invention relates to the use of the compound of formula I for producing a medicament for the treatment for prophylaxis of disorders of lipid metabolism.

The invention further relates to the use of the compound of formula I for producing a medicament for the treatment or prophylaxis of intestation by ectoparasites.

The invention relates to a medicine comprising an effective amount of the compound of formula I.

The defined alkyl radicals and partly or completely fluorinated alkyl radicals may be both straight-chain and branched. Groups C_aH_{2a-1} and their analogs as far as $C_{yy}H_{2yy-1}$ mean either the corresponding alkenyls, cycloalkyls, cycloalkylalkyls or alkylcycloalkyls.

Appropriate heteroaryls are, in particular, 2- or 3-thienyl, 2- or 3-furyl, 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1-, 3-, 4- or 5-pyrazolyl, 1,2,3-triazol-1-, -4- or 5-yl, 1,2,4-triazol-1-, -3- or -5-yl, 1- or 5-tetrazolyl, 2-, 4- or 5-oxazolyl, 3-, 4- or 5-isoxazolyl, 1,2,3-oxadiazol-4- or 5-yl, 1,2,4-oxadiazol-3-or 5-yl, 1,3,4-oxadiazol-2-yl or -5-yl, 2-, 4- or 5-thiazolyl, 3-, 4- or 5-isothiazolyl, 1,3,4-thiadiazol-2- or -5-yl, 1,2,4-thiadiazol-3- or -5-yl, 1,2,3-thiadiazol-4- or 5-yl, 2-, 3- or 4-pyridyl, 2-, 4-, 5- or 6-pyrimidinyl, 3- or 4-pyridazinyl, pyrazinyl, 1-, 2-, 3-, 4-, 5-, 6- or 7-indolyl, 1-, 2-, 4- or 5-benzimidazolyl, 1-, 3-, 4-, 5-, 6- or 7-indazolyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolyl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 3-, 4-, 5-, 6-, 7- or 8-cinnolinyl, 2-, 3-, 5-, 6-, 7- or 8-quinoxalinyl, 1-, 4-, 5-, 6-, 7- or 8-phthalazinyl. The corresponding

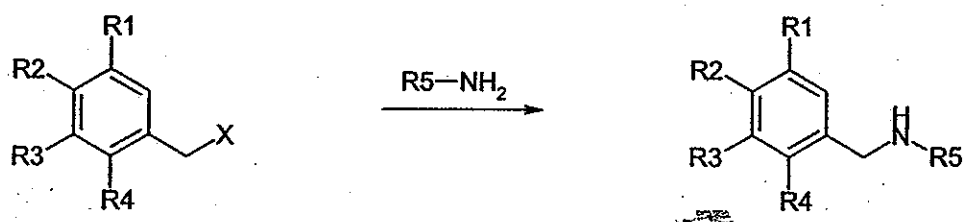
N-oxides of these compounds are additionally encompassed, that is to say, for example, 1-oxy-2-, 3- or 4-pyridyl.

Of these, the 5- or 6-membered heterocycles are preferred. The particularly preferred heterocycles are imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl and oxazolyl.

The terminal CH_3 groups in an alkyl chain are also regarded as CH_2 units and are in this connection viewed as CH_2 groups.

Methods for preparing the compounds used are also described.

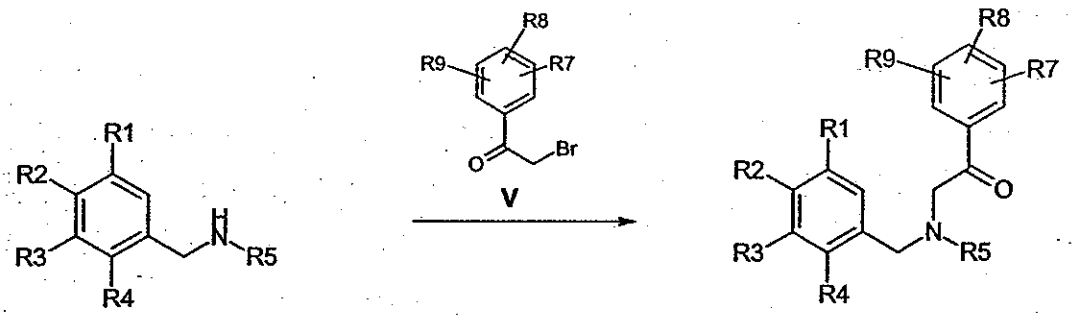
Thus, the substances described herein can be prepared starting from the benzylamine precursors IV. These in turn can, if not obtainable commercially, be synthesized by standard processes from the corresponding benzyl chlorides or bromides III.



X = Cl, Br

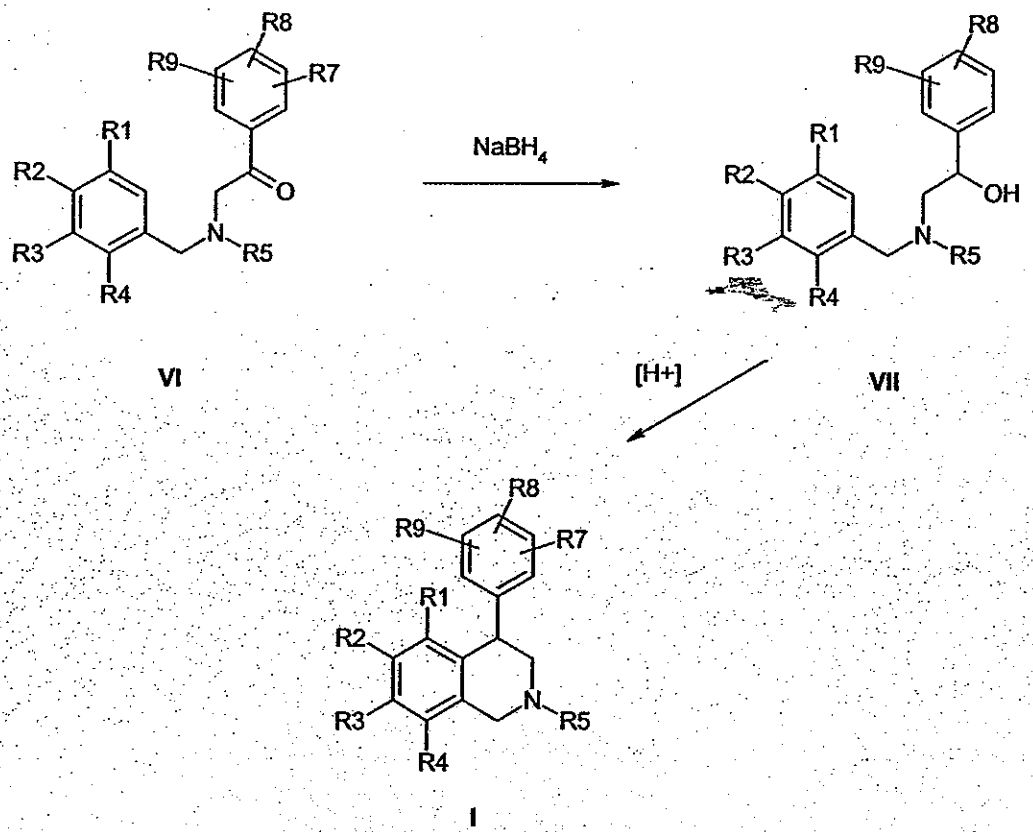
III IV

The benzylamines IV obtained in this way are alkylated in a manner known to the skilled worker with the appropriately substituted alpha-bromoacetophenone compounds V.



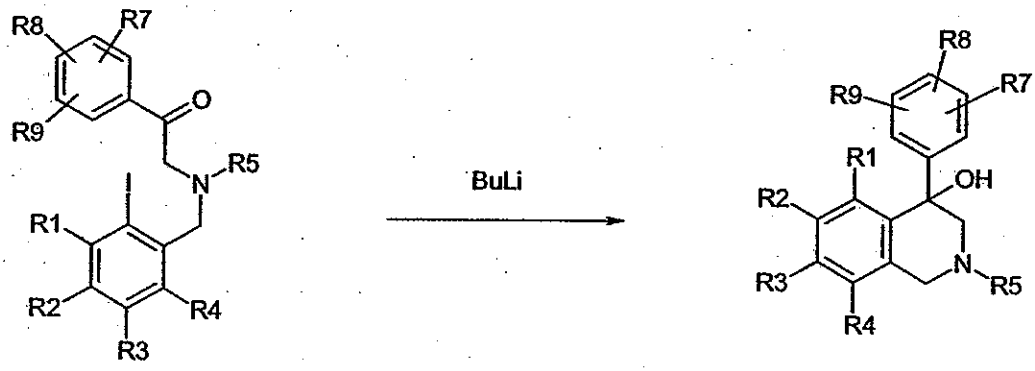
IV VI

The alpha-bromacetophenone compounds V can be obtained from the corresponding acetophenone precursors by bromination in processes known from the literature. The desired tetrahydroisoquinolines I can be obtained by known processes by reduction of the carbonyl group in VI and subsequent acid-catalyzed cyclization of the corresponding alcohols VII (cf. Tetrahedron Lett.; 1989, 30, 5837; Org. Prep. Proced. Int.; 1995, 27, 513).



VI VII I

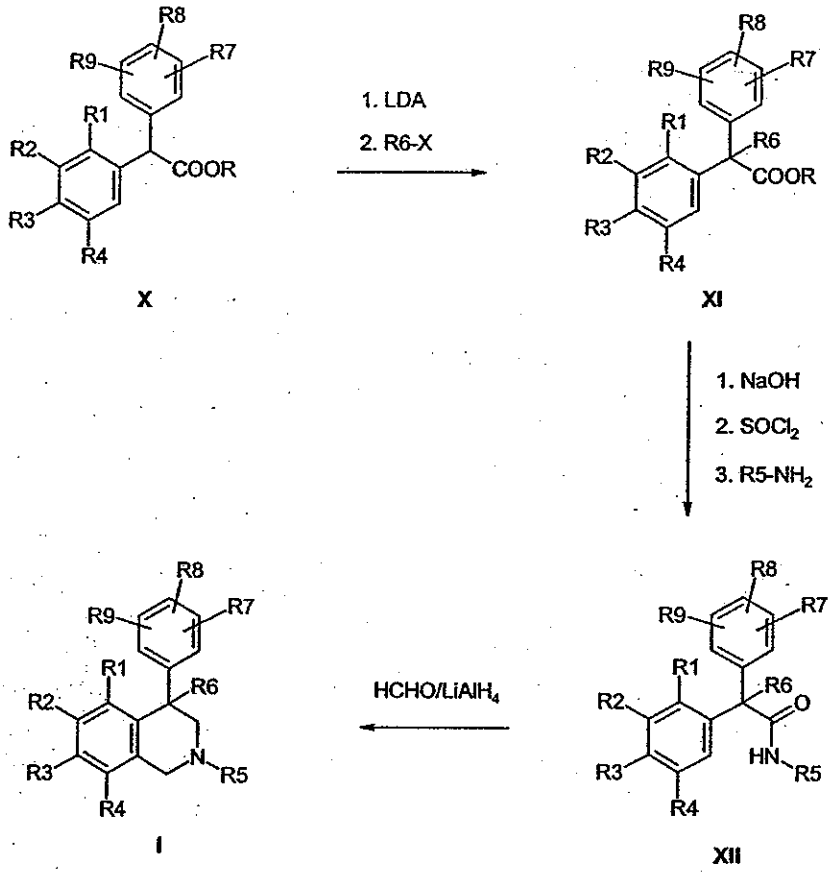
When R6 is not equal to H, the desired compounds of the formula I can be prepared for example from the iodides VIII by halogen/metal exchange and subsequent nucleophilic attack of the intermediate organolithium species on the carbonyl group (cf. Chem. Pharm. Bull.; 1995, 43, 1543).



VIII IX

The tertiary alcohols synthesized in this way can be converted by known methods into other derivatives.

Alkyl-branched analogs (I) are prepared by alkylating the corresponding diphenylacetic esters X in the alpha position by known methods. The desired product XI can be converted by standard processes into the corresponding amides XII, which are converted into the desired tetrahydroisoquinolines I in a Pictet-Spengler-analogous reaction (cf. Tetrahedron; 1987, 43, 439; Chem. Pharm. Bull.; 1985, 33, 340).



Compounds of the type I are described in the published specifications WO 01 32 624 and WO 01 32 625 as norepinephrine, dopamine and serotonin reuptake inhibitors. However, these patent applications protect exclusively compounds in which R1 and R2 may be exclusively H. It has emerged, however, with the compounds according to the invention that at least for R2 it is necessary that R2 is not equal to H. In addition, it was not possible to detect by means of an exemplary compound of the compounds according to the invention any inhibitory properties on the described receptors, so that the described compounds differ distinctly both in structure and in their pharmacological properties from the compounds described in the patent applications mentioned.

In addition, compounds of type I are described in the patent specification EP 11 13 007 as estrogen agonists and antagonists. It was possible to show that the compounds according to the invention show no activity on said receptors, so that the structural differences of the compounds according to the invention result in distinctly different pharmacological properties in this regard too.

It was possible to show that compounds of the formula I are excellent inhibitors of the sodium-hydrogen exchanger (NHE) – especially of the sodium-hydrogen exchanger of subtype 3 (NHE3).

On the basis of these properties, the compounds are suitable for the treatment of disorders caused by oxygen deficiency. The compounds are, as a result of their pharmacological properties, outstandingly suitable as antiarrhythmic medicaments with a cardioprotective component for prophylaxis of infarction and for treatment of infarction, and for the treatment of angina pectoris, in which connection they also inhibit or greatly reduce in a preventive manner the pathophysiological processes associated with the development of ischemia-induced damage, in particular in the induction of ischemia-induced cardiac arrhythmias. Because of their protective effects against pathological hypoxic and ischemic situations, the compounds of the formula I which are used according to the invention can, as a result of inhibition of the cellular Na^+/H^+ exchange mechanism, be used as medicaments for the treatment of all acute or chronic damage induced by ischemia or disorders induced primarily or secondarily thereby. This relates to the use thereof as medicaments for surgical interventions, e.g. in organ transplantations, in which cases the compounds can be used both to protect the organs in the donor before and during removal, to protect removed organs for example on treatment with or storage thereof in physiological bath fluids, as well as during the transfer into the recipient organism. The compounds are likewise valuable medicaments with a protective action during the performance of angioplastic surgical interventions, for example on the heart as well as peripheral vessels. In accordance with their protective action against ischemia-induced damage, the compounds are also suitable as medicaments for the treatment of ischemias of the nervous system, especially of the CNS, in which connection they are suitable for example for the treatment of stroke or of cerebral edema. In addition, the compounds of the formula I which are used according to the invention are likewise suitable for the treatment of types of shock, such as, for example, of allergic, cardiogenic, hypovolemic and bacterial shock.

In addition, the compounds induce an improvement in the respiratory drive and are therefore used to treat respiratory conditions associated with the following clinical conditions and diseases: disturbance of central respiratory drive (e.g. central sleep apnea, sudden infant death, postoperative hypoxia), muscle-related breathing disorders, breathing disorders after long-term ventilation, breathing disorders associated with altitude adaptation, obstructive and mixed type of sleep apnea, acute and chronic pulmonary disorders with hypoxia and hypercapnia.
The compounds additionally increase the tone of the muscles of the upper airways, so that snoring is suppressed.

A combination of an NHE inhibitor with a carbonic anhydrase inhibitor (e.g. acetazolamide), the latter inducing metabolic acidosis and thus itself increasing respiratory activity, proves to be advantageous due to an enhanced effect and reduced use of active ingredient.

It has emerged that the compounds used according to the invention have a mild laxative effect and accordingly can be used advantageously as laxatives or if there is a risk of constipation, in which case the prevention of the ischemic damage associated with constipation in the intestinal region is particularly advantageous.

It is additionally possible to prevent the formation of gall stones.

The compounds of the formula I used according to the invention are furthermore distinguished by a strong inhibitory effect on the proliferation of cells, for example of fibroblast cell proliferation and the proliferation of smooth muscular muscle cells. The compounds of the formula I are therefore suitable as valuable therapeutic agents for diseases in which cell proliferation represents a primary or secondary cause, and can therefore be used as antiatherosclerotic agents, agents to prevent late complications of diabetes, cancers, fibrotic disorders such as pulmonary fibrosis, hepatic fibrosis or renal fibrosis, organ hypertrophies and hyperplasias, in particular for prostate hyperplasia or prostate hypertrophy.

The compounds used according to the invention are effective inhibitors of the cellular sodium-proton antiporter (Na/H exchanger) which is elevated in numerous disorders (essential hypertension, atherosclerosis, diabetes, etc.), also in those cells which are readily amenable to measurements, such as, for example, in erythrocytes, platelets or leukocytes. The compounds used according to the invention are therefore suitable as excellent and simple scientific tools, for example in their use as diagnostic agents for determining and distinguishing different types of hypertension, but also of atherosclerosis, of diabetes, proliferative disorders etc. The compounds of the formula I are moreover suitable for preventive therapy to prevent the development of high blood pressure, for example of essential hypertension.

It has additionally been found that NHE inhibitors show a beneficial effect on serum lipoproteins. It is generally acknowledged that blood lipid levels which are too high, so-called hyperlipoproteinemias, represent a considerable risk factor for the development of arteriosclerotic vascular lesions, especially coronary heart disease. The reduction of elevated serum lipoproteins therefore has exceptional importance for the prophylaxis and regression of atherosclerotic lesions. The compounds used according to the invention can therefore be used for the prophylaxis and regression of atherosclerotic lesions by eliminating a causal risk factor. With this protection of the vessels against the syndrome of endothelial dysfunction, compounds of the formula I are valuable medicaments for the prevention and treatment of coronary vasospasms, of atherogenesis and of atherosclerosis, of left-ventricular hypertrophy and of dilated cardiomyopathy, and thrombotic disorders.

Said compounds are therefore advantageously used for producing a medicament for the prevention and treatment of sleep apneas and muscle-related respiratory disorders; for producing a medicament for the prevention and treatment of snoring; for producing a medicament for lowering blood pressure; for producing a medicament for the prevention and treatment of disorders induced by ischemia and reperfusion of central and peripheral organs, such as acute renal failure, stroke, endogenous states of shock, intestinal disorders etc.; for producing a medicament for the treatment of late damage from diabetes and chronic renal disorders, in particular of all inflammations of

the kidneys (nephritides) which are associated with increased protein/albumin excretion; for producing a medicament for the treatment of infection by ectoparasites in human and veterinary medicine; for producing a medicament for the treatment of said disorders in combinations with hypotensive substances, preferably with angiotensin converting enzyme (ACE) inhibitors, with diuretics and saluretics such as furosemide, hydrochlorothiazide, pseudoaldosterone antagonists and aldosterone antagonists; with adenosine receptor modulators, in particular with adenosine receptor activators (A2 agonists); and with angiotensin receptor antagonists.

The administration of sodium-proton exchange inhibitors of the formula I as novel medicaments for lowering elevated blood lipid levels, and the combination of sodium-proton exchange inhibitors with hypotensive medicaments and/or medicaments with hypolipidemic activity is claimed.

Medicaments which comprise a compound I can in this connection be administered orally, parenterally, intravenously, rectally, transdermally or by inhalation, the preferred administration being dependent on the particular characteristics of the disorder. The compounds I may moreover be used alone or together with pharmaceutical excipients, both in veterinary medicine and in human medicine.

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, flavorings, preservatives, solubilizers or colors.

For a form for oral administration, the active compounds are mixed with additives suitable for this purpose, such as carriers, stabilizers or inert diluents, and converted by conventional methods into suitable dosage 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. It is moreover possible

for the preparation to take place both as dry granules and as wet granules. Examples of suitable oily carriers or solvents are vegetable or animal oils such as sunflower oil or fish liver oil.

For subcutaneous or intravenous administration, the active compounds used are converted, if desired with the substances customary for this purpose, such as solubilizers, emulsifiers or other excipients, into a solution, suspension or emulsion. 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 a mixture 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 ingredient of the formula I in a pharmaceutically acceptable solvent such as, in particular, ethanol or water, or a mixture of such solvents.

The formulation may, 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, % by weight.

The dosage of the active ingredient of the formula I to be administered, and the frequency of administration, depend on the potency and duration of action of the compounds used; additionally also on the nature and severity of the disorder to be treated and on the sex, age, weight and individual responsiveness of the mammal to be treated.

On average, the daily dose of a compound of the formula I for a patient weighing about 75 kg is at least 0.001 mg/kg, preferably 0.01 mg/kg, to a maximum of 10 mg/kg, preferably 1 mg/kg, of body weight. For acute episodes of the disorder, for example immediately after suffering a myocardial infarction, higher and, in particular, more frequent dosages may also be necessary, e.g. up to 4 single doses a day. Up to

200 mg a day may be necessary, in particular on i.v. administration, for example for a patient with infarction in the intensive care unit.

Descriptions of experiments and examples:

List of abbreviations used:

R_t	retention time
TFA	trifluoroacetic acid
HPLC	high performance liquid chromatography
eq	equivalent
LCMS	liquid chromatography mass spectroscopy
MS	mass spectroscopy
CI	chemical ionization
RT	room temperature
THF	tetrahydrofuran
TOTU	O-[(ethoxycarbonyl)-cyanomethyleneamino]-N,N,N',N'-tetramethyluronium tetrafluoroborate
DMSO	dimethyl sulfoxide
abs.	absolute
decomp.	decomposition
DMF	dimethylformamide

General:

The retention times (R_t) indicated below relate to LCMS measurements with the following parameters:

Method A:

stationary phase:	Merck Purospher 3μ2 x 55 mm
mobile phase:	95% H_2O (0.05% TFA)→ 95% acetonitrile; 4 min; 95% acetonitrile; 1.5 min → 5% acetonitrile; 1 min; 0.5 ml/min, 30°C.

Method B:

stationary phase:	Merck Purospher 3μ2 x 55 mm

mobile Phase: 0 min 90% H_2O (0.05% TFA) 2.5 min-95% acetonitrile; 95% acetonitrile to 3.3 min; 10% acetonitrile 3.4 min; 1 ml/min.

Method B1:

stationary phase: YMC, J'sphere ODS H80 4μ 2 x 20 mm

mobile phase 0 min 90% H_2O (0.05% TFA) 1.9 min-95% acetonitrile; 95% acetonitrile to 2.4 min; 10% acetonitrile 2.45 min; 1 ml/min.

Method C:

stationary phase: Merck LiChroCart 55-2 Purospher STAR RP 18e

solvent: solvent A: acetonitrile/water 90:10 + 0.5% HCOOH

solvent B: acetonitrile/water 10:90 + 0.5% HCOOH

flow rate: 0.75 ml/min

time[min]	solvent B[%]
0.00	95.0
0.50	95.0
1.75	5.0
4.25	5.0
4.50	95.0
5.00	95.0

stop time: 6.20 min

temperature: 40°C

Method D:

stationary phase: Merck RP18 Purospher STAR, 55 x 2 mm, 3 μ particle size.

solvent: solvent A: acetonitrile + 0.08% HCOOH

solvent B: water + 0.1% HCOOH

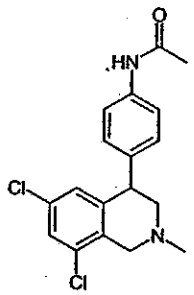
flow rate: 0.45 ml/min

time[min]	solvent B[%]
0	95

5	5
7	5
8	95
9	5

temperature: room temperature

Example 1: N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide



Intermediate 1: 2,4-Dichlorobenzyl-(methyl)-amine
is prepared by methods known from the literature (J. Med. Chem.; 1984, 27, 1111).

Intermediate 2: N-[4-(2-Bromo-acetyl)-phenyl]-acetamide
is synthesized in a manner known to the skilled worker by bromination of N-(4-acetyl-phenyl)-acetamide.
The starting compound (0.256 mol) is introduced into 300 ml of acetic acid and, at 60°C, a solution of 39.9 g of bromine (1.0 eq) in 60 ml of acetic acid is added dropwise. After 1.5 h, the reaction mixture is allowed to cool to room temperature and is added to 1 l of ice-water. The precipitate is filtered off with suction, washed with water and dried, with 60 g of the title compound being isolated (melting point: 192°C).

Intermediate 3: N-{4-[2-(2,4-Dichloro-benzylamino)-acetyl]-phenyl}-acetamide;
37.1 g (0.195 mol) of intermediate 1 are introduced into 400 ml of dioxane, and a solution of 60 g (0.234 mol) of intermediate 2 in 600 ml of dioxane is added. 134 ml of triethylamine are added, and the mixture is stirred at room temperature for 4 h. After standing overnight, the precipitate is filtered off and the filtrate is concentrated in

vacuo. The residue is taken up in ethyl acetate, washed with $NaHCO_3$ and H_2O, dried with $MgSO_4$ and concentrated. The oily residue resulting thereby is triturated with an ethyl acetate/ether mixture, resulting in 36 g of intermediate 3 in the form of a crystalline solid (melting point: 115-117°C).

Intermediate 4:

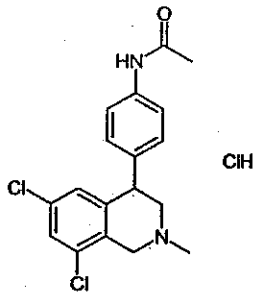
N-{4-[2-(2,4-Dichloro-benzylamino)-1-hydroxy-ethyl]-phenyl}-acetamide;

36 g (0.099 mol) of intermediate 3 are dissolved in 500 ml of methanol and, at 0°C, 7.8 g (2 eq) of sodium borohydride are added. The mixture is then stirred at 0°C for 30 min and at room temperature for a further hour. For workup, the reaction mixture is concentrated and the residue is partitioned between 1 N HCl and ethyl acetate. The aqueous phase is separated off, adjusted to pH 9 and extracted twice with ethyl acetate. The combined organic phases are dried with $MgSO_4$ and concentrated. The crude product obtained in this way can be reacted further without further purification.

N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

20 g (0.054 mol) of intermediate 4 are dissolved in 250 ml of dichloromethane and, at 0°C, 250 ml of conc. H_2SO_4 are added dropwise. The mixture is stirred at 0°C for 2 h and at room temperature for 1 h. For workup, the reaction mixture is added to ice-water, and the precipitate is filtered off with suction. The precipitate is taken up in 300 ml of 1 N NaOH and extracted three times with ethyl acetate. Drying of the organic phases and concentration affords a crude product which is triturated with diisopropyl ether, whereupon 11.7 g of the compound of the example are isolated as a crystalline solid (melting point: 205-206°C).

1a: N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide-hydrochloride;



An analytical sample (100 mg) of the title compound from example 1 is suspended in 10 ml of 2 N HCl, and THF is added until a clear solution is produced. It is concentrated in vacuo, and the residue is triturated with ether and filtered off with suction, whereupon the title compound is obtained as a crystalline solid (R_t = 3.807 min (method A); melting point.: 125°C with decomposition).

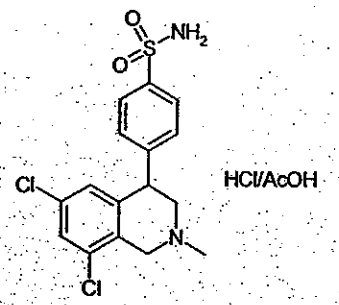
Example 2:

2a: (+)-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide hydrochloride;

2b: (+)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide hydrochloride;

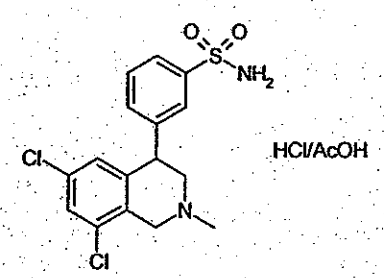
2c: (-)-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide acetate;

2d: (-)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide acetate;



(+ and -)

2a/2c



(+ and -)

2b/2d

Intermediate 1: 2,4-Dichlorobenzyl-(methyl)-amine is prepared by methods known from the literature (J. Med. Chem.; 1984, 27, 1111).

Intermediate 2: 2-[(2,4-Dichloro-benzyl)-methyl-amino]-1-phenyl-ethanone;
Intermediate 1 is reacted with 2-bromo-1-phenyl-ethanone in the manner described in example 1, intermediate 3. Workup in an analogous manner and purification on silica gel affords the desired alkylation product in good yield as a yellowish oil (R_t = 4.188 min (method A); MS(Cl^+) = 308.2/310.2).

Intermediate 3: 2-[(2,4-Dichloro-benzyl)-methyl-amino]-1-phenyl-ethanol;
Intermediate 2 is reduced with sodium borohydride in the manner described in example 1, intermediate 4. Once monitoring of the reaction indicates complete conversion, the mixture is concentrated and the residue is taken up in ethyl acetate. It is washed twice with H_2O, dried with $MgSO_4$ and freed of solvent. The crude product, which is obtained in quantitative yield, can be reacted further without further purification (R_t = 4.149 min (method A); MS(Cl^+) = 310.2/312.2).

Intermediate 4: 6,8-Dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
20 g (64.5 mmol) of intermediate 3 are dissolved in 55 ml of dichloromethane and cooled to 0°C. This solution is added dropwise to 55 ml of precooled conc. H_2SO_4 and then stirred at room temperature for two hours. For workup, the mixture is poured onto ice and made strongly alkaline with 6 N NaOH. Three extractions with dichloromethane are carried out. The combined organic phases are dried with $MgSO_4$ and concentrated. The oily crude product is purified on silica gel, resulting in intermediate 4 in a yield of 53% (R_t = 4.444 min (method A); MS(Cl^+) = 292.2/294.2).

4a: (-)-6,8-Dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline trifluoroacetate;
4b: (+)-6,8-Dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline trifluoroacetate;
Intermediate 4 is separated into the two enantiomers by HPLC on a chiral phase.
chiral column: Chiralpak OD 250 x 4.6 cm;
solvent: n-heptane/isopropanol 7:3 + 0.1% TFA;
flow rate: 1 ml/min;
R_t((-)-enantiomer/4a) = 9.340 min;
R_t((+)-enantiomer/4b) = 20.327 min.

2a: (+)-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide hydrochloride;

2b: (+)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide hydrochloride;

A suspension of 500 mg (1.7 mmol) of intermediate 4a in 10 ml of dichloromethane is introduced at 0°C into 1.2 ml of chlorosulfonic acid. The mixture is stirred at 0°C for one hour and at room temperature for a further hour. A further 5 ml of chlorosulfonic acid is added and the mixture is stirred at room temperature for one hour. For workup, it is poured onto ice and adjusted to pH 8 with $NaHCO_3$. Three extractions with ethyl acetate are carried out. The combined organic phases are dried with Na_2SO_4 and freed of solvent. The crude product obtained in this way is heated in 20 ml of conc. NH_3 solution at 90°C for three hours. After the conversion is complete, the reaction solution is concentrated and the residue is partitioned between H_2O and ethyl acetate. The organic phase is separated off and the aqueous phase is extracted once more with ethyl acetate. The combined organic phases are dried with Na_2SO_4 and the solvent is removed in vacuo. Subsequent chromatography on silica gel affords 335 mg of a mixture of example 2a and 2b in the form of a yellow amorphous solid. Further purification on a preparative HPLC affords 212 mg of the para-substituted title compound 2a, plus 58 mg of the meta isomer 2b.

Conditions for the preparative HPLC.

chiral column: Chiralpak AS 250 x 4.6 mm;

solvents: n-heptane/ethanol/methanol/acetonitrile 20:1.5:0.5:0.5

flow rate: 1 ml/min;

R_t(main fraction) = 14.145 min (→2a);

R_t(subsidiary fraction) = 11.623 min (→2b).

Both fractions were dissolved in methanol/2 N HCl mixture and freeze dried, and it was possible to obtain the title compounds 2a and 2b in the form of crystalline solids.

(R_t(2a) = 3.630 min (method A); MS(2a),(ES^+) =371.3/373.3 (M^++H)/ 412.3/ 414.3 (M^++CH_3CN); R_t (2b) = 3.668 min (method A); MS(2b),(ES^+) =371.3/373.3 (M^++H)/ 412.3/ 414.3 (M^++CH_3CN).

2c: (-)-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide acetate;

2d: (-)-3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide acetate;

The title compound is synthesized by the method described under 2a/2b, using intermediate 4b as starting compound. The purification and separation from the meta isomer which is to be expected takes place under the following conditions:

chiral column: Chiralpak AS 250 x 4.6/12 mm;

solvent: acetonitrile

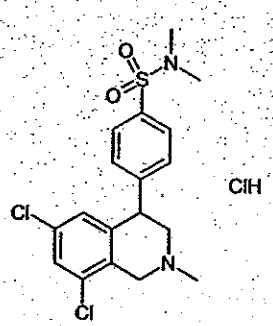
flow rate: 1 ml/min;

R_t(main fraction)= 4.394 min (→2c);

R_t(subsidiary fraction) = 4.130 min (→2d).

The purified products are each taken up in a 10% acetic acid solution and freeze dried, resulting in the desired acetates as slightly yellowish solids (R_t(2c) = 3.656 min (method A); MS(ES^+) =371.1/373.1 (M^++H)/ 412.1/414.1 (M^++CH_3CN)); (R_t(2d) = 1.562 min (method B); MS(ES^+) =371.1/373.1 (M^++H)/ 412.1/414.1 (M^++CH_3CN)).

Example 3: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N,N-dimethyl-benzenesulfonamide, hydrochloride;



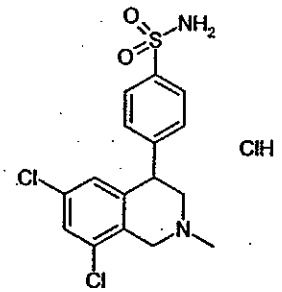
6,8-Dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline (intermediate 4, example 2) was introduced in portions into chlorosulfonic acid (6.6 ml). The mixture was subsequently stirred at 40°C for one hour. The reaction mixture was then cooled to room temperature and an ice/water mixture was added. The precipitate which separated out during this was filtered off with suction and taken up in ethyl acetate which, after washing with saturated brine was dried over magnesium sulfate. Subsequent concentration afforded 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonyl chloride as a solid crude product, a portion of which (150 mg) was directly introduced in portions into dimethylamine solution (5 ml, approx. 40% in water) cooled to 10°C. The resulting suspension was subsequently stirred at this temperature for 1.5 h. Then ice-water was added and, after extraction three times with ethyl acetate, the combined ethyl acetate phases were washed with saturated brine and dried over magnesium sulfate. The residue was taken up with water and, after addition of 2 N HCl, freeze dried. The crude product obtained in this way was then purified by preparative HPLC.

Conditions:
stationary phase: Merck Purospher RP18 (10μM) 250 x 25 mm
mobile phase: 90% H_2O (0.05% TFA)→ 90% acetonitrile; 40 min; flow rate: 25 ml/min

The fractions containing the product were combined, the acetonitrile was stripped off in a rotary evaporator, and the aqueous phase was washed with saturated potassium carbonate solution and then extracted three times with ethyl acetate. The combined ethyl acetate phases were washed with saturated brine, dried over magnesium sulfate and concentrated. The residue was taken up in water and, after addition of 2 N HCl, freeze dried. 80 mg of a pale solid were obtained. This consisted of ~80% of the desired compound, in addition to ~20% of a regioisomer (R_t = 4.000 min (method A); MS(Cl^+) = 399.1).

Example 4:

4a: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide, hydrochloride;



Intermediate 1: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-benzenesulfonyl chloride

At 0°C, 1 mmol of 6,8-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline (intermediate 4, example 2) is introduced into 1 ml of chlorosulfonic acid and stirred at room temperature for 3 hours. For workup, the reaction mixture is poured onto ice, adjusted to pH 7 to 8 with 1 N NaOH and extracted twice with ethyl acetate. The combined ethyl acetate phases are dried with Na_2SO_4 and concentrated in a rotary evaporator. The crude product obtained in this way is reacted further without further purification.

Intermediate 2: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-sulfonamide

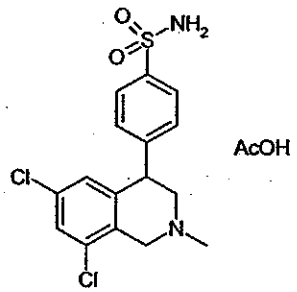
319 mg of intermediate 1 are suspended in 6 ml of 25% strength ammonia and heated to 90°C. After 3 h, the mixture is diluted with H_2O and extracted with ethyl acetate. The organic phase is separated off and dried with Na_2SO_4, resulting in 165 mg of the title compound.

4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide, hydrochloride;

145 mg of intermediate 2 are suspended in 15 ml of diethyl ether, and 1 ml of ethereal HCl is added. After stirring at room temperature for 30 minutes, the precipitate is

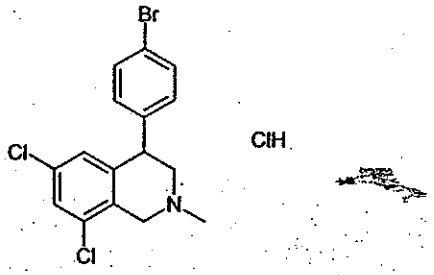
filtered off with suction and dried, resulting in 136 mg of the hydrochloride in the form of a yellowish solid.

4b: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide, acetate;



255 mg of intermediate 2, example 8, are mixed with 5 ml of glacial acetic acid, and 50 ml of H_2O is added. Filtration of sparingly soluble constituents is followed by freeze drying, resulting in 250 mg of the title compound.

Example 5: 4-(4-Bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline, hydrochloride;



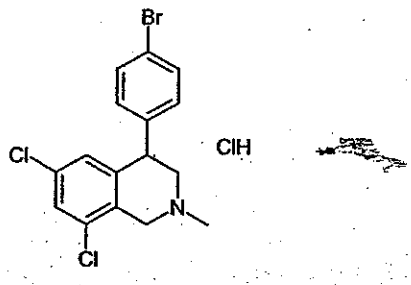
Intermediate 1:

1-(4-Bromo-phenyl)-2-[(2,4-dichloro-benzyl)-methyl-amino]-ethanone; (2,4-Dichloro-benzyl)-methyl-amine (see example 1, intermediate 1) and 2-bromo-1-(4-bromo-phenyl)-ethanone are reacted in analogy to the method described in example 1, intermediate 3. After analogous workup and chromatography on silica gel, the alkylation product can be isolated in a yield of 69%.

Intermediate 2: 1-(4-Bromo-phenyl)-2-[(2,4-dichloro-benzyl)-methyl-amino]-ethanol;
Intermediate 1 is reduced to the corresponding alcohol with 2 equivalents of $NaBH_4$ in analogy to the manner described for intermediate 4, example 1, and the alcohol can be isolated in a yield of 86%.

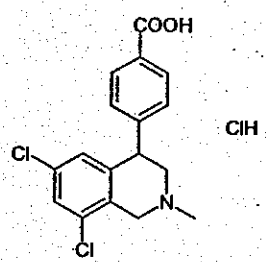
Intermediate 3: 4-(4-Bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
5.45 g (14.0 mmol) of 1-(4-bromo-phenyl)-2-[(2,4-dichloro-benzyl)-methyl-amino]-ethanol are introduced into 15 ml of dichloromethane and, at 0°C, 15 ml of conc. H_2SO_4 are added. After stirring at room temperature for 2 hours, the reaction mixture is poured onto ice and made alkaline with 6 N NaOH. Three extractions with dichloromethane are carried out. The combined organic phases are dried with $MgSO_4$ and concentrated. For further purification, the residue is chromatographed on silica gel, resulting in 2.6 g of the title compound as a yellowish oil.

4-(4-Bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline, hydrochloride;



300 mg of 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline are stirred in 2 N HCl at room temperature. The resulting precipitate is filtered off with suction and dried.

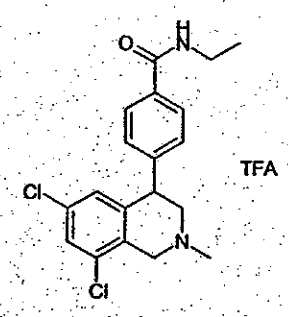
Example 6: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;



4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;

5.57 g (15 mmol) of 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline (example 5, intermediate 3) are dissolved in 150 ml of abs. DMF/benzene (1:1). After the solution has been degassed, under argon 1.18 g (4.5 mmol) of triphenylphosphine and 1.17 g (9 mmol) of $Ca(HCO_2)_2$ are added. After renewed flushing with argon, 867 mg (0.75 mmol) of $Pd(PPh_3)_4$ are added and carbon monoxide is passed into the solution. The mixture is stirred at 120°C. After six hours at 120°C and standing overnight under argon, a further 867 mg (0.75 mmol) of $Pd(PPh_3)_4$ were added and stirring at 120°C and passing carbon monoxide into the solution were continued for eight hours. After again standing overnight, 135 mg of $PdCl_2$ were added and reaction was allowed to take place under the same conditions. For workup, the solvent is removed in vacuo and the residue is taken up in ethyl acetate. Three extractions with 2 N NaOH are carried out. The combined aqueous phases are adjusted to pH 6 with 6 N HCl and extracted three times with ethyl acetate. The organic phases are dried with $MgSO_4$ and freed of solvent. The residue is purified on silica gel using a dichloromethane/methanol mixture, resulting in 420 mg of the title compound (R_t = 4.025 min (method A); MS(Cl^+) = 336.1/338.1).

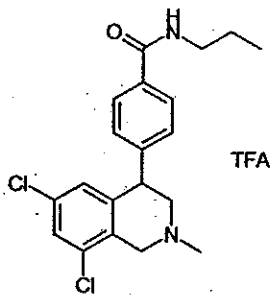
Example 7: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide, trifluoroacetate;



146 mg (0.43 mmol) of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid (see example 6) are dissolved in 5 ml of DMF, and 1.0 equivalent of triethylamine is added. At 0°C, a solution of 141 mg (0.43 mmol) TOTU in 3 ml of DMF is added. The mixture is stirred at 0°C for 30 min and at room temperature for 30 min. This solution is then added at 0°C to a solution of 0.28 ml of 2 M ethylamine solution and 0.06 ml (0.043 mmol) of triethylamine in 5 ml of DMF, and the reaction mixture is

stirred at room temperature for three hours. For workup, the solvent is distilled off in vacuo, and the residue is taken up in ethyl acetate and washed twice with 1 N KOH and once with H_2O. The organic phase is dried with Na_2SO_4 and concentrated. Chromatography on silica gel (dichloromethane/methanol 95:5) is used for further purification. Further purification on a preparative HPLC (acetonitrile/H_2O/trifluoroacetic acid) affords the desired carboxamide as trifluoroacetate (R_t = 4.169 min (method A); MS(Cl^+) = 363.3/365.3).

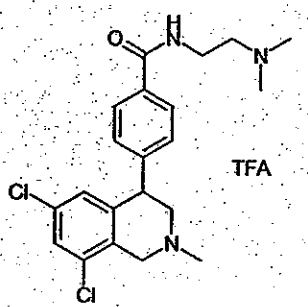
Example 8: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide, trifluoroacetate;



The title compound can be prepared by the method described in example 7 starting from n-propylamine and 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid (see example 6).

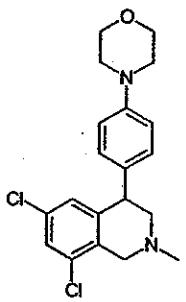
(R_t = 1.881 min (method B); MS(Cl^+) = 377.3/379.3).

Example 9: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide, trifluoroacetate;



was prepared in analogy to example 7 starting from example 6 and N1,N1-dimethylethane-1,2-diamine by a TOTU-mediated coupling reaction (R_t = 1.449 min (method B); MS(Cl^+) = 406.3/408.3).

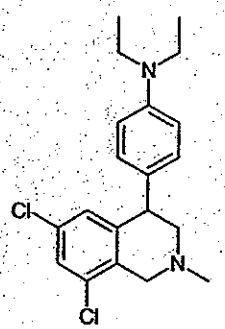
Example 10: 6,8-Dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline, trifluoroacetate;



TFA

456 mg (1.4 mmol) of Cs_2CO_3, 6.75 mg (0.03 mmol) of palladium acetate and 28 mg (0.045 mmol) of 2,2-bis-(diphenylphosphino)-1,1-binaphthyl are introduced into 5 ml of abs. toluene. Under argon, a solution of 0.104 ml (1.2 mmol) of morpholine in 2.5 ml of abs. DMF, and a solution of 371 mg (1.0 mmol) of 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline in 2.5 ml of abs. toluene are added, and the mixture is stirred at 100°C for a total of 9 hours. For workup, the solvent is removed, the residue is taken up in dichloromethane, and insoluble constituents are filtered off. After concentration of the filtrate, the residue is chromatographed on silica gel (CH_2Cl_2 /methanol 95:5), resulting in 350 mg of the desired morpholine derivative. After a further purification on a preparative HPLC it is possible to isolate 160 mg of the corresponding trifluoroacetate in the form of a colorless solid.

Example 11: [4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-phenyl]-diethyl-amine, trifluoroacetate;

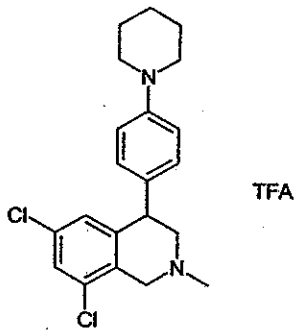


TFA

The procedure is analogous to the method described in example 10 starting from diethylamine and 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline (example 5, intermediate 3). Reaction time: 2 days at 100°C; three times

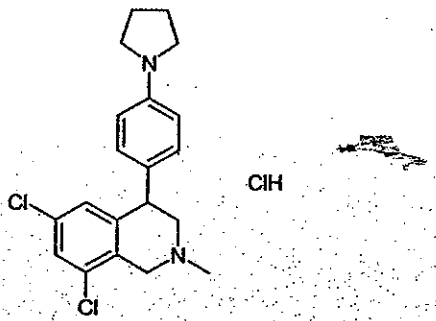
the amount of Pd catalyst and phosphine ligand. The desired trifluoroacetate can be isolated as a colorless solid after preparative HPLC.

Example 12: 6,8-Dichloro-2-methyl-4-(4-piperidin-1-yl-phenyl)-1,2,3,4-tetrahydro-isoquinoline, trifluoroacetate;



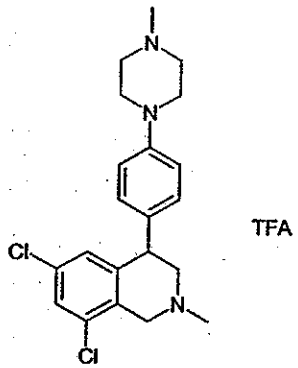
The desired piperidine derivative can be obtained starting from piperidine and 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline (example 5, intermediate 3) in analogy to the method described in example 10.

Example 13: 6,8-Dichloro-2-methyl-4-(4-pyrrolidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline, hydrochloride;



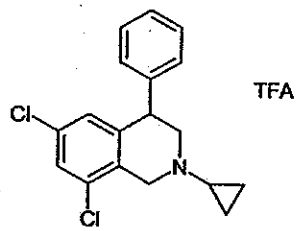
The reaction is carried out in analogy to the method described in example 10, starting from pyrrolidine and 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline (example 5, intermediate 3). The product obtained after purification by chromatography is taken up in the DMSO/acetonitrile mixture, whereupon a precipitate separates out. This is filtered off, dissolved in 2 N HCl and freeze dried, resulting in the title compound of a colorless solid.

Example 14: 6,8-Dichloro-2-methyl-4-[4-(4-methyl-piperazin-1-yl)-phenyl]-1,2,3,4-tetrahydro-isoquinoline, trifluoroacetate;



Reaction of N-methyl-piperazine and 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline (example 5, intermediate 3) by the method described in example 10 affords the title compound in the form of a colorless solid.

Example 15: 6,8-Dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline, trifluoroacetate;



Intermediate 1:

Cyclopropyl-(2,4-dichloro-benzyl)-amine;

5.25 g (30 mmol) of 2,4-dichlorobenzaldehyde are introduced into 140 ml of methanol and, at room temperature, a solution of 1.71 g (30 mmol) of cyclopropylamine is added. The mixture is stirred at room temperature for 40 min and then 1.42 g (37.5 mmol) of $NaBH_4$ are added in portions. After standing overnight, the solvent is removed and the residue is taken up in 2 N HCl. Two extractions with ethyl acetate are carried out. The aqueous phase is made alkaline with NaOH and again extracted twice with ethyl acetate. The organic phases are dried with $MgSO_4$ and concentrated. The crude product obtained in this way, in the form of a slightly yellowish oil, can be reacted further without further purification.

Intermediate 2: 2-[Cyclopropyl-(2,4-dichloro-benzyl)-amino]-1-phenyl-ethanone;

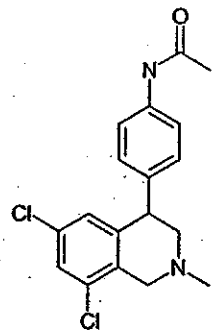
Intermediate 1 is reacted with alpha-bromoacetophenone in the presence of triethylamine in dioxane by the method described in example 1, intermediate 3. For workup, the solvent is distilled off, and the residue is taken up in ethyl acetate. It is washed twice with H_2O and twice with 2 N HCl, dried with $MgSO_4$ and concentrated. The crude product obtained in this way can be reacted further without further purification.

Intermediate 3: 2-[Cyclopropyl-(2,4-dichloro-benzyl)-amino]-1-phenyl-ethanol; Intermediate 2 is reduced with $NaBH_4$ in analogy to the method described in example 1, intermediate 4. For workup, the mixture is concentrated, and the residue is partitioned between 1 N HCl and ethyl acetate. The aqueous phase is separated off and extracted once more with ethyl acetate. The combined organic phases are dried with $MgSO_4$ and the solvent is removed in vacuo.

6,8-Dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline, trifluoroacetate; Intermediate 3 (1.9 g) is dissolved without further purification in 10 ml of dichloromethane and cyclized with conc. H_2SO_4 by the method described in example 1. For workup, the reaction mixture is poured onto ice. The organic phase is separated off, and the aqueous phase is extracted once more with dichloromethane. The combined organic phases are dried with $MgSO_4$ and freed of solvent. Chromatography on silica gel (n-heptane/ethyl acetate 5:1 → 3:1) affords 200 mg of a yellowish oil, which is subjected to further purification on a preparative HPLC. This results in 184 mg of the title compound as trifluoroacetate.

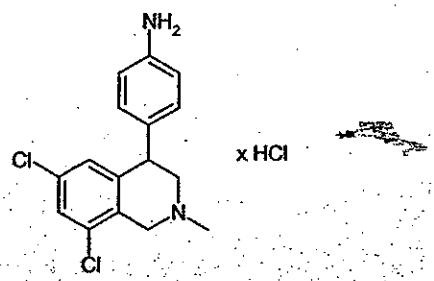
Example 16: 16a: (-)-N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
16b: (+)-N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

(+ and -)



500 mg of the title compound from example 1 are separated on a chiral phase, resulting in about 250 mg of the two enantiomeric acetamides 16a and 16b.
chiral column: Chiralpak OD 250 x 4.6 mm;
solvent: acetonitrile;
flow rate: 1 ml/min;
R_t((-)-enantiomer/16a) = 5.856 min;
R_t((+)-enantiomer/16b) = 8.613 min.

Example 17: 4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine, hydrochloride;



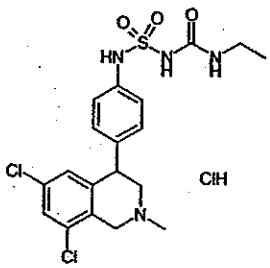
Intermediate 1:
4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
3.0 g (8.6 mmol) of N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 1) are dissolved in 100 ml of 20% strength sodium ethanolate solution and heated under reflux for four hours. A further 2.0 g (29.4 mmol) of solid sodium ethanolate are added, and the mixture is heated under reflux for three more hours. For workup, the solvent is removed in vacuo, and the residue is taken up in 200 ml of H_2O and extracted twice with dichloromethane. The combined organic phases are dried with $MgSO_4$ and concentrated. Further purification by

chromatography on silica gel (ethyl acetate/heptane 1:1) results in the aniline as a yellowish oil in quantitative yield.

4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine, hydrochloride;

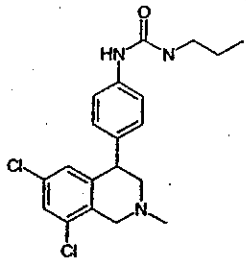
200 mg (0.65 mmol) of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine are dissolved in 30 ml of ethanolic HCl. The clear solution is concentrated in vacuo. The residue is triturated in ether, filtered off with suction and dried, whereupon it was possible to isolate 208 mg of the desired hydrochloride.

Example 18: N-Ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea, hydrochloride



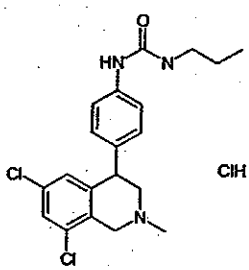
1.0 mmol of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide (example 4, intermediate 2) is mixed with 350 mg (2.5 eq) of K_2CO_3 in 15 ml of dry acetone and stirred at room temperature for 1.5 hours. A solution of 2.5 eq of ethyl isocyanate in acetone is added dropwise at room temperature, and the solution is heated to reflux. For workup, the mixture is concentrated in vacuo, and the residue is taken up in H_2O and extracted twice with ethyl acetate. The aqueous phase is acidified with 6 N HCl, and the resulting precipitate is filtered off with suction. Washing with ethyl acetate and drying in vacuo affords the title compound in good yield.

Example 19: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propylurea;



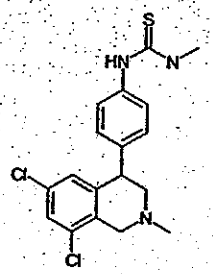
A solution of 0.17 g (2.0 mmol) of n-propyl isocyanate in toluene is added dropwise to a stirred solution of 500 mg (1.63 mmol) of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (see example 17) in 15 ml of toluene. After one hour at 40°C, a further 0.17 g of n-propyl isocyanate is added, and the mixture is stirred at 80°C for one hour. For workup, the solvent is removed and the residue is triturated with H_2O and ether. Drying affords 503 mg of the desired n-propylurea.

19a: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propyl-urea, hydrochloride;



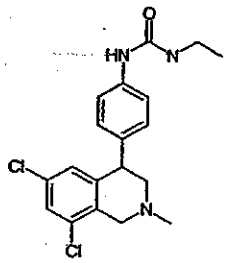
450 mg of 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propyl-urea are dissolved in a mixture of 2 N HCl and THF. The clear solution is concentrated in vacuo, and the residue is triturated with ether and filtered off with suction. Drying affords 473 mg of the desired hydrochloride.

Example 20: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl- thiourea;



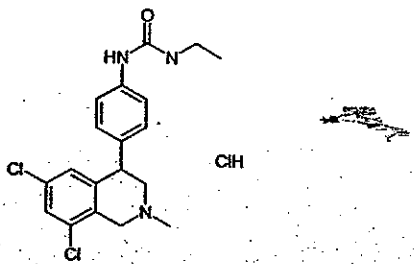
Proceeding in analogy to the method described in example 19 and starting from 500 mg (1.63 mmol) of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (see example 17) and 220 mg (3.0 mmol) of methyl isothiocyanate allows 245 mg of the desired thiourea to be isolated.

Example 21: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethylurea;



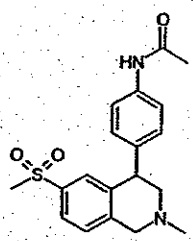
Preparation takes place in analogy to a method described in example 19, starting from 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (500 mg; 1.63 mmol) and ethyl isocyanate (284 mg/4 mmol).

21a: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea, hydrochloride;



Conversion into the corresponding hydrochloride takes place in analogy to the method described in example 19a.

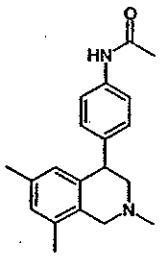
Example 22: N-[4-(6-Methanesulfonyl-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;



Intermediate 1: (4-Methanesulfonyl-benzyl)-methyl-amine
is synthesized starting from 1-bromomethyl-4-methanesulfonylbenzene and methylamine in a manner known to the skilled worker.

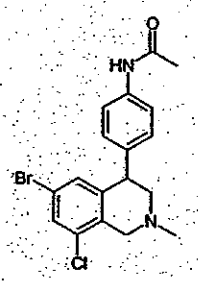
The title compound is prepared in analogy to the synthetic route indicated in example 1, starting from (4-methanesulfonyl-benzyl)-methyl-amine (intermediate 1) and N-[4-(2-bromo-acetyl)-phenyl]-acetamide (example 1, intermediate 2).

Example 23: N-[4-(2,6,8-Trimethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;



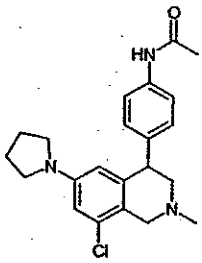
The synthetic route detailed in example 1 is followed, starting from (2,4-dimethyl-benzyl)-methyl-amine, which can be prepared from 1-bromomethyl-2,4-dimethyl-benzene and methylamine in a manner known to the skilled worker, and N-[4-(2-bromo-acetyl)-phenyl]-acetamide (example 1, intermediate 2).

Example 24: N-[4-(6-Bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;



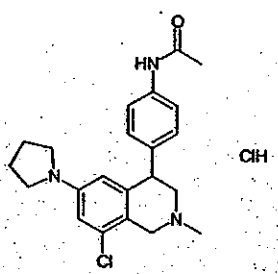
The synthetic route detailed in example 1 is followed, starting from (4-bromo-2-chloro-benzyl)-methyl-amine, which can be prepared from 4-bromo-1-bromomethyl-2-chloro-benzene and methylamine in a manner known to the skilled worker, and N-[4-(2-bromo-acetyl)-phenyl]-acetamide (example 1, intermediate 2).

Example 25: N-[4-(8-Chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;



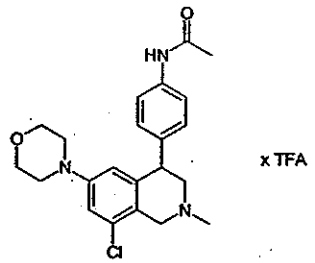
1.02 g (3.12 mmol) of Cs_2CO_3, 8.8 mg (0.04 mmol) of palladium acetate and 36.1 mg (0.06 mmol) of 2,2-bis-diphenylphosphino-1,1-binaphthyl are introduced into 6.5 ml of abs. toluene under argon. At room temperature, a solution of 512 mg (1.3 mmol) of N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 24) in 4 ml of abs. DMF, and a solution of 111 mg (1.56 mmol) of pyrrolidine in 4 ml of DMF are added, and the mixture is heated at 100°C for 7 hours. For workup, the solvent is removed in vacuo, and the residue is taken up in dichloromethane. Insoluble constituents are filtered off, and the filtrate is concentrated. The residue is chromatographed on silica gel with a dichloromethane/methanol mixture, and it is possible to isolate 360 mg of the compound of the example.

25a: N-[4-(8-Chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide, hydrochloride;



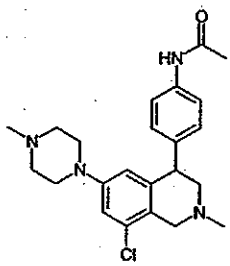
320 mg of N-[4-(8-chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide are dissolved in 20 ml of ethanolic HCl, stirred at room temperature for 30 min and concentrated. The residue is taken up in H_2O and freeze dried.

Example 26: N-[4-(8-Chloro-2-methyl-6-morpholin-4-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide, trifluoroacetate;



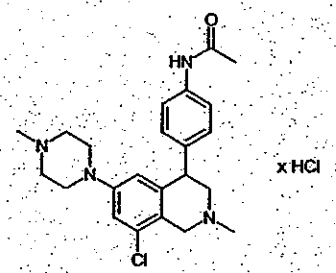
Preparation takes place in analogy to the method described in example 25, starting from N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 24) and morpholine. The chromatography on silica gel was followed by a further purification on a preparative HPLC.

Example 27: N-{4-[8-Chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;



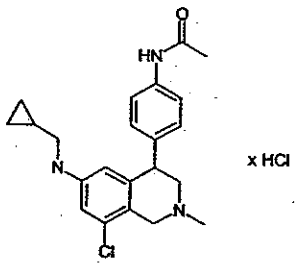
Preparation takes place in analogy to the method described in example 25, starting from N-[4-(6-Bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 24) and N-methyl-piperazine.

27a: N-{4-[8-Chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide, hydrochloride;



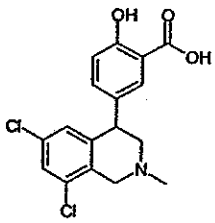
220 mg of N-{4-[8-Chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide are dissolved in a little methanol, diluted with 2 N HCl and freeze dried, resulting in 226 mg of the desired hydrochloride.

Example 28: N-{4-[8-Chloro-6-(cyclopropylmethyl-amino)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide, hydrochloride;



Preparation takes place in analogy to the method described in example 25, starting from N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 24) and C-cyclopropyl-methylamine. The chromatography on silica gel was followed by a further purification on a preparative HPLC. The purified compound was dissolved in 1 N HCl, diluted with H_2O and freeze dried.

Example 29: 5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;



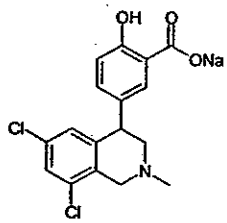
Intermediate 1: Ethyl 5-acetyl-2-hydroxy-benzoate
is prepared from 5-acetyl-2-hydroxy-benzoic acid by acid-catalyzed esterification in a manner known to the skilled worker.

Intermediate 2: Ethyl 5-(2-bromo-acetyl)-2-hydroxy-benzoate
is prepared from ethyl 5-acetyl-2-hydroxy-benzoate by a known method in analogy to the process described in example 1, intermediate 2.

Intermediate 3: Ethyl 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoate
The title compound is synthesized by the synthetic route described in example 1, starting from ethyl 5-(2-bromo-acetyl)-2-hydroxy-benzoate and 2,4-dichlorobenzyl-(methyl)-amine (see example 1, intermediate 1).

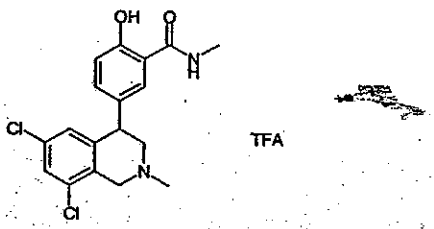
5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid; 6.8 g (18 mmol) of ethyl 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoate are hydrolyzed in an ethanol/2 N KOH mixture in a manner known to the skilled worker, resulting in 5.4 g of the free acid.

29a: 5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid, sodium salt;



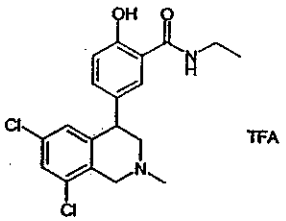
352 mg (1 mmol) of the free acid 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid are dissolved in 10 ml of 0.1 M NaOH, diluted with H_2O and freeze dried, resulting in 375 mg of the title compound.

Example 30: 5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-N-methyl-benzamide, trifluoroacetate;



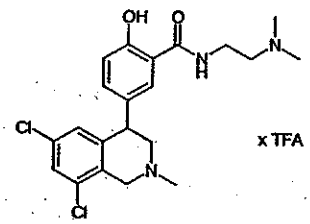
The title compound can be prepared starting from 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid in a TOTU-mediated reaction with methylamine in analogy to the method described in example 7.

Example 31: 5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-ethyl-2-hydroxy-benzamide, trifluoroacetate;



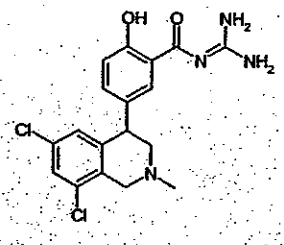
The title compound can be prepared starting from 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid in a TOTU-mediated reaction with ethylamine in analogy to the method described in example 7.

Example 32: 5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)- 2-hydroxy-benzamide, trifluoroacetate;



The title compound can be prepared starting from 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid in a TOTU-mediated reaction with N1,N1-dimethyl-ethane-1,2-diamine in analogy to the method described in example 7.

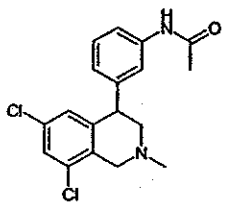
Example 33: N-[5-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoyl]-guanidine;



2.52 g of potassium tert-butoxide are added to a solution of 2.39 g (25 mmol) of guanidine hydrochloride in 15 ml of abs. DMF and stirred at room temperature for 45 min. A solution of 950 mg (2.5 mmol) of ethyl 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoate (example 29, intermediate 3) in 10 ml of abs. DMF is added, and the mixture is stirred at room temperature for four hours. After no further increase in conversion is detectable, the precipitate is removed by filtration with suction and the solvent is removed in vacuo. The residue is taken up in

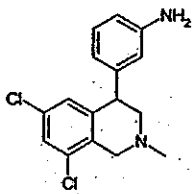
2 N HCl and extracted twice with dichloromethane. The aqueous phase is adjusted to a pH of about 10 with KOH, whereupon the desired acylguanidine separates out as a colorless precipitate. Filtration with suction and drying affords 793 mg of the title compound.

Example 34: N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;



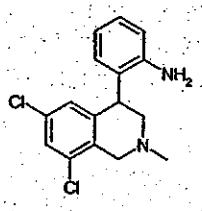
N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide; The desired meta-acetanilide is prepared in analogy to the synthetic route indicated for example 1, starting from N-(3-acetyl-phenyl)-acetamide and 2,4-dichlorobenzyl-(methyl)-amine (example 1, intermediate 1) in four analogous stages.

Example 35: 3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;



Acetyl is eliminated from N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide (example 34) by the method described in example 17, intermediate 1, in the presence of sodium ethanolate.

Example 36: 2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;



Intermediate 1: N-[2-(2-Bromo-acetyl)-phenyl]-acetamide;

31 g (0.175 mol) of N-(2-Acetylphenyl)-acetamide (prepared by acylation of 2-aminoacetophenone with acetyl chloride as described by Fuerstner, Alois; Jumbam, Denis N.; Tetrahedron; 48; 29; 5991-6010, (1992)) are dissolved in 200 ml of glacial acetic acid. 127 ml of 33% strength HBr in glacial acetic acid are added and then, at room temperature, 8.75 ml (0.175 mol) of bromine are slowly run in. The mixture is stirred at room temperature overnight. The mixture is stirred into 1.5 l of ice-water, and the precipitated product is filtered off with suction, thoroughly washed with ice-water and dried in vacuo. The crude product contains, according to HPLC and NMR, some precursor and dibrominated product, but is pure enough (about 85% strength) for further reaction.
Yield: 43 g

Intermediate 2: N-(2-{2-[(2,4-Dichloro-benzyl)-methyl-amino]-acetyl}-phenyl)-acetamide;
12.4 g (65.24 mmol) of 2,4-dichloro-N-methylbenzylamine (example 1, intermediate 1) are dissolved in 200 ml of dioxane. To this are added 19.96 g of the crude product from the preceding bromination, likewise dissolved in 200 ml of dioxane, and 45 ml of triethylamine. The mixture is stirred at room temperature overnight and then filtered. The filtrate is evaporated, and the residue is taken up in ethyl acetate and washed with saturated sodium bicarbonate solution and brine, dried over sodium sulfate and concentrated in a rotary evaporator. The crude product (20.4 g) is pure enough according to NMR for further reaction.

Intermediate 3: N-(2-{2-[(2,4-Dichloro-benzyl)-methyl-amino]-1-hydroxy-ethyl}-phenyl)-acetamide;
20 g of the crude product from the preceding stage (about 50 mmol) are dissolved in 200 ml of methanol and cooled to < 5°C in an icebath. To this are added, while stirring vigorously, 4.3 g (109 mmol) of sodium borohydride in portions so that the internal temperature does not exceed 10°C. The mixture is then stirred in the icebath for 30 min and at RT for 1 h. After standing overnight, the mixture is evaporated, and the residue is taken up in ethyl acetate, washed 3× with water and 1× with brine, dried

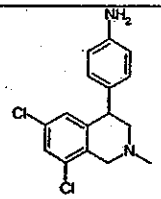
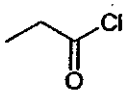
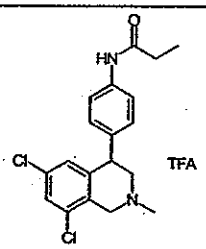
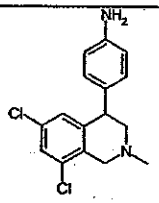
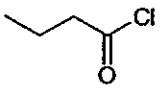
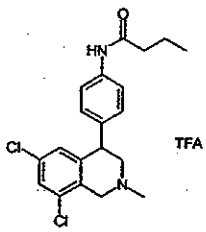
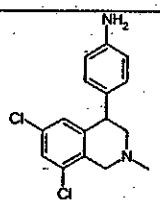
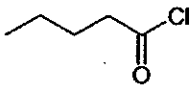
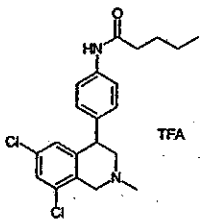
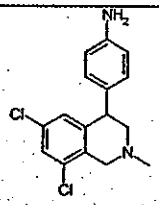
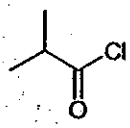
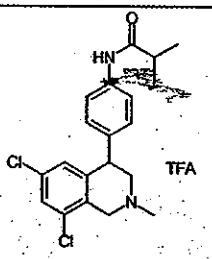
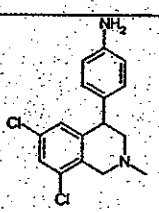
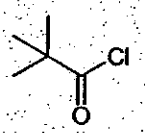
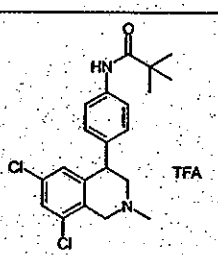
over sodium sulfate and concentrated in a rotary evaporator. The crude product (19.4 g) is reacted further without purification.

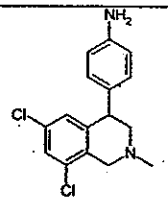
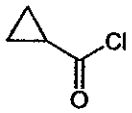
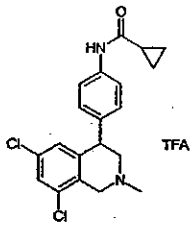
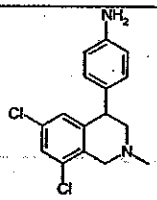
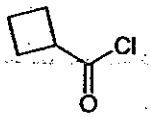
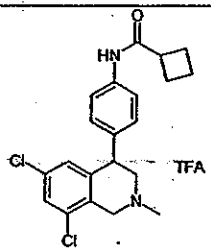
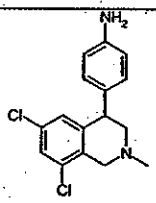
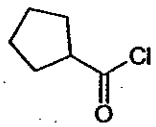
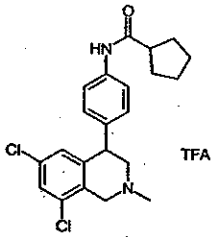
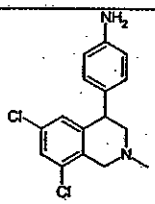
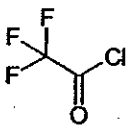
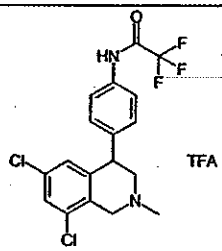
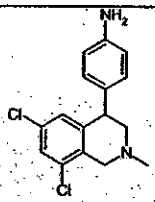
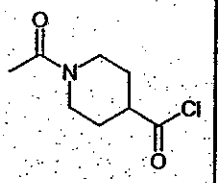
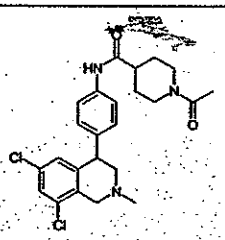
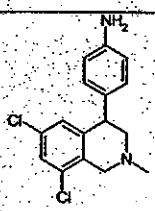
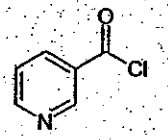
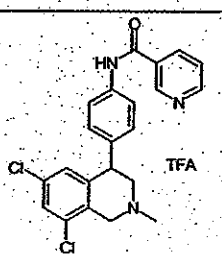
Intermediate 4: 1-(2-Amino-phenyl)-2-[(2,4-dichloro-benzyl)-methyl-amino]-ethanol;
10g of the crude product from the preceding stage are dissolved in 300 ml of methanol. 200 ml of conc. hydrochloric acid are added, and the mixture is stirred at 50°C for 10 h. The mixture is allowed to cool and is poured into water, and the pH is adjusted to 10-12 with 20% strength NaOH. The product is extracted with ethyl acetate, and the combined extracts are washed with brine, dried over sodium sulfate and evaporated. The crude product (9.9 g) contains some sodium chloride, but this does not interfere with further reaction.

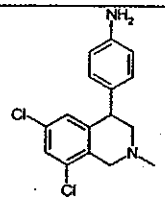
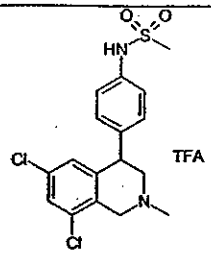
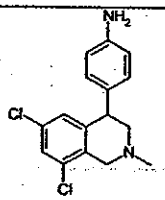
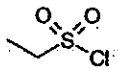
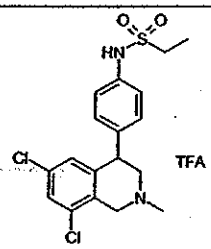
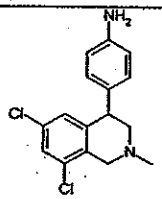
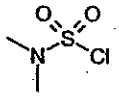
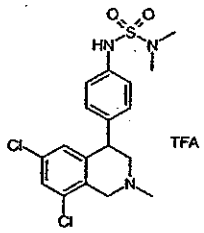
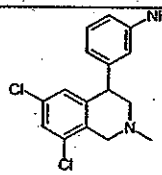
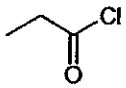
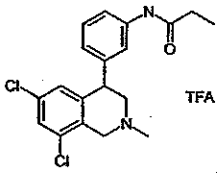
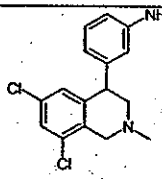
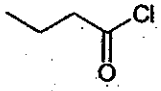
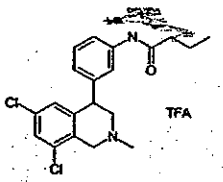
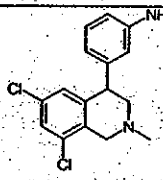
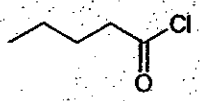
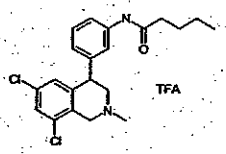
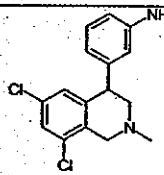
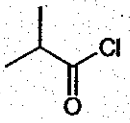
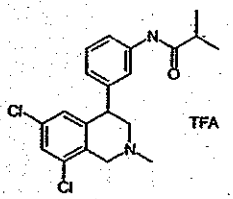
2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
9.9 g of the crude product from the preceding stage are dissolved in 350 ml of chloroform. While cooling in an icebath, 123 ml of conc. sulfuric acid are added dropwise. The mixture is stirred in the icebath for 2 h and is then allowed slowly to reach RT and is finally heated at 50°C overnight. The cooled mixture is poured onto ice and made alkaline (pH > 10) with sodium hydroxide solution. The organic phase is separated off, the aqueous phase is back-extracted 2× with methylene chloride, and the combined organic phases are washed with water and NaCl, dried over sodium sulfate and evaporated.

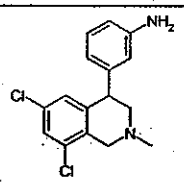
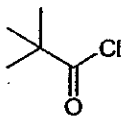
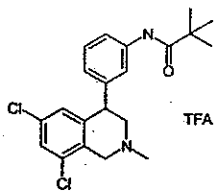
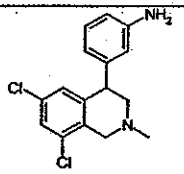
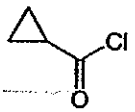
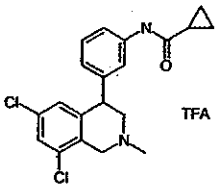
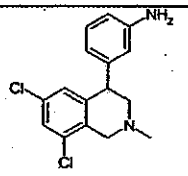
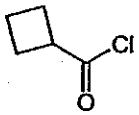
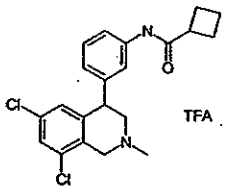
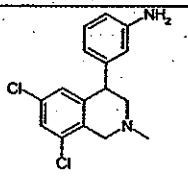
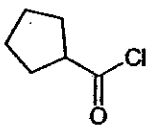
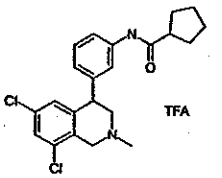
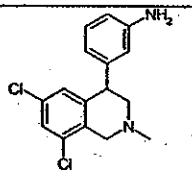
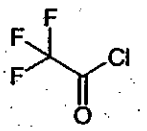
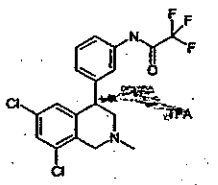
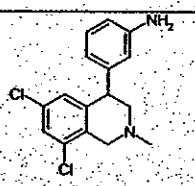
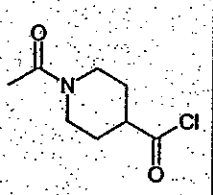
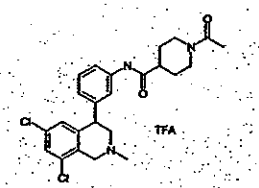
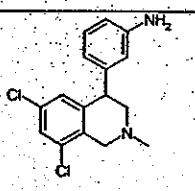
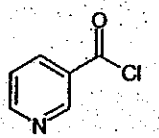
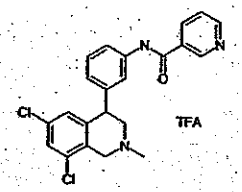
General method for preparing the compounds of examples 37 to 77:
154 mg (0.5 mmol) of the title compounds from example 35, example 36 or example 17, intermediate 1, are introduced into 5 ml of dichloromethane, and 0.076 ml (0.55 mmol) of triethylamine is added. At 0°C, a solution of 1.1 equivalents (0.55 mmol) of an acid chloride in 5 ml of dichloromethane is added, and the mixture is stirred overnight while warming up. For workup, it is filtered and freed of solvent. The residue is dissolved in 20 ml of ethyl acetate and washed once each with 5% strength $NaHCO_3$ solution and 5% strength NaCl solution, and dried. Evaporation of the solvent is followed by final purification on a preparative HPLC.

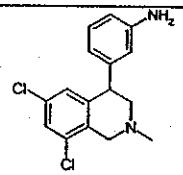
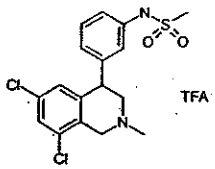
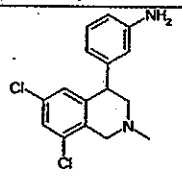
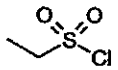
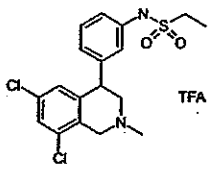
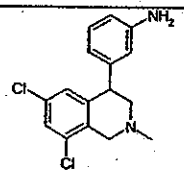
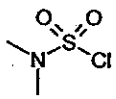
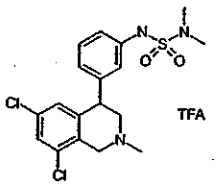
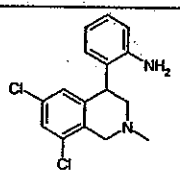
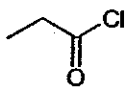
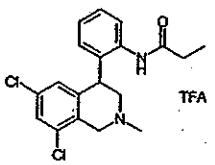
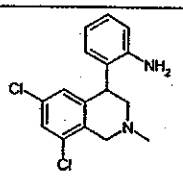
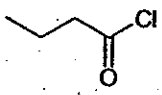
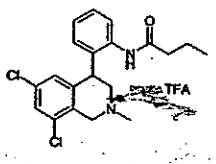
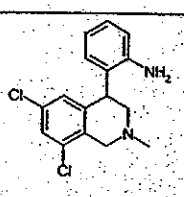
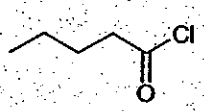
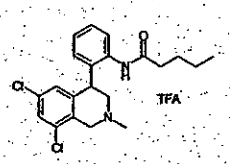
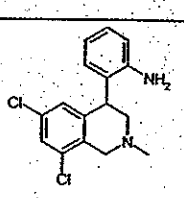
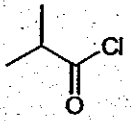
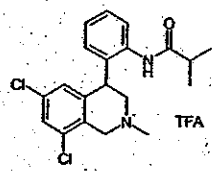
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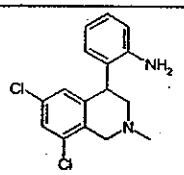
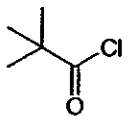
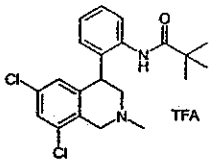
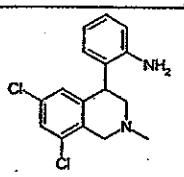
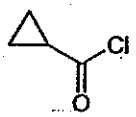
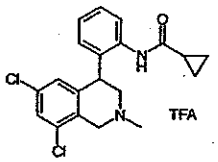
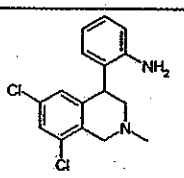
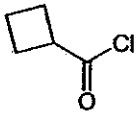
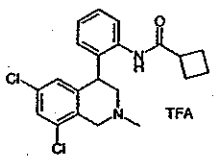
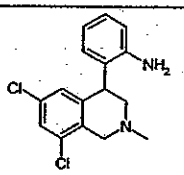
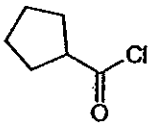
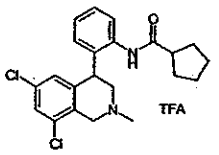
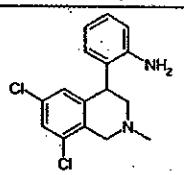
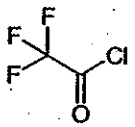
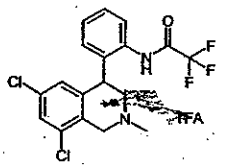
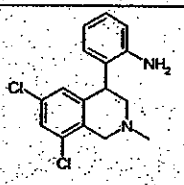
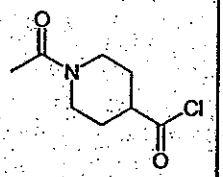
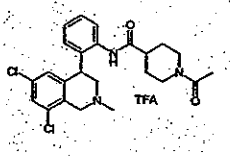
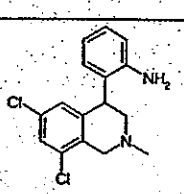
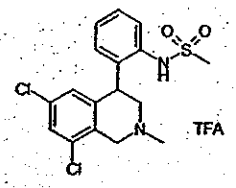
Example	Precursor 1/ aniline	Precursor 2/ acid chloride	Product
37	 Ex. 17, Int. 1		
38	 Ex. 17, Int. 1		
39	 Ex. 17, Int. 1		
40	 Ex. 17, Int. 1		
41	 Ex. 17, Int. 1		

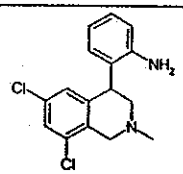
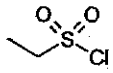
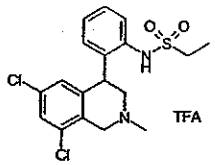
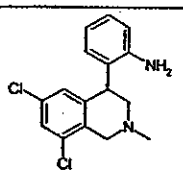
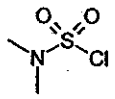
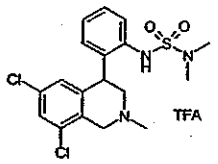
42	 Ex. 17, Int. 1		 TFA
43	 Ex. 17, Int. 1		 TFA
44	 Ex. 17, Int. 1		 TFA
45	 Ex. 17, Int. 1		 TFA
46 *	 Ex. 17, Int. 1		
47	 Ex. 17, Int. 1		 TFA

48	 Ex. 17, Int. 1		 TFA
49	 Ex. 17, Int. 1		 TFA
50	 Ex. 17, Int. 1		 TFA
51	 Ex. 35		 TFA
52	 Ex. 35		 TFA
53	 Ex. 35		 TFA
54	 Ex. 35		 TFA

55	 Ex. 35		 TFA
56	 Ex. 35		 TFA
57	 Ex. 35		 TFA
58	 Ex. 35		 TFA
59	 Ex. 35		
60	 Ex. 35		 TFA
61	 Ex. 35		 TFA

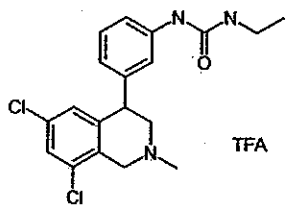
62	 Ex. 35		
63	 Ex. 35		
64	 Ex. 35		
65	 Ex. 36		
66	 Ex. 36		
67	 Ex. 36		
68	 Ex. 36		

69	 Ex. 36		
70	 Ex. 36		
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73	 Ex. 36		
74	 Ex. 36		
75	 Ex. 36		

76	 Ex. 36		
77	 Ex. 36		

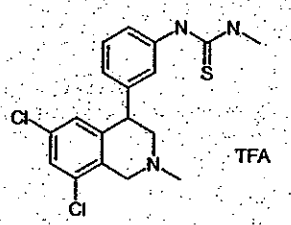
*) Product precipitates from the reaction solution and requires no further purification

Example 78: 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea, trifluoroacetate;



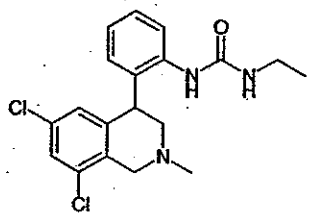
0.355 mmol of the compound of example 35 is dissolved in 5 ml of dry acetonitrile, and 0.39 mmol of ethyl isocyanate is added. After standing overnight with exclusion of moisture, the solvent is removed and the crude product is purified on a preparative HPLC, resulting in the title compound as a colorless solid.

Example 79: 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea, trifluoroacetate;



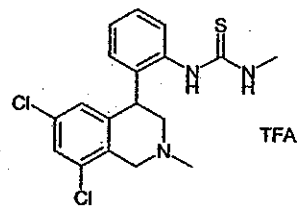
The title compound is synthesized starting from the compound of example 35 and methyl isothiocyanate by the method described in example 78.

Example 80: 1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;



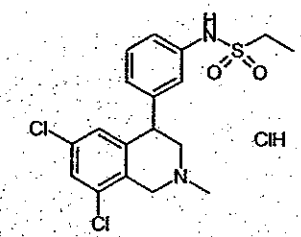
The process is analogous to example 78, starting from the compound of example 36 and ethyl isocyanate. For workup, the resulting precipitate is filtered off with suction and washed with acetonitrile, resulting in the desired ethylurea as a colorless solid.

Example 81: 1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea, trifluoroacetate;



The compound of example 36 and methyl isothiocyanate are reacted in analogy to the method described in example 78.

Example 82: N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide, hydrochloride;

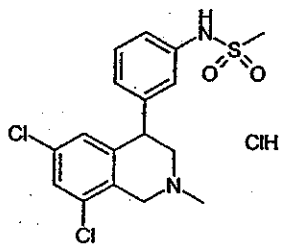


307.1 mg (1 mmol) of the compound of example 35 are dissolved in 10 ml of pyridine and at 0°C, 0.19 g (1.5 mmol) of ethanesulfonyl chloride, and a catalytic amount of DMAP are added. The mixture is stirred at room temperature.

For workup, the solvent is removed in vacuo, the residue is taken up in ethyl acetate and washed with H_2O. The organic phase is dried with $MgSO_4$ and concentrated. The

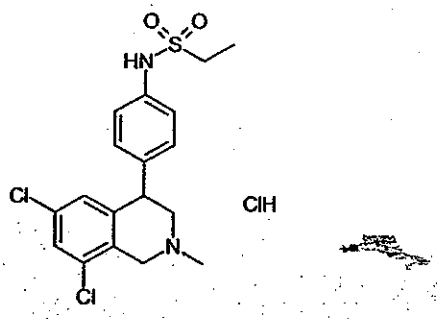
crude product is chromatographed on silica gel. The sulfonamide obtained in this way is dissolved in a THF/2 N HCl mixture and again concentrated in vacuo, resulting in 208 mg of the desired hydrochloride.

Example 83: N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide, hydrochloride;



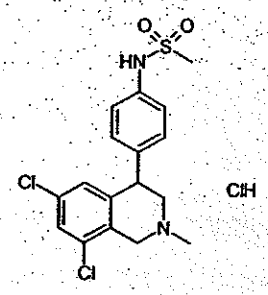
The process is analogous to the method described in example 82, starting from the compound of example 35 and methanesulfonyl chloride.

Example 84: N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide, hydrochloride;



The process is analogous to the method described in example 82, starting from the compound of example 17, intermediate 1, and ethanesulfonyl chloride.

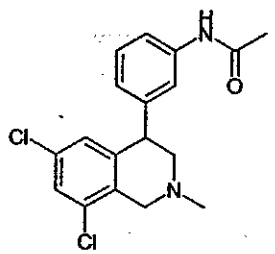
Example 85: N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide, hydrochloride;



The process is analogous to the method described in example 82, starting from the compound of example 17, intermediate 1, and methanesulfonyl chloride.

Example 86: 86a: (-)-N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
86b: (+)-N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

(+ and -)



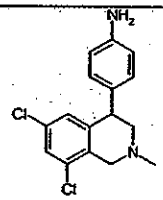
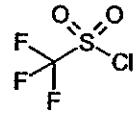
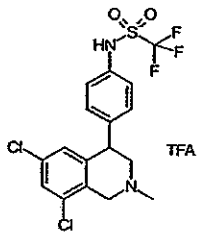
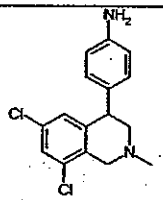
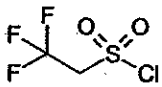
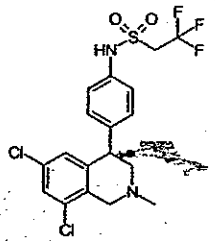
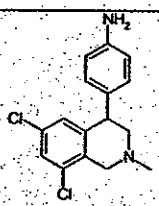
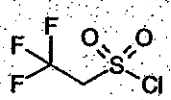
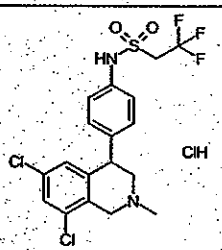
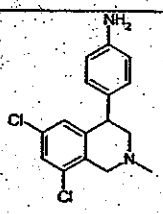
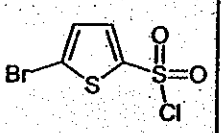
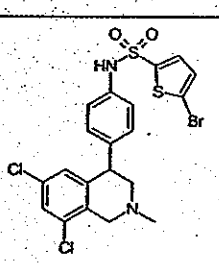
2.0 g of the title compound from example 34 are separated on a chiral phase, resulting in about 1.0 g of the two enantiomeric acetamides 86a and 86b.
chiral column: Chiralpak ADH/31 250 x 4.6 mm;
solvent: acetonitrile;
flow rate: 1 ml/min;
R_t((-)-enantiomer/86a) = 5.541 min;
R_t((+)-enantiomer/86b) = 7.033 min.

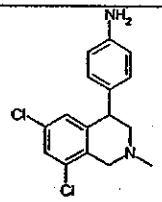
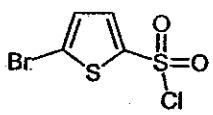
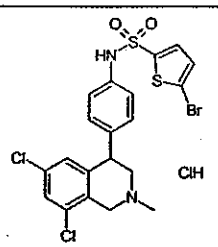
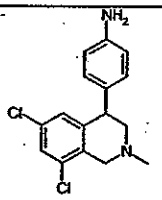
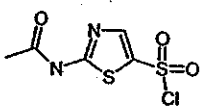
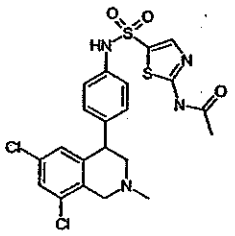
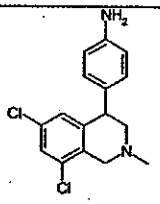
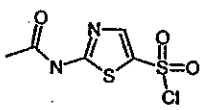
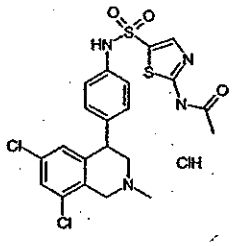
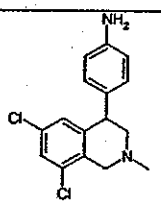
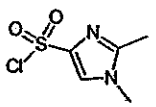
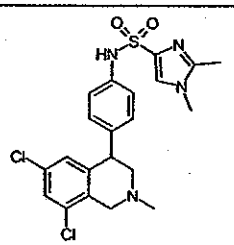
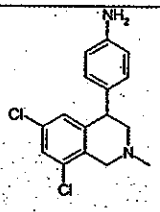
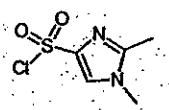
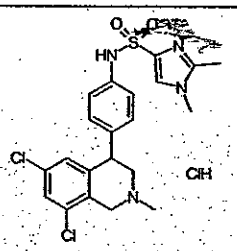
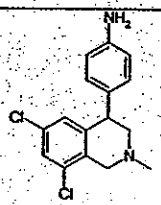
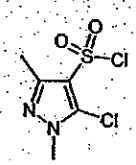
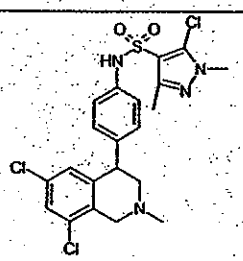
General method for preparing the compounds of examples 87 to 98
1.0 mmol of 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (example 17, intermediate 1) or 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (example 35) is introduced into 10 ml of pyridine and, at 0°C, a solution of 1.2 equivalents of the appropriate sulfonyl chloride (see table 2) in 5 ml of dichloromethane is added dropwise. The mixture is stirred at room temperature. A catalytic amount of DMAP is added depending on the progress of the reaction and, where appropriate, the reaction temperature is increased to 50°C until no further increase in conversion can be detected. For workup, the mixture is concentrated and the residue is partitioned between ethyl acetate and saturated $NaHCO_3$ solution. The

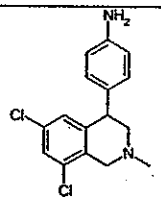
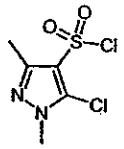
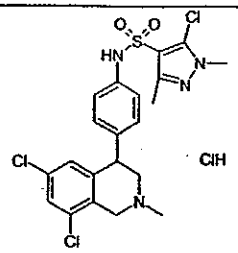
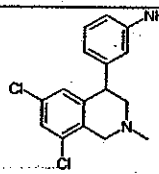
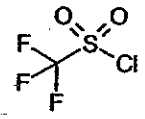
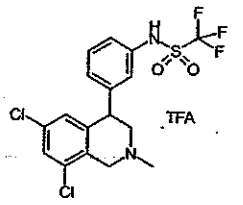
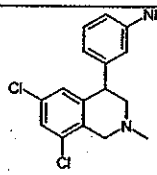
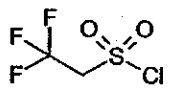
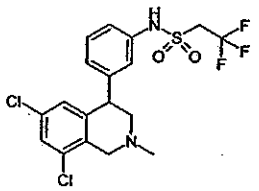
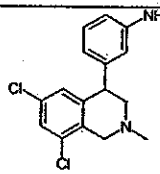
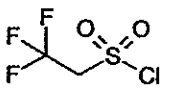
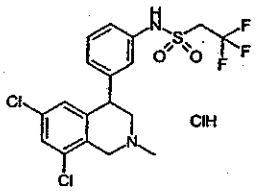
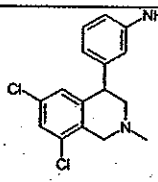
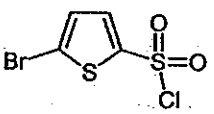
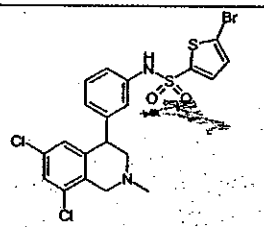
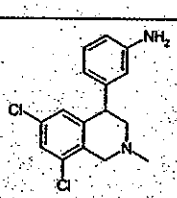
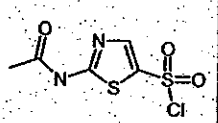
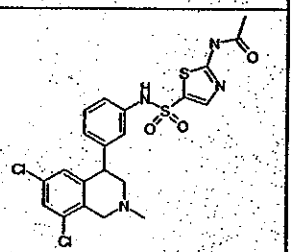
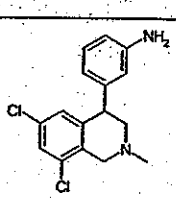
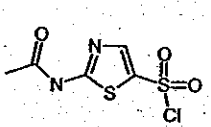
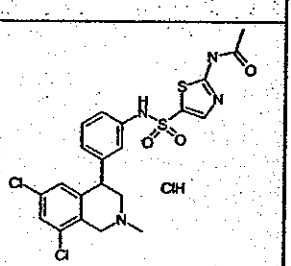
organic phase is separated off and washed once more with saturated $NaHCO_3$ solution and H_2O, dried with Na_2SO_4 and concentrated. For further purification, the crude product obtained in this way is chromatographed on silica gel. The products obtained in this way are converted into the corresponding hydrochlorides by dissolving the substances in 2 N HCl or ethanolic HCl and freeing off solvent, resulting in the desired HCl salts.

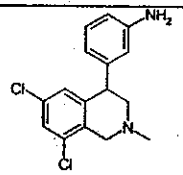
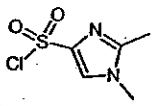
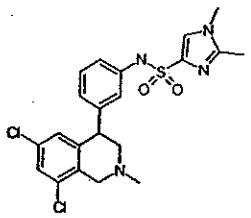
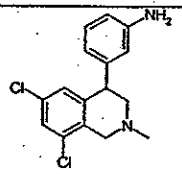
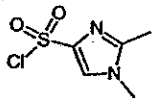
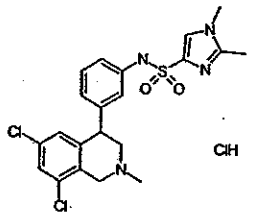
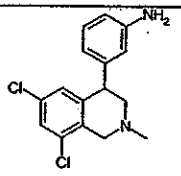
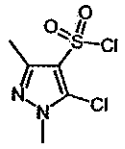
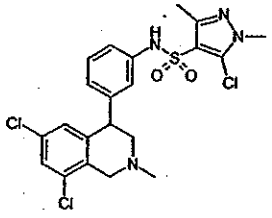
Purification in a preparative HPLC system results in the corresponding products as trifluoroacetates.

Table 2:

Example	Precursor 1/ aniline	Precursor 2/ acid chloride	Product
87	 Ex. 17, Int. 1		
88	 Ex. 17, Int. 1		
88a	 Ex. 17, Int. 1		
89	 Ex. 17, Int. 1		

89a	 Ex. 17, Int. 1		
90	 Ex. 17, Int. 1		
90a	 Ex. 17, Int. 1		
91	 Ex. 17, Int. 1		
91a	 Ex. 17, Int. 1		
92	 Ex. 17, Int. 1		

92a	 Ex. 17, Int. 1		
93	 Ex. 35		
94	 Ex. 35		
94a	 Ex. 35		
95	 Ex. 35		
96	 Ex. 35		
96a	 Ex. 35		

97	 Ex. 35		
97a	 Ex. 35		
98	 Ex. 35		

General method for synthesizing the compounds of examples 99 to 110

Preparation of the amine component

4.0 mmol of the aromatic aldehyde (see table 3) are stirred with 8.0 mmol of the aliphatic amine (see table 3) in methanol at room temperature for 2 hours and then, depending on the progress of the reaction, 0.67 to 2.0 eq of $NaBH_4$ are added in portions. After standing at room temperature overnight, the solvent is removed and the residue is taken up in 1 N HCl. It is extracted with dichloromethane. The aqueous phase is adjusted to a pH of 11 to 12 with NaOH and again extracted with dichloromethane. The organic phases are dried with $MgSO_4$ and concentrated in a rotary evaporator. Further purification takes place by chromatography on silica gel or on a preparative HPLC.

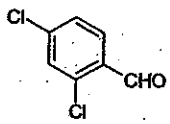
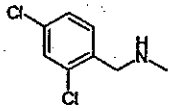
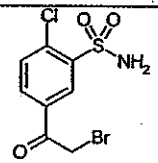
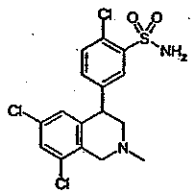
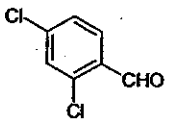
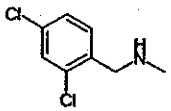
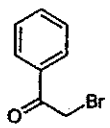
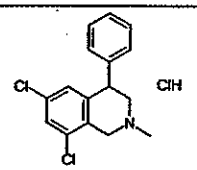
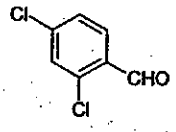
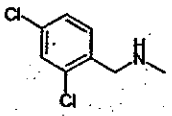
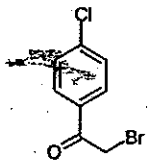
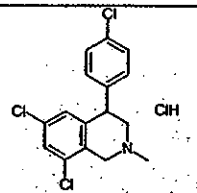
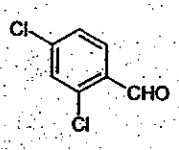
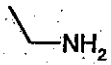
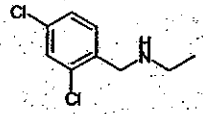
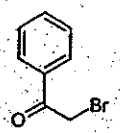
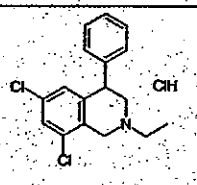
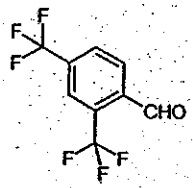
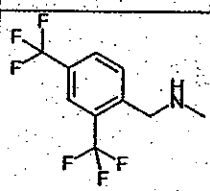
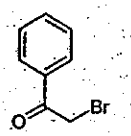
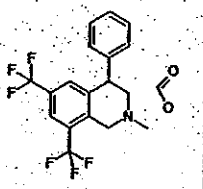
Preparation of the bromo ketone component

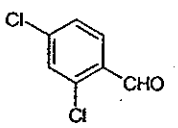
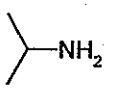
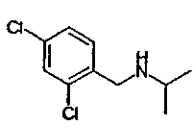
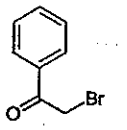
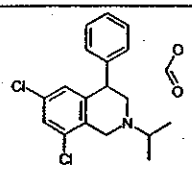
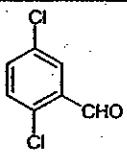
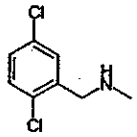
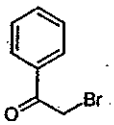
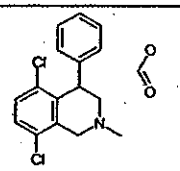
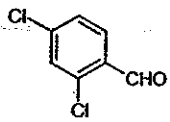
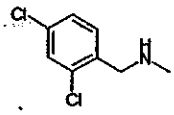
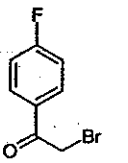
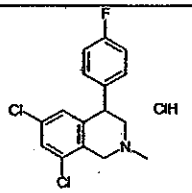
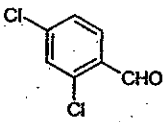
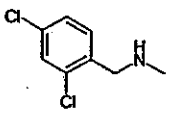
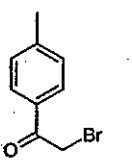
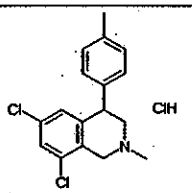
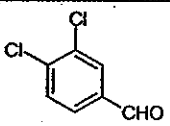
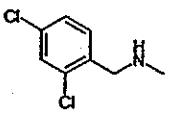
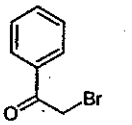
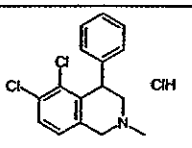
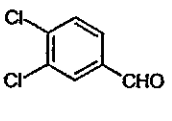
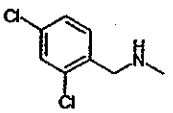
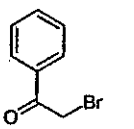
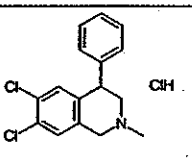
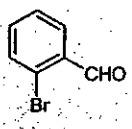
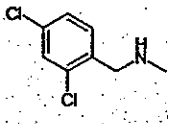
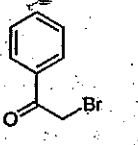
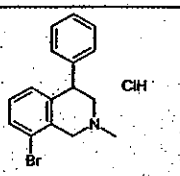
The bromo ketone building blocks are synthesized by methods known from the literature, starting from commercial acetophenones by treatment with bromine in glacial acetic acid in analogy to example 1, intermediate 2.

The compounds of examples 100 to 111 can be prepared starting from the amine and bromo ketone components shown in table 3 in analogy to the synthetic route shown in example 1 (alkylation of the amine component by the bromo ketone component, subsequent reduction with $NaBH_4$ and final H_2SO_4-mediated cyclization).

The resulting tetrahydroisoquinolines can be converted into the corresponding salts in a manner known to the skilled worker.

Table 3:

Example No.	Aromatic aldehyde	Aliphatic amine	Amine component	Bromo ketone component	Compound of example
99				 *)	
100					
101					
102					
103					

104					
105		—NH_2			
106		—NH_2			
107		—NH_2			
108		—NH_2			
109		—NH_2			
110		—NH_2			

*) Synthesis described in: Lang et al., DE-A 24 36 263

General method for preparing the compounds of examples 111 to 124

0.358 mmol of the acids indicated in table 4 are dissolved in 1 ml of DMF, and 0.221 ml (1.30 mmol) of diisopropylethylamine is added. At 0°C, a solution of 128 mg (0.390 mmol) of TOTU in 1 ml of DMF is added dropwise. After addition of a solution of 100 mg (0.325 mmol) of the amine component indicated in table 4, in 2 ml of DMF, the mixture is stirred at room temperature overnight. For workup, insoluble constituents are filtered off and washed with 20 ml of ethyl acetate. The filtrate is washed twice with

saturated $NaHCO_3$ solution and once with 5% strength NaCl solution, dried and concentrated.

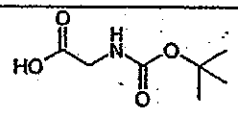
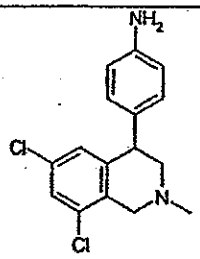
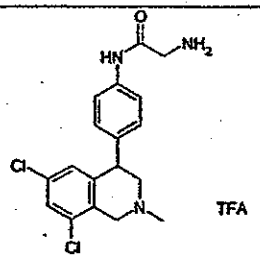
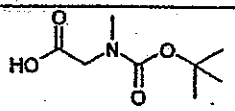
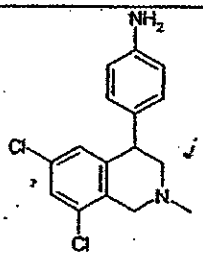
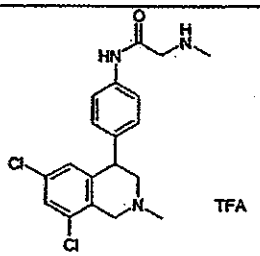
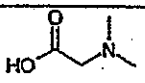
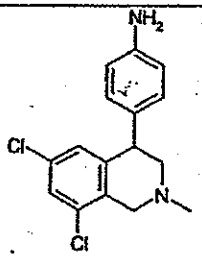
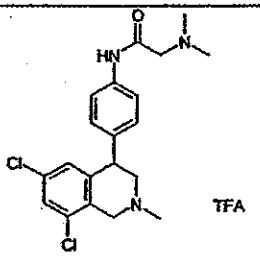
The crude products which still contain Boc protective groups are deprotected without further purification (see below: general method for eliminating the Boc protective groups). Workup of building blocks without Boc protection is followed by purification by preparative HPLC, with the desired compounds of the examples being obtained as trifluoroacetates.

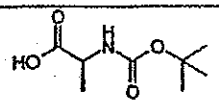
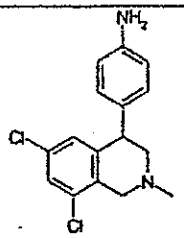
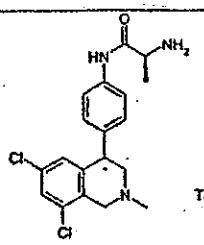
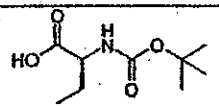
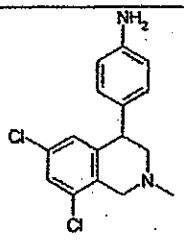
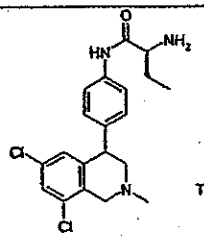
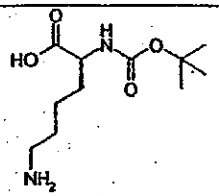
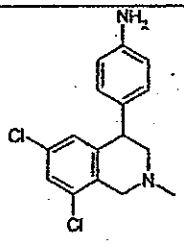
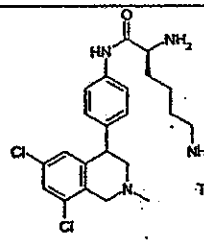
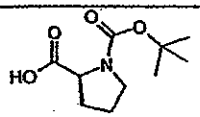
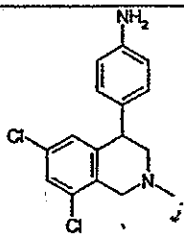
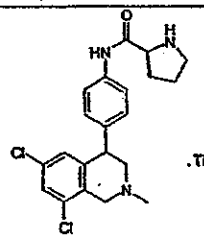
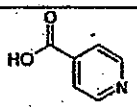
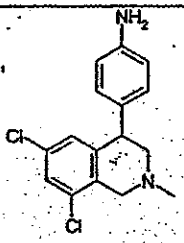
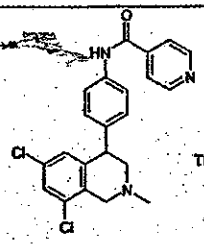
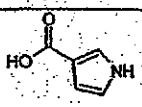
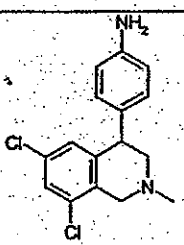
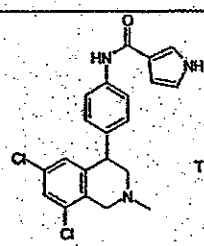
General method for preparing the compounds of examples 124 to 147
0.358 mmol of the acids indicated in table 4 are dissolved in 1 ml of DMF, and 0.221 ml (1.30 mmol) of diisopropylethylamine is added. At 0°C, 151 mg (0.975 mmol) of diethylcarbodiimide, a solution of 132 mg (0.975 mmol) of HOBt in 1 ml of DMF, and 20 mg (0.162 mmol) of DMAP are added. After addition of a solution of the amine component indicated in table 4, in 2 ml of DMF, the mixture is stirred at room temperature overnight. For workup, insoluble constituents are filtered off and washed with 20 ml of ethyl acetate. The filtrate is washed twice with saturated $NaHCO_3$ solution and once with 5% strength NaCl solution, dried and concentrated.

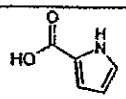
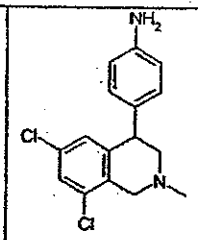
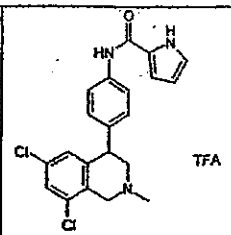
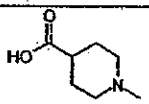
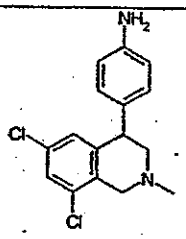
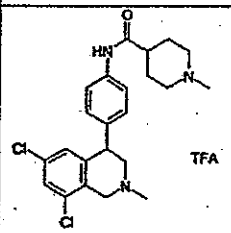
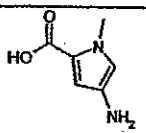
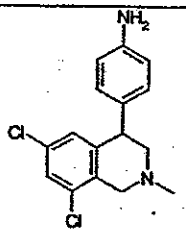
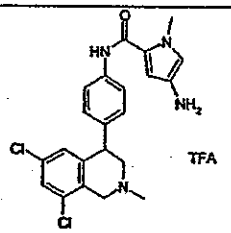
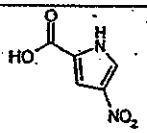
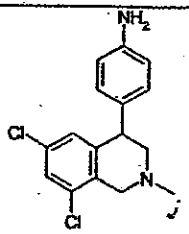
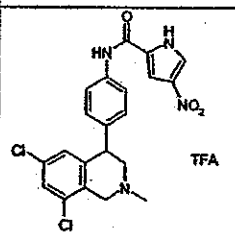
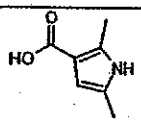
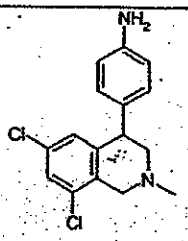
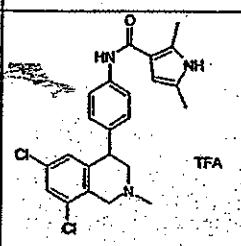
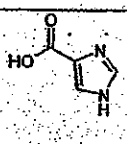
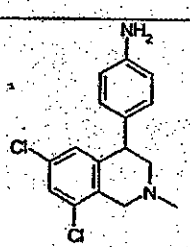
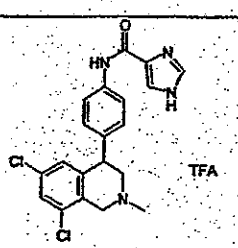
The crude products which still contain Boc protective groups are deprotected without further purification (see below: general method for eliminating the Boc protective groups). Workup of building blocks without Boc protection is followed by purification by preparative HPLC, with the desired compounds of the examples being obtained as trifluoroacetates.

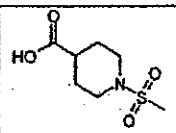
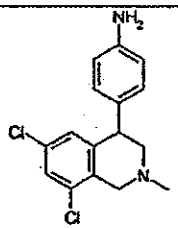
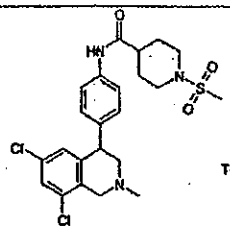
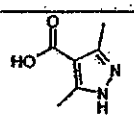
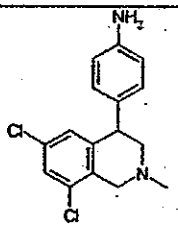
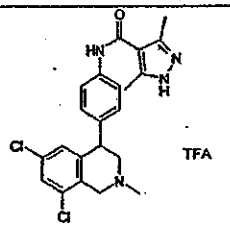
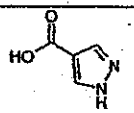
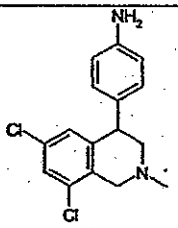
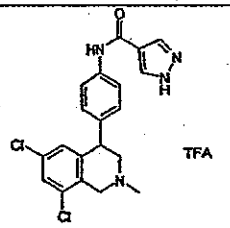
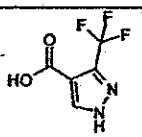
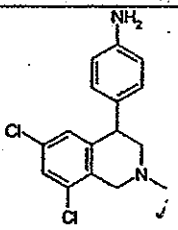
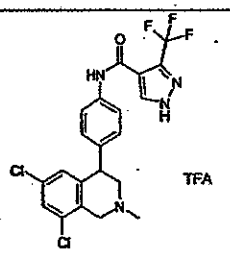
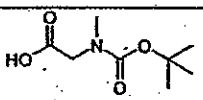
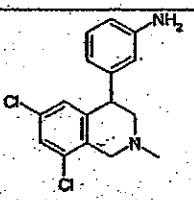
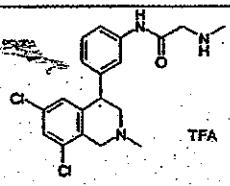
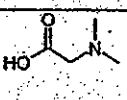
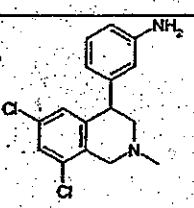
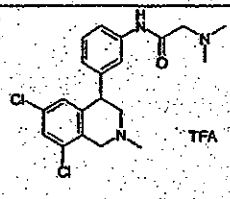
General method for eliminating Boc protective groups
The resulting crude products are stirred in 5 ml of a 10% strength solution of trifluoroacetic acid in dichloromethane at room temperature for one hour. The residue from evaporation in vacuo is purified on a preparative HPLC, with the desired compounds of the examples being obtained as trifluoroacetates.

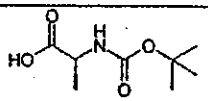
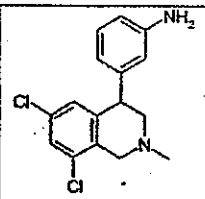
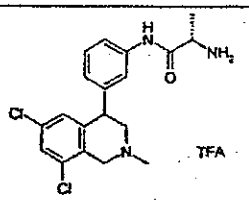
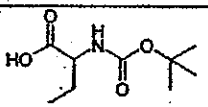
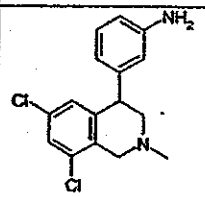
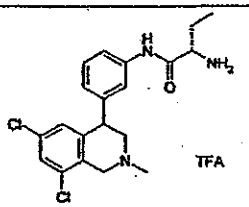
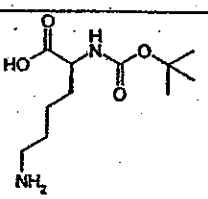
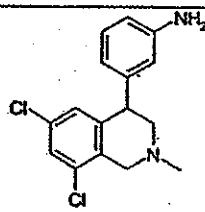
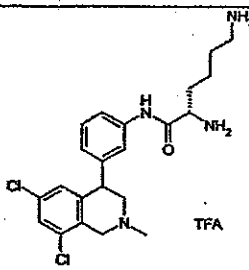
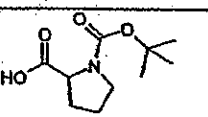
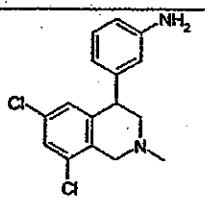
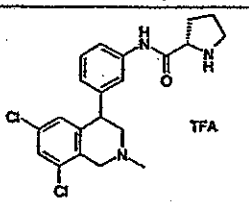
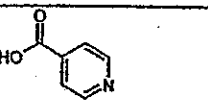
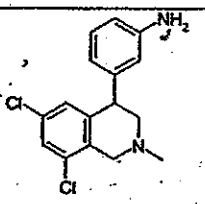
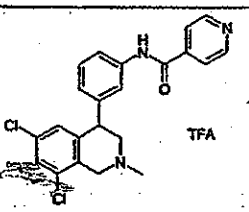
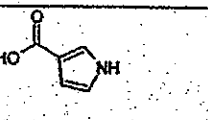
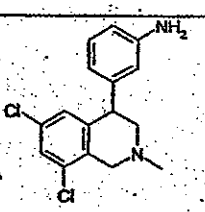
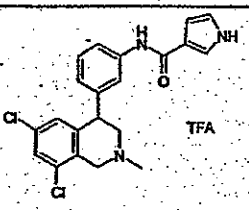
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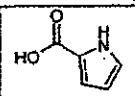
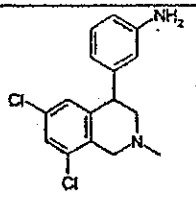
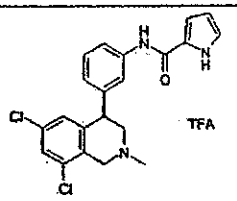
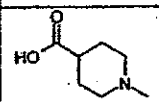
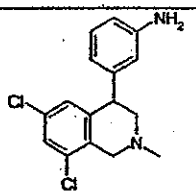
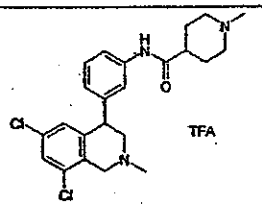
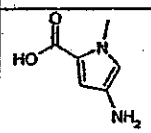
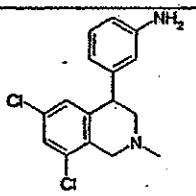
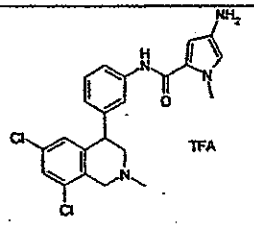
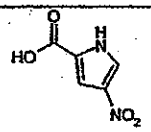
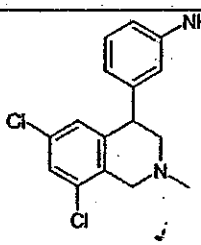
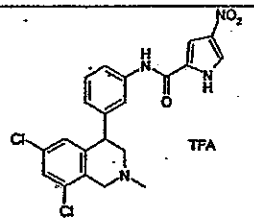
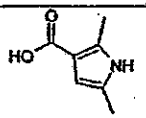
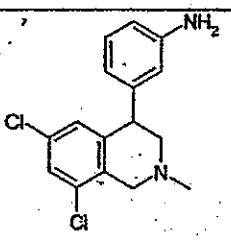
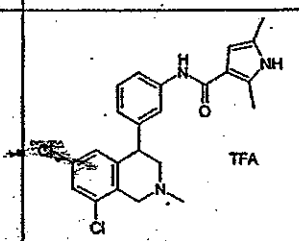
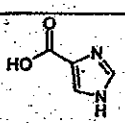
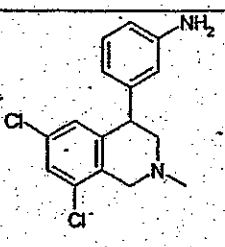
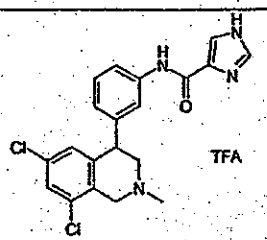
Example No.	Acid component	Amine component	Compound of example
111		 Ex. 17, int. 1	 TFA
112			 TFA
113			 TFA

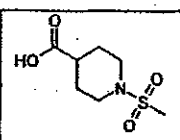
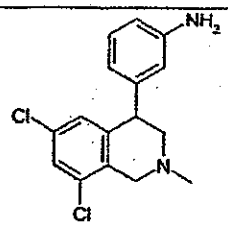
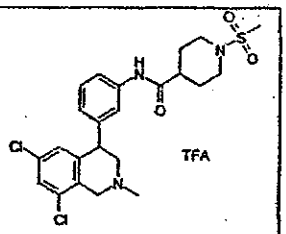
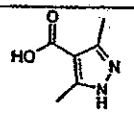
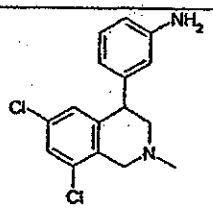
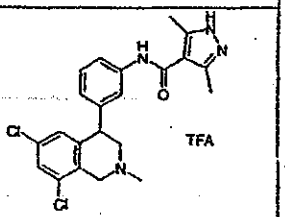
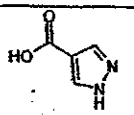
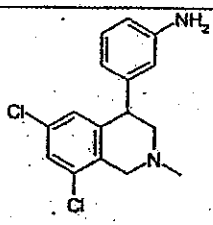
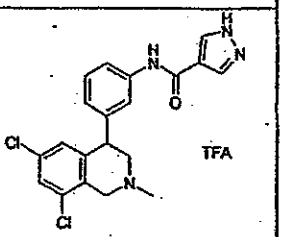
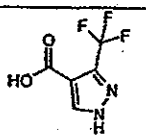
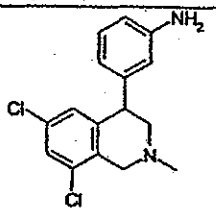
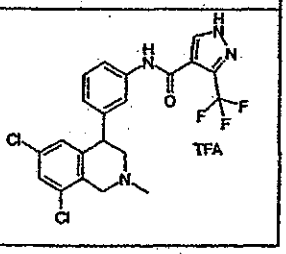
114			 TFA
115			 TFA
116			 TFA
117			 TFA
118			 TFA
119			 TFA

120			 TFA
121			 TFA
122			 TFA
123			 TFA
124			 TFA
125			 TFA

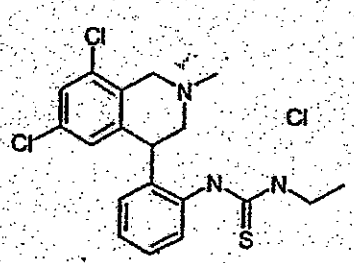
126			 TFA
127			 TFA
128			 TFA
129			 TFA
130		 Ex. 35	 TFA
131			 TFA

132			
133			
134			
135			
136			
137			

138			
139			
140			
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142			
143			

144			
145			
146			
147			

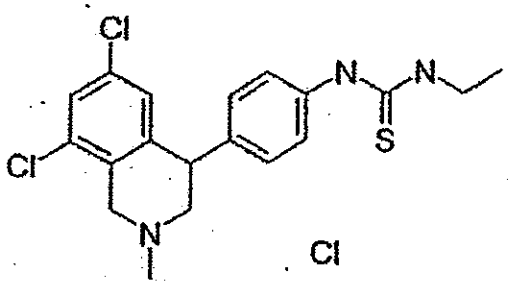
Example 148: 1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea, hydrochlorides;



2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (95 mg, compound of example 36) is introduced into 4 ml of acetonitrile and, while stirring, 27 mg of ethyl isothiocyanate are added. After standing at room temperature for 15 hours, the solvent is removed in vacuo, and the residue is purified on a preparative

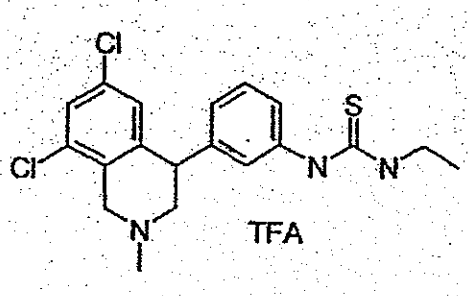
HPLC. The trifluoroacetate obtained in this way is taken up in water and made alkaline with K_2CO_3. The aqueous phase is extracted with ethyl acetate. The organic phase is separated off, dried with $MgSO_4$ and concentrated. The residue is taken up in dilute HCl and freeze dried, resulting in 36 mg of the title compound.

Example 149: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea, hydrochlorides;



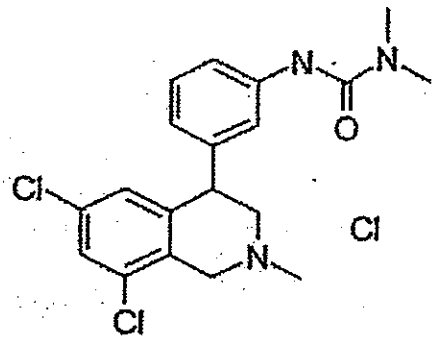
4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (50 mg, compound of example 17, intermediate 1) are introduced into 4 ml of THF, and ethyl isothiocyanate (14 mg) is added. After heating to reflux for 2 hours, the reaction solution is concentrated and heated at 85°C to 2 hours. The crude product obtained in this way is purified on a preparative HPLC. Further treatment of the trifluoroacetate obtained in this way as described in example 148 affords 33 mg of the desired hydrochloride after freeze drying.

Example 150: 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea, trifluoroacetate;



3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (50 mg, compound of example 35) are dissolved in 3 ml of THF and, while stirring, 14 mg of ethyl isothiocyanate are added. After heating to reflux for 2 hours, the reaction solution is concentrated and heated at 85°C for 2 hours. The crude product obtained in this way is purified on a preparative HPLC, becoming 66 mg of the title compound.

Example 151: 3-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea, hydrochloride;



Intermediate 1: 4-nitrophenyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate, hydrochlorides;

3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (350 mg, compound of example 35) are dissolved in 17.5 ml of dichloromethane and, while stirring, 230 mg of 4-ntirophenyl chloroformate are added. After 4.5 hours, a further 0.1 equivalent (23 mg) of 4-nitrophenyl chloroformate were added, and the solution was stirred overnight. For workup, the resulting precipitate is filtered off and washed with dichloromethane. The title compound obtained in this way can be reacted further without further purification.

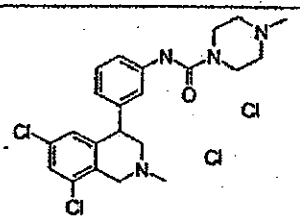
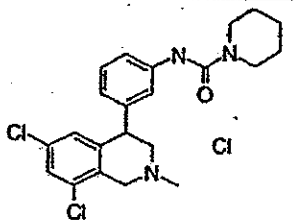
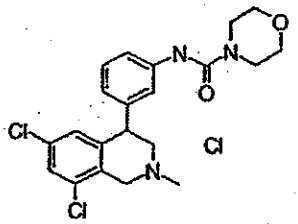
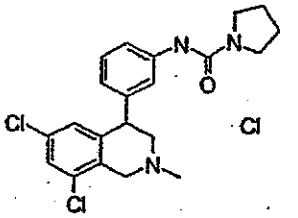
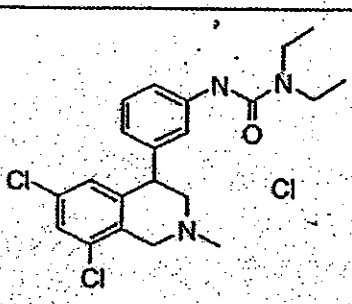
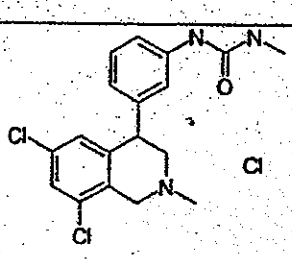
3-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea, hydrochloride;

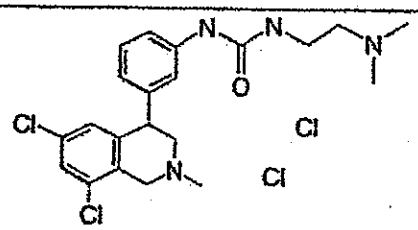
35 mg of 4-nitrophenyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate hydrochlorides (intermediate 1) are suspended in 3.5 ml of dichloromethane and, while stirring, a solution of 3.7 mg of dimethylamine in 1ml of dichloromethane is added dropwise. After 1 hours, the mixture is diluted with

dichloromethane and washed with aqueous K_2CO_3 solution. The organic phase is separated and washed twice with saturated K_2CO_3 solution, dried with $MgSO_4$ and concentrated. The residue is taken up in dilute HCl and freeze dried, resulting in 29 mg of the title compound.

The following examples are prepared in analogy to the method described in example 151, starting from intermediate 1 and the appropriate amine components:

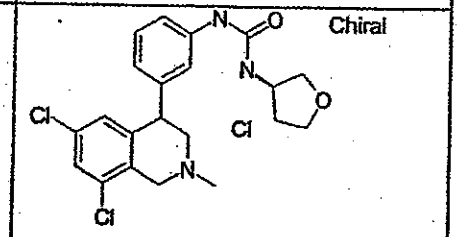
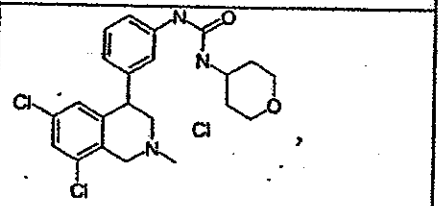
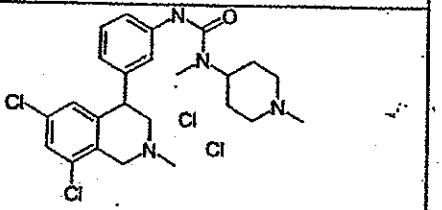
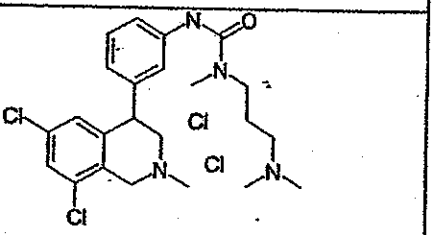
Table 5:

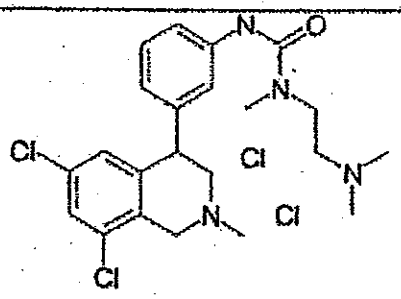
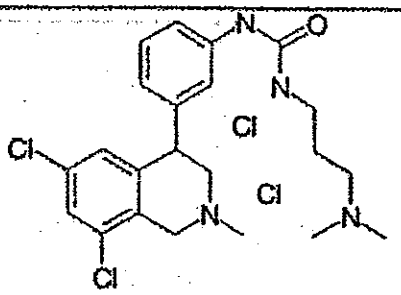
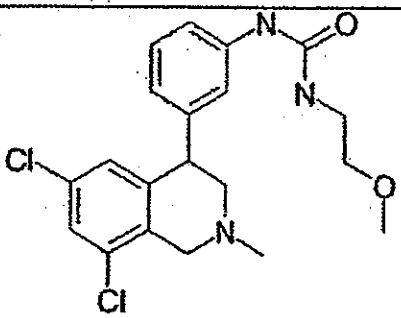
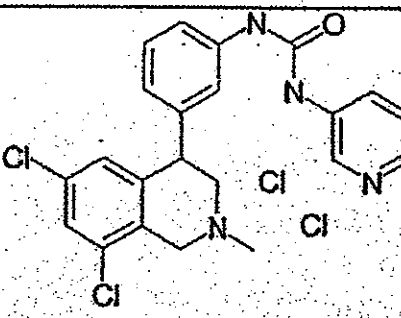
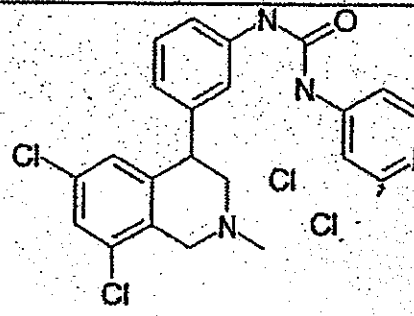
Example No.:	Structure
152	
153	
154	
155	
156	
157	

158	

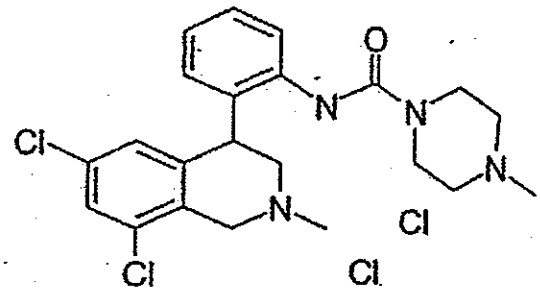
The following examples were prepared in analogy to the method described in example 151. THF was used as solvent, and the reactions were carried out in a closed reaction vessel. Reaction temperatures of 85°C were necessary for examples 159 to 166. Compound of example 167 was purified by preparative HPLC.

Table 6:

Example No.:	Structure
159	 Chiral
160	
161	
162	

163	
164	
165	
166	
167	

Example 168: N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methylpiperazine-1-carboxamide, hydrochloride;



Intermediate 1: 4-Nitrophenyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate, hydrochlorides;

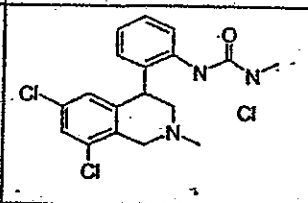
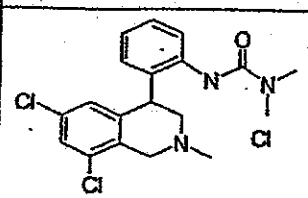
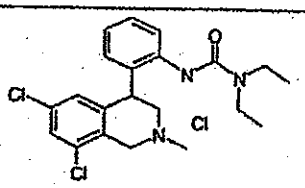
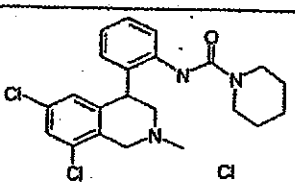
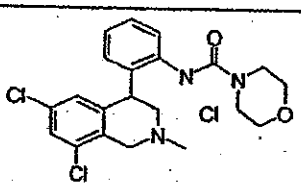
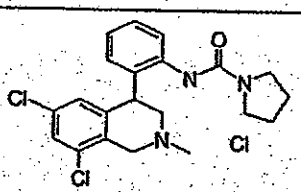
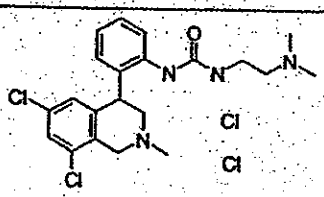
[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (200 mg, comparative example 36) are dissolved in 10 ml of dichloromethane and, while stirring, 131 mg of 4-nitrophenyl chloroformate are added. After 3.5 hours, the resulting precipitate is filtered off with suction and washed with dichloromethane. The crude product obtained in this way is recrystallized from dichloromethane, resulting in 159 mg of the title compound.

N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methylpiperazine-1-carboxamide, hydrochloride;

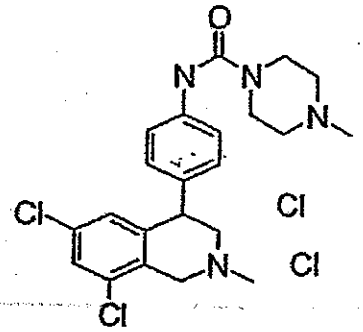
15 mg of 4-nitrophenyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate hydrochlorides are suspended in 2 ml of dichloromethane, and a solution of 3.2 mg of 1-methylpiperazine in 1 ml of dichloromethane is added. After 1 hours, the mixture is diluted with dichloromethane and washed with aqueous K_2CO_3 solution. The organic phase is separated and washed twice with saturated K_2CO_3 solution, dried with $MgSO_4$ and concentrated. The residue is taken up in dilute HCl and freeze dried, resulting in 13 mg of the title compound.

The following examples are prepared in analogy to the method described for example 168.

Table 7:

Example No.:	Structure
169	
170	
171	
172	
173	
174	
175	

Example 176: N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide, hydrochlorides;



Intermediate 1: 4-Nitrophenyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate, hydrochlorides;

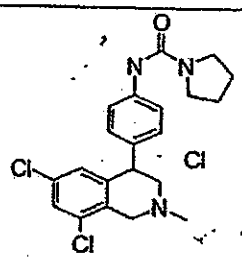
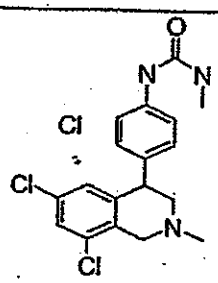
4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (200 mg, compound of example 17, intermediate 1) are dissolved in 10 ml of dichloromethane and, while stirring, 131 mg of 4-nitrophenyl chloroformate are added. After 4.5 hours, the resulting precipitate is filtered off with suction and washed with dichloromethane. The crude product obtained in this way is recrystallized twice from dichloromethane, resulting in 254 mg of the title compound.

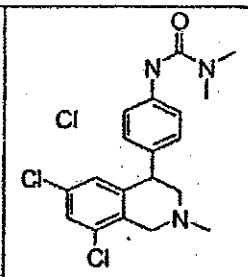
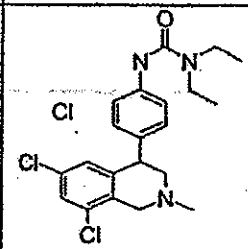
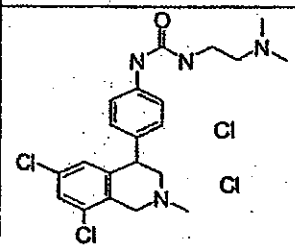
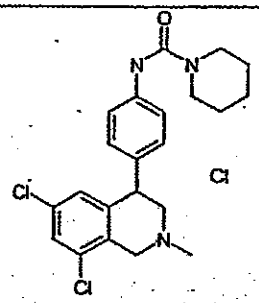
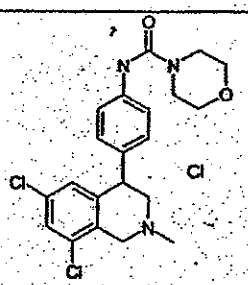
N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide, hydrochlorides;

15 mg of 4-nitrophenyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate hydrochloride are suspended in 2 ml of dichloromethane, and a solution of 3.2 mg of 1-methylpiperazine in 1 ml of dichloromethane is added. After stirring for 5 hours and standing overnight, the mixture is diluted with dichloromethane and washed with aqueous K_2CO_3 solution. The organic phase is separated and washed twice with saturated K_2CO_3 solution, dried with $MgSO_4$ and concentrated. The residue is taken up in dilute HCl and freeze dried, resulting in 13 mg of the title compound.

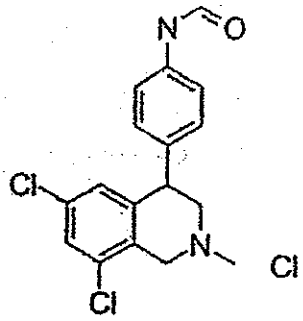
The following examples are prepared in analogy to the method described for example 176.

Table 8:

Example No.:	Structure
177	
178	

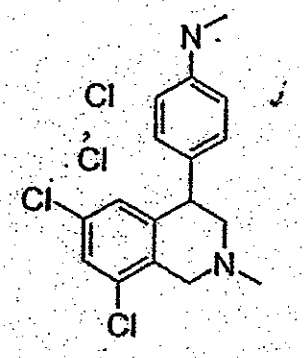
179	
180	
181	
182	
183	

Example 184: N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]formamide, hydrochloride;



4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (200 mg, compound of example 17, intermediate 1) is dissolved in 1 ml of formic acid and heated to reflux for 15 min. After standing overnight, the mixture is added to an ice/water mixture and extracted twice with ethyl acetate. The combined organic phases are dried with $MgSO_4$ and concentrated. The residue is taken up in dichloromethane and washed with saturated $NaHCO_3$ solution. The phases are separated and the aqueous are extracted three times more with dichloromethane. Drying of the organic phases ($MgSO_4$) and removal of the solvent by distillation afford 167 mg of crude product. 10 mg are dissolved in dilute HCl and freeze dried, resulting in 11 mg of the title compound.

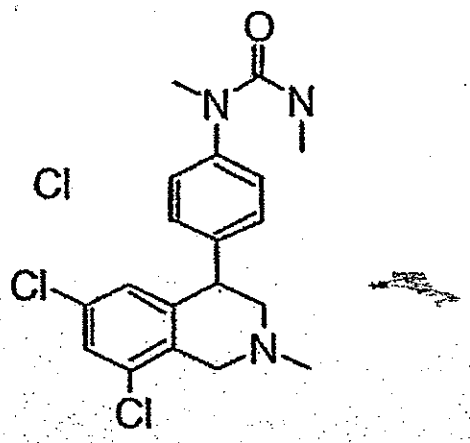
Example 185: [4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]methyl-amine, hydrochloride



N-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]formamide (150 mg, compound of example 184) are dissolved in 2.5 ml of THF and, at 50°C under argon, added dropwise to a solution of 0.45 ml of a 1 M solution of lithium

aluminum hydride/THF in 2.5 ml of THF. The mixture is heated to reflux for 1 hour. After standing overnight, a further 0.22 ml of a 1 M lithium aluminum hydride solution are added at 50°C, and the mixture is heated to reflux for a further hour. For workup, the solvent is removed and the residue is partitioned between dichloromethane and aqueous HCl. The phases are separated and the aqueous are extracted three times with dichloromethane, The combined organic phases are dried with with $MgSO_4$ and concentrated. Further purification takes place on a preparative HPLC. The product obtained in this way is taken up in an $NaHCO_3$ solution and extracted with dichloromethane. Drying of the organic phase with $MgSO_4$ affords 80 mg of the free base. 10 mg are taken up in diluted HCl and freeze dried, resulting in 10 mg of the title compound.

Example 186: 1-[4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea, hydrochlorides;

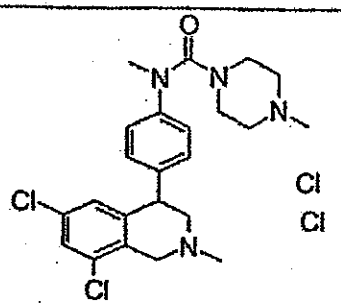
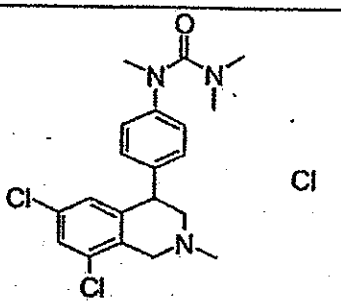
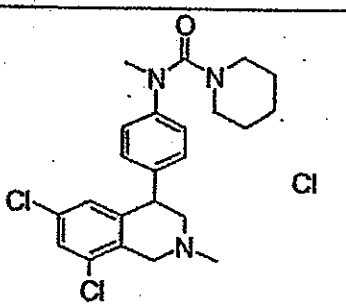
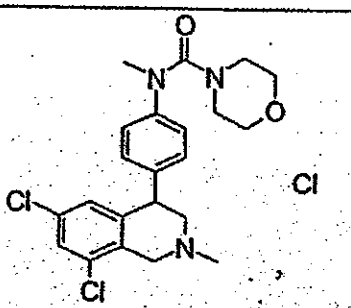
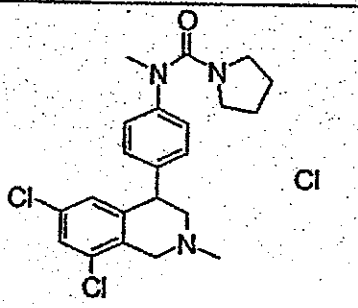


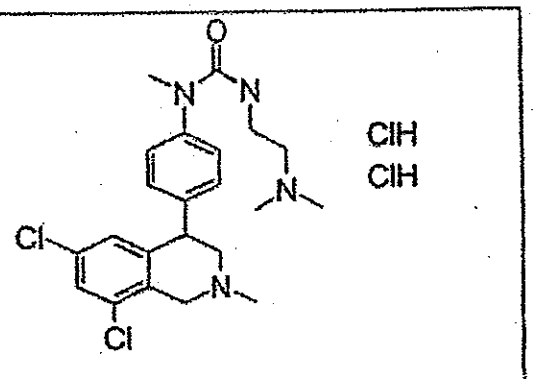
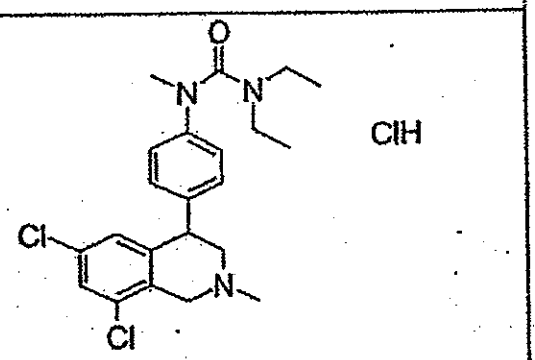
The title compound is prepared by the method described for example 151, starting from [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]methyl-amine (example 185), 4-nitrophenyl chloroformate and methylamine (20 µl, 2 M in THF) resulting in 9 mg of the desired hydrochloride.

The following compounds are prepared in analogy to example 186 starting from [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]methyl-amine (example 185), 4-nitrophenyl chloroformate and the appropriate amine components:

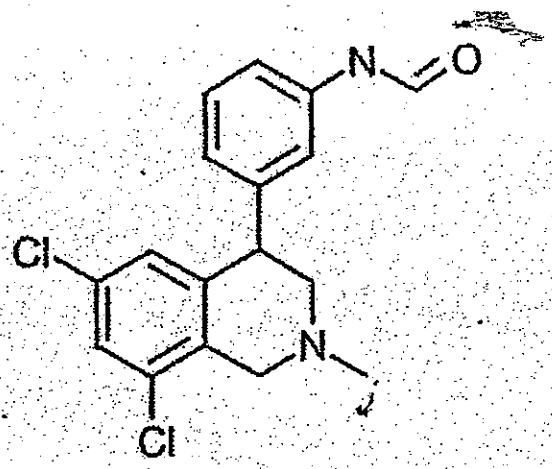
Table 9:

Example No.:	Structure

187	
188	
189	
190	
191	

192	
193	

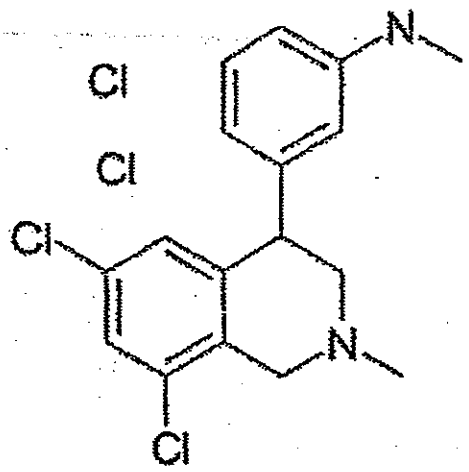
Example 194: N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]formamide



3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (600 mg, compound of example 35) is dissolved in 2.4 ml of formic acid and heated to reflux for 15 min. After standing overnight, the mixture is added to a mixture of ice/water and

saturated $NaHCO_3$ solution and extracted three times with dichloromethane. The combined organic phases are dried with $MgSO_4$ and concentrated, resulting in 588 mg of the title compound.

Example 195: [3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine, hydrochloride;

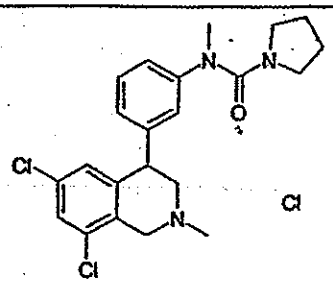


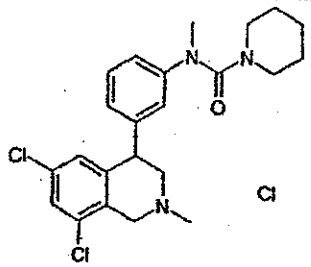
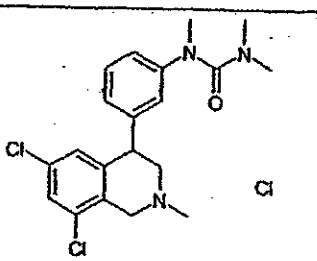
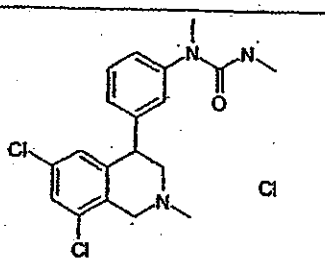
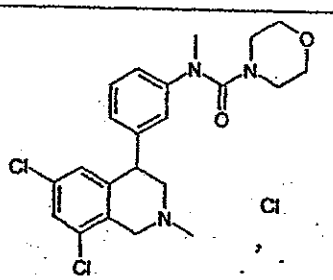
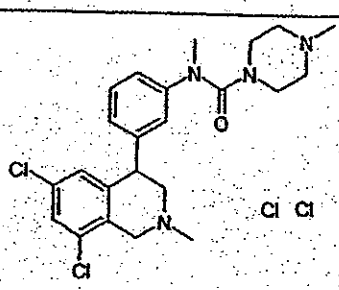
N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]formamide (588 mg, compound of example 194) is dissolved in 10 ml of THF and, at 50°C under argon, added to a solution of 1.8 ml of a 1 M solution of lithium aluminum hydride in THF. The mixture is heated to reflux for 1 hour. After standing overnight, a further 2 ml of a 1 M lithium aluminum hydride solution are added at 50°C, and heated to reflux for a further 30 min. For workup, ice is added and the aqueous phase is extracted four times with ethyl acetate. The combined organic phases are dried with $MgSO_4$ and concentrated. Further purification takes place on a preparative HPLC. The product obtained in this way is taken up in $NaHCO_3$ solution and extracted with ethyl acetate. Drying of the organic phase with $MgSO_4$ affords 270 mg of the free base. 45 mg are taken up in diluted HCl and freeze dried, resulting in 45 mg of the title compound.

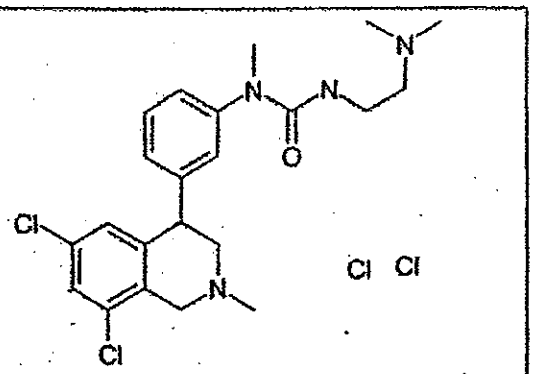
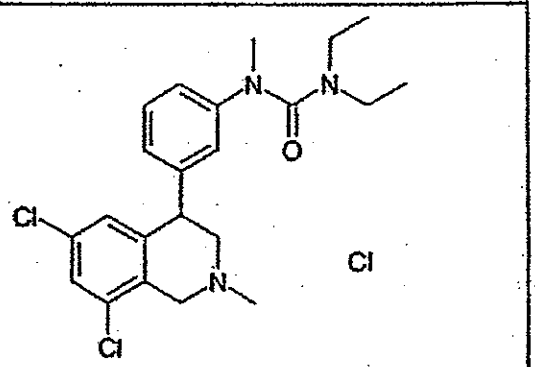
The compounds of the following examples can be prepared starting from [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]methylamine

(example 195), 4-nitrochloroformate and the appropriate amine components by the method described for example 151:

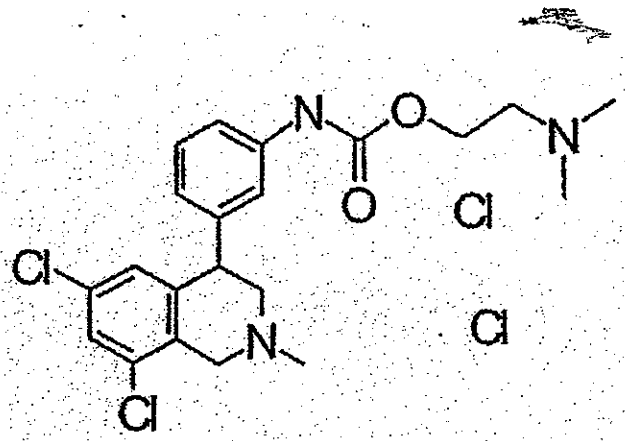
Table 10:

Example No.:	Structure
196	

197	
198	
199	
200	
201	

202	
203	

Example 204: 2-Dimethylaminoethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate, hydrochloride;

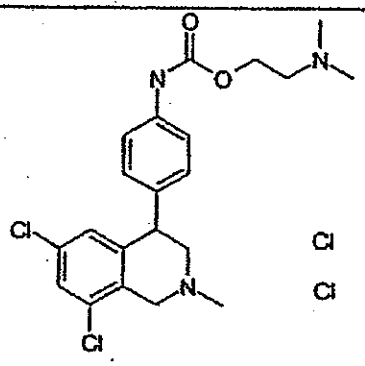
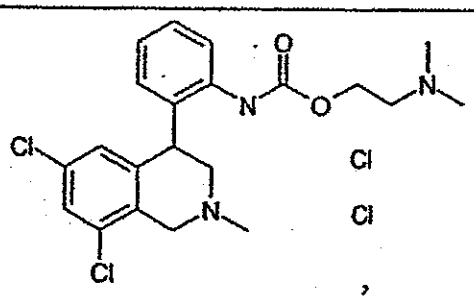


15 mg of 4-nitrophenyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate hydrochloride (see example 151, intermediate 1) are suspended in 1.5 ml of dichloromethane while stirring under an argon atmosphere, and a solution of

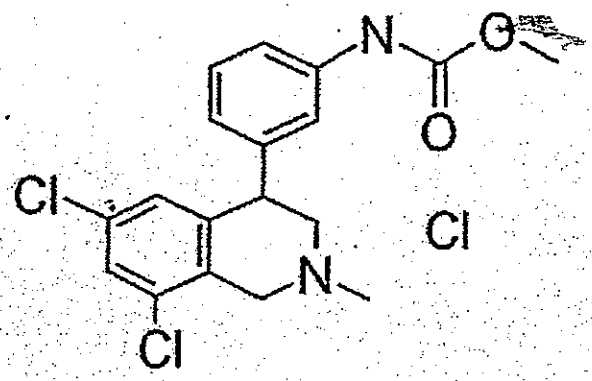
3 mg of 2-dimethylaminoethanol in 0.5 ml of dichloromethane is added, and the mixture is stirred for 6 hours. After standing overnight, water, dichloromethane and saturated $NaHCO_3$ solution are added, and the organic phase is separated. The dichloromethane phase is washed three times with saturated $NaHCO_3$ and dried with $MgSO_4$, and the solvent is removed in vacuo. The crude product obtained in this way is purified on a preparative HPLC. The product fractions are concentrated and partitioned between ethyl acetate and saturated $NaHCO_3$ solution. The organic phase is separated off, dried with $MgSO_4$ and concentrated. The residue is taken up in dilute HCl and freeze dried, resulting in 5 mg of the title compound.

In an analogous manner, the corresponding isomers 2-dimethylaminoethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]carbamate hydrochloride and 2-dimethylaminoethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate hydrochloride are prepared starting from 4-nitrophenyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate hydrochloride and 4-nitrophenyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate hydrochloride.

Table 11:

Example No.:	Structure
205	
206	

Example 207: Methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate, hydrochloride;

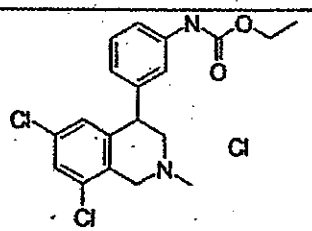
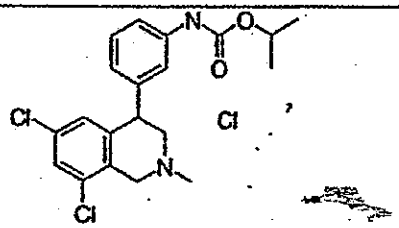
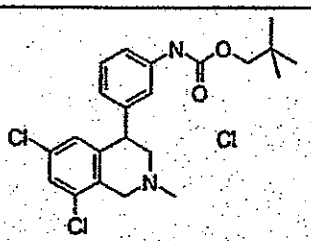


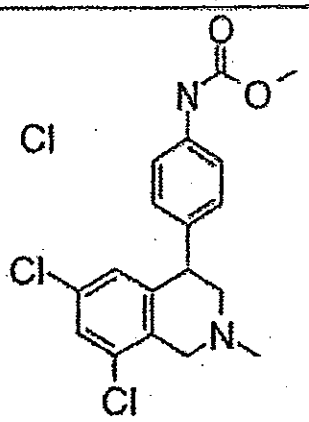
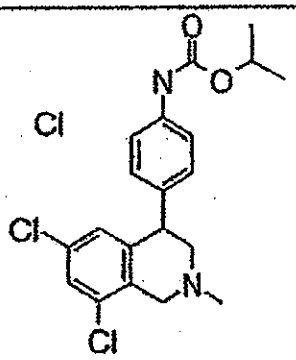
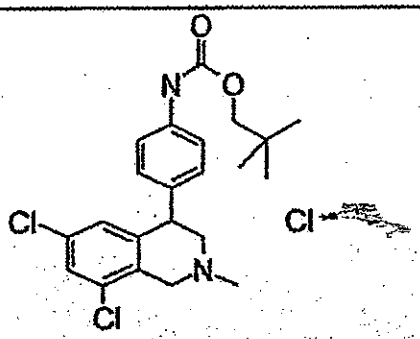
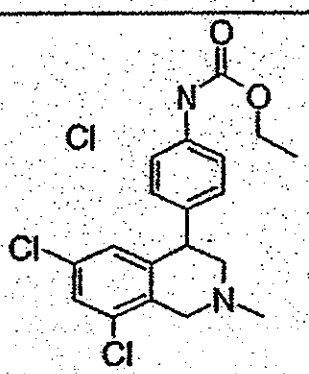
15 mg of 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine (example 35) are introduced under an argon atmosphere into 1.5 ml of dichloromethane while stirring, and a solution of 4.6 mg of methyl chloroformate in 0.5 ml of dichloromethane is added. After stirring for 6 hours and standing overnight, a

further 2.3 mg of methyl chloroformate are added, and the mixture is stirred for 5 hours. For workup, the solvent is removed, and the residue is taken up in dilute HCl and freeze dried, resulting in 20 mg of the title compound.

The following carbamates can be prepared in an analogous manner starting from the appropriate anilines 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine and 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine.

Table 12:

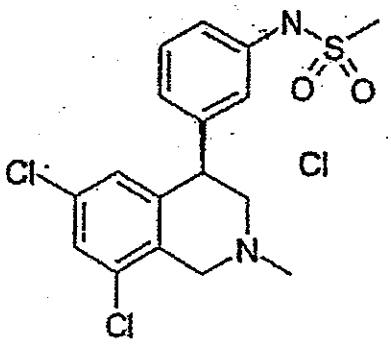
Example No.:	Structure
208	
209	
210	

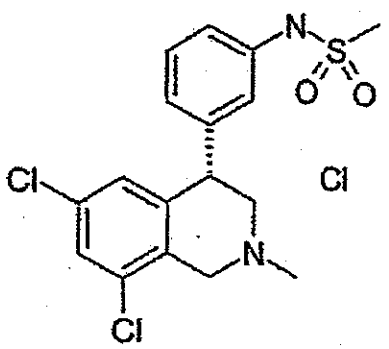
211	
212	
213	
214	

Example

215a: (+)-N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide, hydrochloride;

215b: : (-)-N-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide, hydrochloride;





96 mg of racemic N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]methanesulfonamide (see example 83) are separated into the enantiomers on a chiral preparative HPLC.

chiral column: Chiralpak AD 250 x 50 mm; 20 μ;

solvent: heptane:ethanol:methanol: 10:1:1;

flow rate: 50 ml/min;

the resulting enantiomers are dissolved in dilute HCl and freeze dried, resulting in 37 mg of each of the title compounds 215a and 215b. The enantiomeric purity is determined on a chiral HPLC.

chiral column: Chiralpak AD-H/31 250 x 4.6 mm;

solvent: heptane:ethanol:methanol: 10:1:1;

flow rate: 1 ml/min;

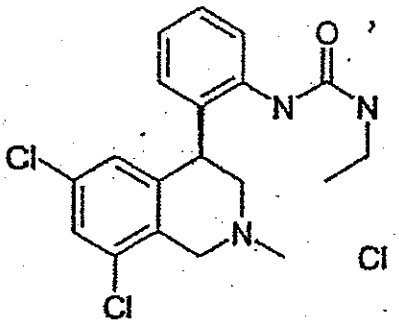
R_t (enantiomer eluting first) = 6.84 min; 100% ee;

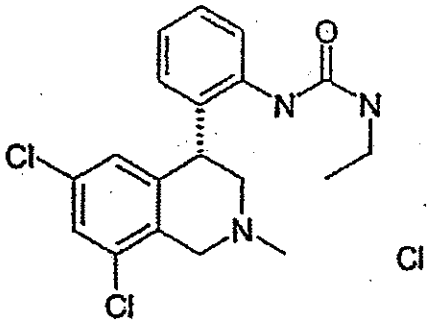
R_t (enantiomer eluting second) = 8.02 min, 100% ee.

Example

216a: (+)-1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethylurea, hydrochloride;

216b: (-)-1-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethylurea, hydrochloride;





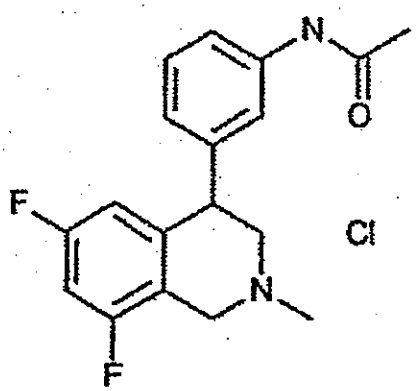
316 mg of racemic 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethylurea (compound of example 80) are separated into the enantiomers on a chiral preparative HPLC.

chiral column: Chiralpak OD 250 × 50 mm, 20 μ;
solvent: heptane:ethanol:isopropanol: 50:2:1; 0.3% diethylamin
flow rate: 50 ml/min;

The enantiomers are subjected separately to further purification on a preparative HPLC. The resulting products are partitioned between saturated $NaHCO_3$ solution and ethyl acetate, and the organic phase is separated off, dried with $MgSO_4$ and freed of solvent. Dissolving the residue in dilute HCl and freeze drying affords 37 mg of the enantiomer eluting first and 58 mg of that eluting second. The enantiomeric purity is determined by analytical HPLC.

chiral column: Chiralpak OD 250 × 4.6 mm;
solvent: heptane:ethanol:isopropanol: 50:2:1; (0.3% diethylamine);
flow rate: 10 ml/min;
R_t (enantiomer eluting first) = 9.22 min; 100% ee;
R_t (enantiomer eluting second) = 9.96 min, 98% ee.

Example 217: N-[3-(6,8-Difluoro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide, hydrochloride;



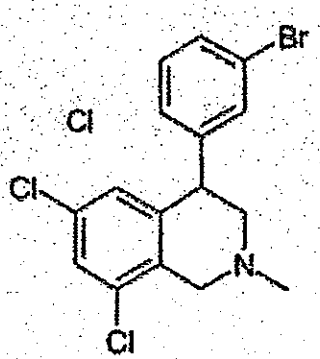
Intermediate 1: 2,4-Difluorobenzylmethylamine

2,4-Difluorobenzylmethylamine can be prepared in a manner known to the skilled worker starting from 2,4-difluorobenzaldehyde (cf. example 1, intermediate 1).

N-[3-(6,8-Difluoro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]acetamide, hydrochloride;

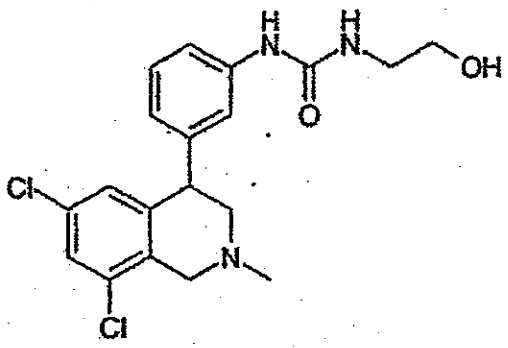
The title compound can be prepared by the synthetic route described in example 1 starting from N-(3-acetylphenyl)acetamide and 2,4-difluorobenzylmethylamine (intermediate 1).

Example 218: 4-(3-Bromophenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro isoquinoline, hydrochloride;



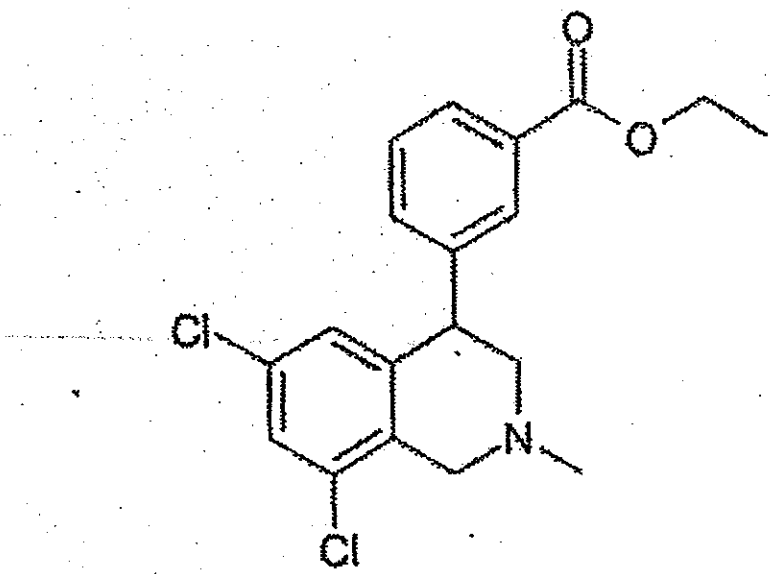
The title compound can be prepared by the synthetic route described in example 1 starting from 2,4-dichlorobenzylmethylamine (see example 1) and 2-bromo-1-(3-bromophenyl)ethanone as alkylating agent.

Example 219: 1-[3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl-3-(2-hydroxyethyl)urea



509 mg (1 mmol) of 4-nitrophenyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroiso-quinolin-4-yl)-phenyl]carbamate hydrochlorides (compound of example 151, intermediate 1) are dissolved in 15 ml of absolute DMF and, at 0°C, a solution of 67.2 mg (1.1 mmol) of 2-aminoethanol in 10 ml of DMF is added. The mixture is stirred at room temperature for three hours and then the solvent is removed in vacuo. The residue is partitioned between ethyl acetate and saturated $NaHCO_3$ solution. The organic phase is separated off and the aqueous is extracted twice more with ethyl acetate. The combined organic phases are washed with saturated NaCl solution, dried with $MgSO_4$ and concentrated. Chromatography on silica gel (dichloromethane/methanol) affords 265 mg of the title compound.

Example 220: Ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate



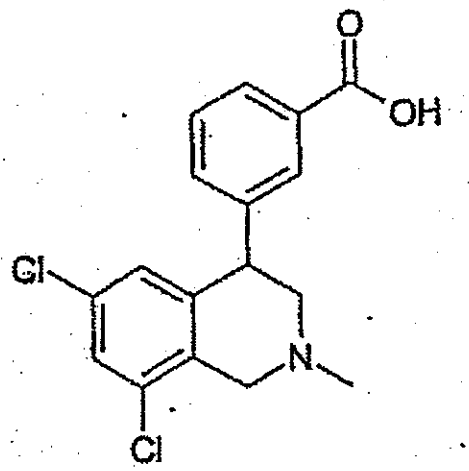
Intermediate 1: 3-Acetylbenzoic acid is prepared in a manner known to the skilled worker from 3-acetylbenzonitrile by hydrolysis of the nitrile group.

Intermediate 2: Ethyl 3-acetylbenzoate is prepared from intermediate 1 in a manner known to the skilled worker.

Intermediate 3: Ethyl 3-(2-bromoacetyl)benzoate is synthesized in analogy to the method described in example 1, intermediate 2, from ethyl 3-acetylbenzoate (intermediate 2).

Ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate, Starting from ethyl 3-(2-bromoacetyl)benzoate (intermediate 3) and 2,4-dichlorobenzyl-methylamine (example 1, intermediate 1) it is possible to proceed further in analogy to the synthetic route described in example 1, resulting in ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzoate after alkylation reaction, reduction and ring-closure reaction.

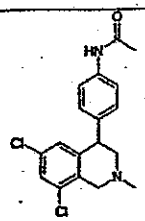
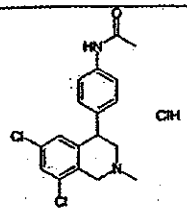
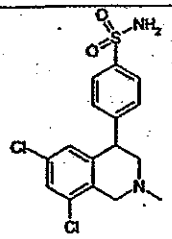
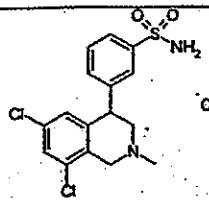
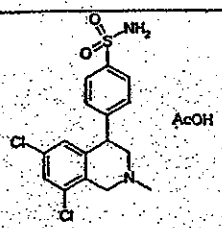
Example 221: 3-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)benzoic acid;

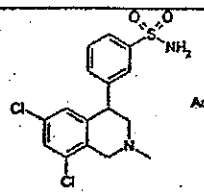
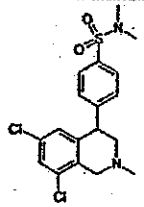
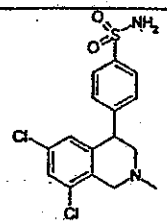
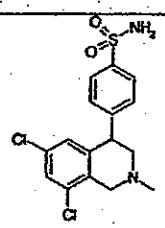
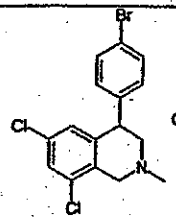
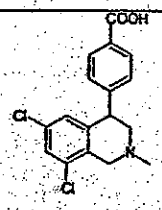


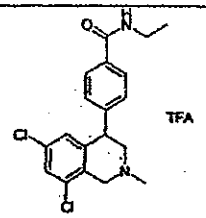
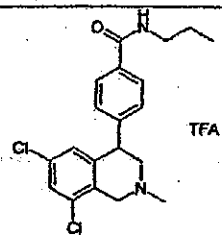
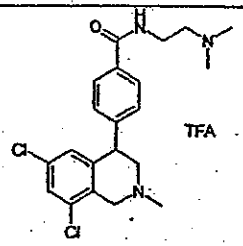
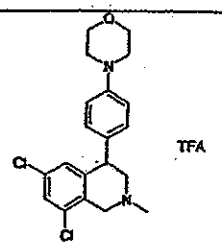
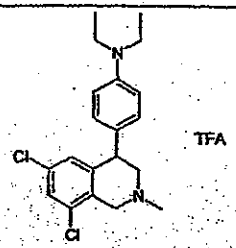
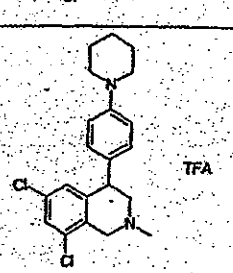
500 mg of ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate (compound of example 220) are dissolved in 15 ml of methanol, and 10 ml of 2 N of KOH are added. After one hour at 50°C, the mixture is concentrated in vacuo and the residue is partitioned between water and ether. The aqueous phase is adjusted to a pH of about 6 with 2 N HCl, and the resulting precipitate is filtered off with suction. Drying affords 304 mg of the title compound as a colorless solid.

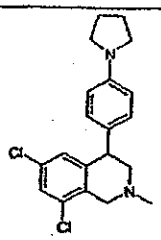
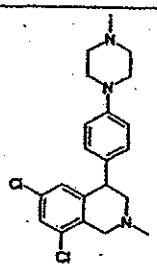
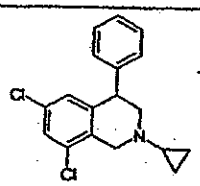
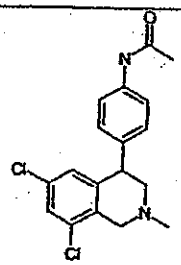
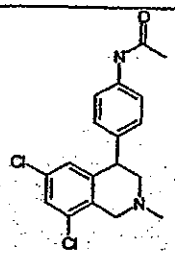
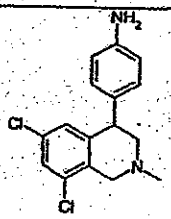
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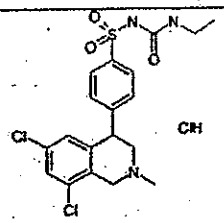
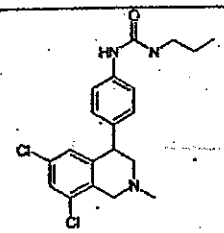
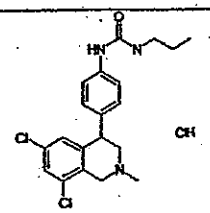
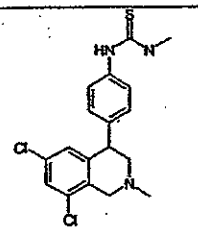
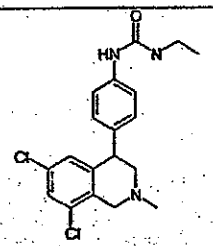
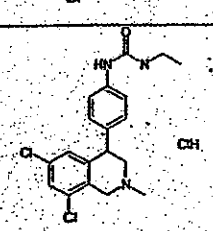
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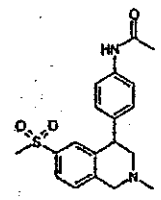
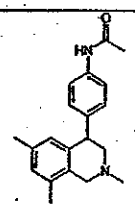
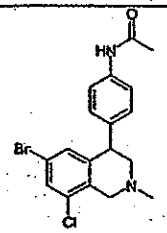
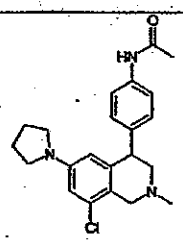
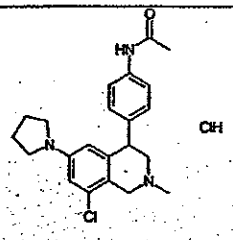
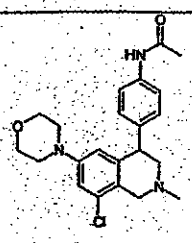
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1a		1,60	B	349,2/351,2	ESI	m.p.: 125 °C (decomp.)
2a		3,63	A	371,3/373,3 412,3/414,3	ESI	(+) enantiomer
2b		3,67	A	371,3/373,3 412,3/414,3	ESI	(+) enantiomer
2c		3,66	A	371,1/373,1 412,1/414,1	ESI	(-) enantiomer

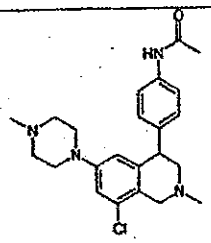
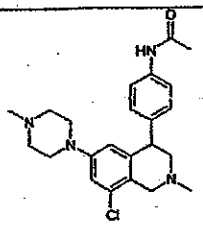
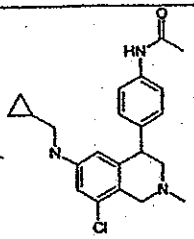
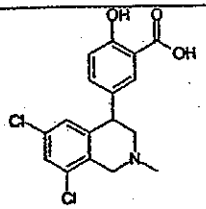
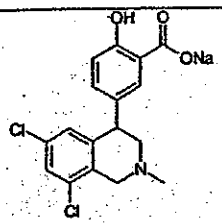
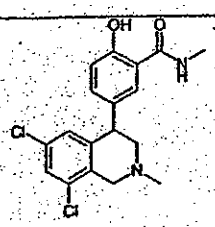
2d	 AcOH	1,56	B	371,1/373,1 412,1/414,1	ESI	(-) enantiomer
3	 ClH	4,00	A	399,1/401,1	Cl	
4a	 ClH	3,59	A	371,2/373,2 412,2/414,2	ESI	
4b	 AcOH	1,58	B	371,0/372,0/ 373,0/373,9	ESI	
5	 ClH	4,57	A	369,9/371,9/ 373,9	Cl	
6	 ClH	4,03	A	336,1/338,1	Cl	

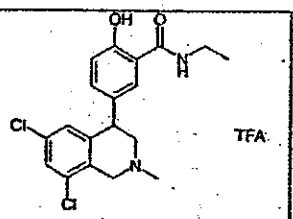
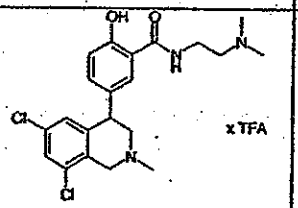
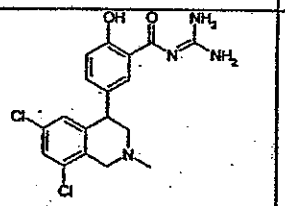
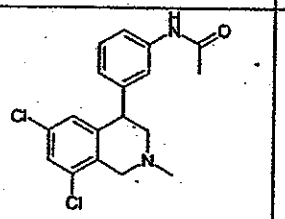
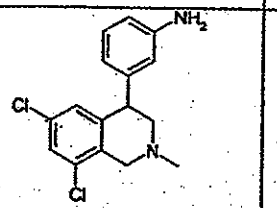
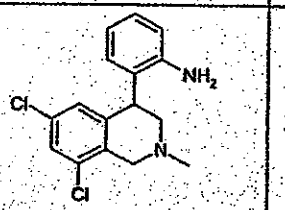
7	 TFA	4,17	A	363,3/365,3	Cl	
8	 TFA	1,88	B	377,3/379,3	Cl	
9	 TFA	1,45	B	406,3/408,3	Cl	
10	 TFA	4,37	A	377.1/379,1	Cl	
11	 TFA	4,05	A	363,2/365,2	ESI	
12	 TFA	3,79	A	375,2/377,2	ESI	

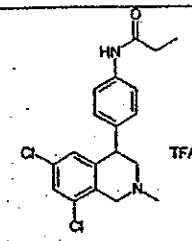
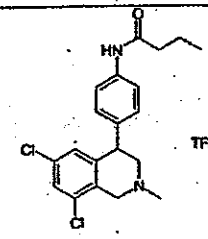
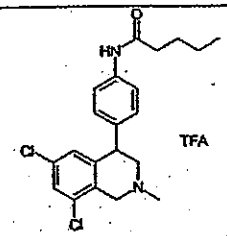
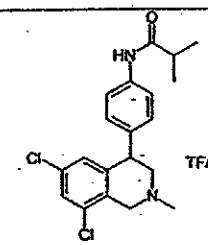
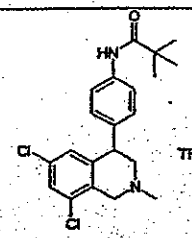
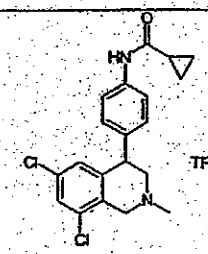
13	 CIH	4,92	A	361,2/363,2	ESI	
14	 TFA	4,08	A	390,2/392,2	ESI	
15	 TFA	4,80	A	318,2/320,2	Cl	
16a		1,61	B	349,1/350,1/ 351,1	ESI	(-) enantiomer
16b		1,61	B	349,1/350,1/ 351,1	ESI	(+) enantiomer
17	 x HCl	0,91	B	307,1/309,0	ESI	

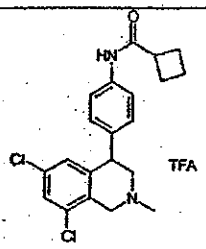
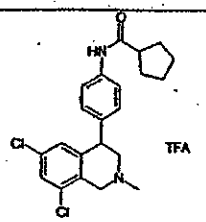
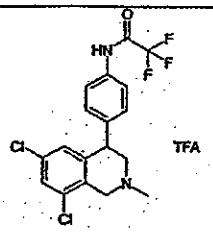
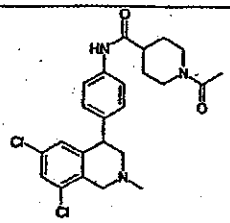
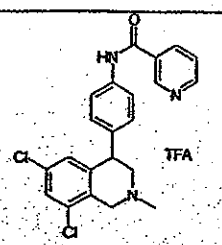
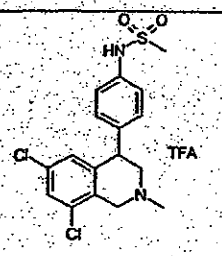
18		1,63	B	442,0/444,0	ESI	
19		4,00	A	392,2/394,2	ESI	
19a		1,80	B	392,1/394,1	ESI	
20		1,67	B	380,1/382,2	ESI	
21		1,68	B	378,3/380,2	ESI	m.p.: 218-220 °C
21a		1,68	B	378,1/379,1/ 380,1	ESI	

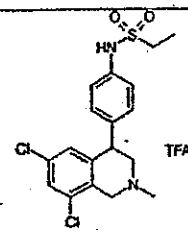
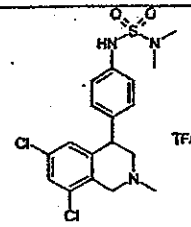
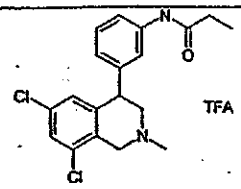
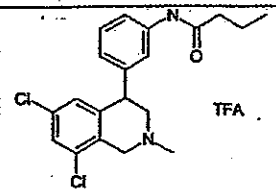
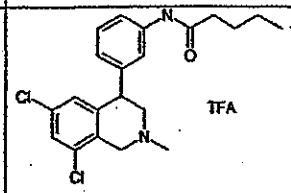
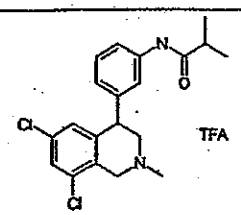
22		0,32	B	359,1 717,3/718,3/ 719,3	ESI	
23		1,60	B	309,2/310,1	ESI	
24		1,67	B	393,0/394,0/396,0/397,0	ESI	
25		1,85	B	384,1/386,1	ESI	
25a		1,78	B	384,1/385,1/ 386,2	ESI	
26		1,46	B	400,1/401,2/ 401,2	ESI	

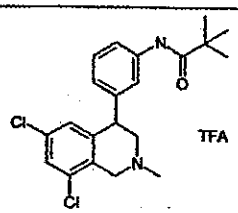
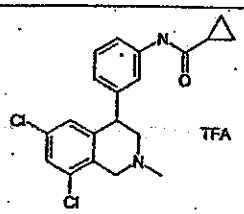
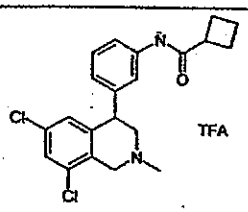
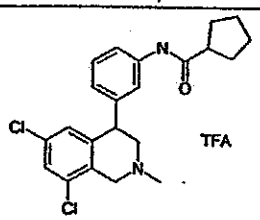
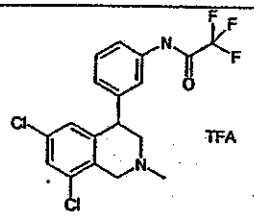
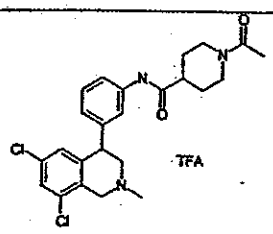
27		0.27	B	413,2/414,2/ 415,2	ESI	
27a	 xHCl	0,25	B	413,2/414,2/ 415,2	ESI	
28	 xHCl	1,65	B	384,2/385,2 386,2	ESI	
29		1,67	B	352,0/353,0/ 354,0	ESI	
29a		1,68	B	352,0/353,0/ 354,0	ESI	
30	 TFA-	1,68	B	365,1/366,1/ 367,0/368,0	ESI	

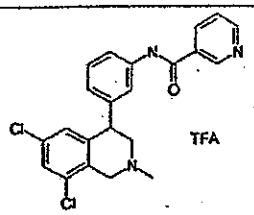
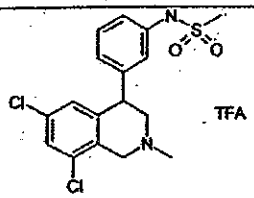
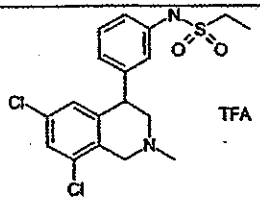
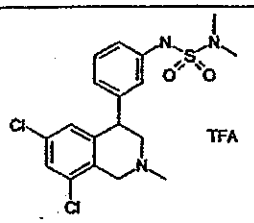
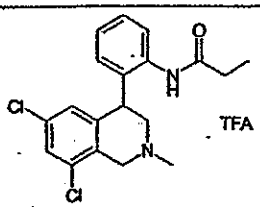
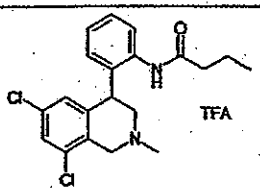
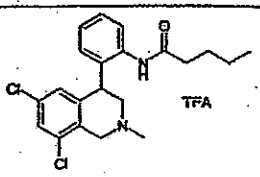
31	 TFA	1,79	B	379,1/380,1/ 381,1	ESI	
32	 xTFA	1,47	B	422,1/423,1/ 424,1/425,1	ESI	
33		1,46	B	393,1/394,1/ 395,1	ESI	
34		1,63	B	349,0/350,1/ 351,0	ESI	
35		1,17	B	307,0/308,1/ 309,1	ESI	
36		1,66	B	307,0/308,0/ 309,1	ESI	

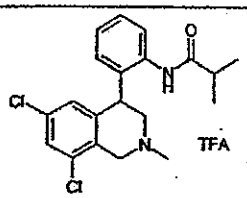
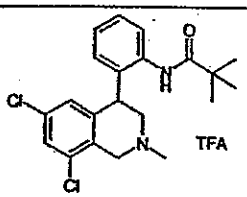
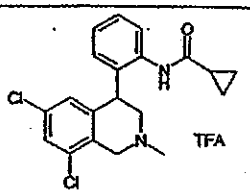
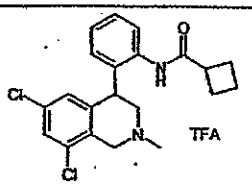
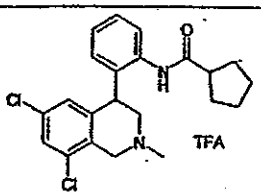
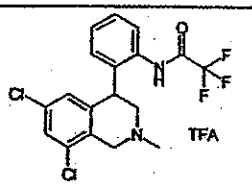
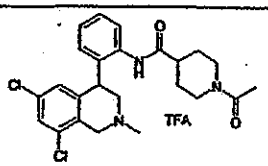
37		2,35	C	363,3/365,3	ESI	
38		2,43	C	377,3/379,3	ESI	
39		2,49	C	391,3/393,3	ESI	
40		2,43	C	377,3/379,3	ESI	
41		2,48	C	391,3/393,3	ESI	
42		2,40	C	375,3/377,3	ESI	

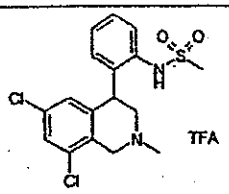
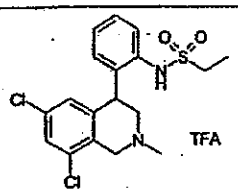
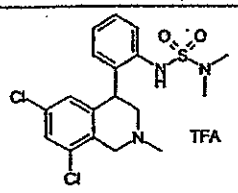
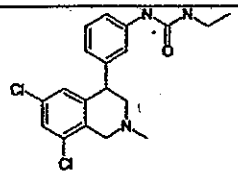
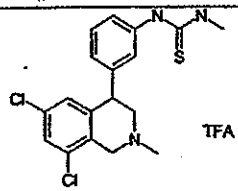
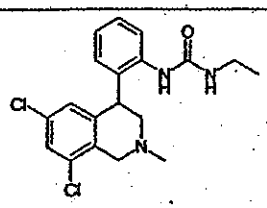
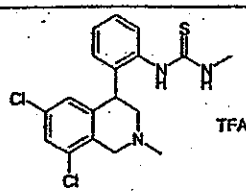
43		2,45	C	389,3/391,3	ESI	
44		2,52	C	403,4/405,4	ESI	
45		2,49	C	403,2/404,2	ESI	
46		2,36	C	460,4/462,4	ESI	
47		2,35	C	412,2/414,3	ESI	
48		2,29	C	385,3/387,3	ESI	

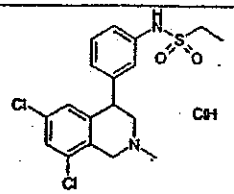
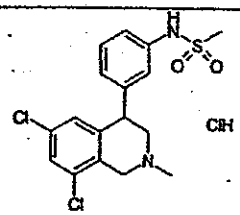
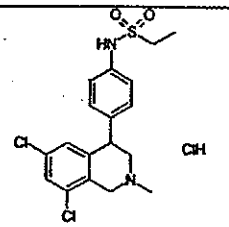
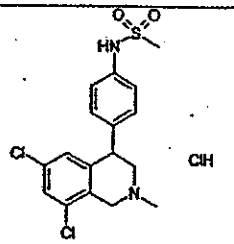
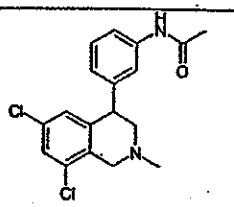
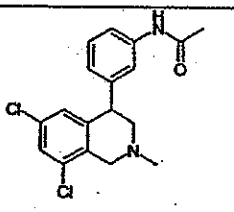
49	 TFA	2,37	C	399,3/401,3	ESI	
50	 TFA	2,42	C	414,4/416,4	ESI	
51	 TFA	2,37	C	363,3/365,3	ESI	
52	 TFA	2,44	C	377,3/379,3	ESI	
53	 TFA	2,51	C	391,3/393,3	ESI	
54	 TFA	2,44	C	377,3/379,3	ESI	

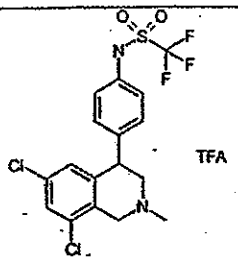
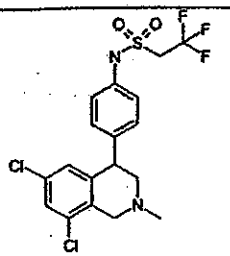
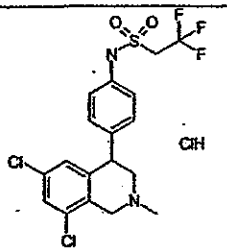
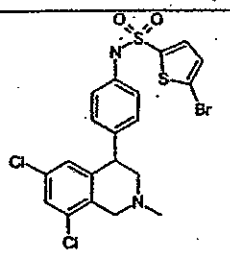
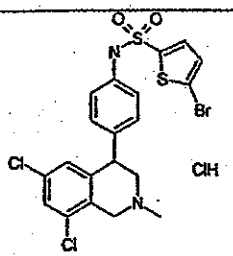
55	 TFA	2,49	C	391,3/393,3	ESI	
56	 TFA	2,41	C	375,3/377,3	ESI	
57	 TFA	2,47	C	389,3/391,3	ESI	
58	 TFA	2,52	C	403,4/405,4	ESI	
59	 TFA	2,48	C	403,2/404,2	ESI	
60	 TFA	2,34	C	460,4/462,4	ESI	

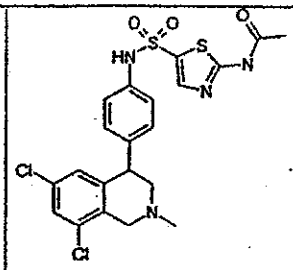
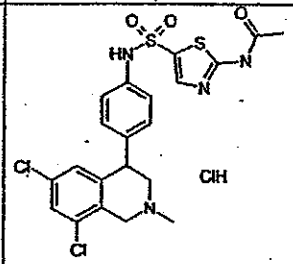
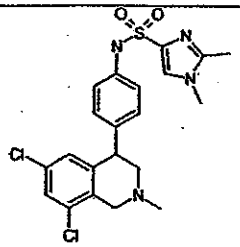
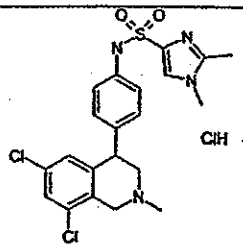
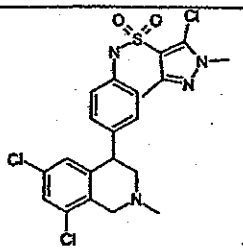
61		2,36	C	412,2/414,3	ESI	
62		2,32	C	385,3/387,3	ESI	
63		2,38	C	399,3/401,3	ESI	
64		2,41	C	414,4/416,4	ESI	
65		2,30	C	363,3/365,3	ESI	
66		2,41	C	377,3/379,3	ESI	
67		2,52	C	391,3/393,3	ESI	

68		2,41	C	377,3/379,3	ESI	
69		2,45	C	391,3/393,3	ESI	
70		2,36	C	375,3/377,3	ESI	
71		2,44	C	389,3/391,3	ESI	
72		2,51	C	403,4/405,4	ESI	
73		2,70	C	403,2/404,2	ESI	
74		2,30	C	460,4/462,4	ESI	

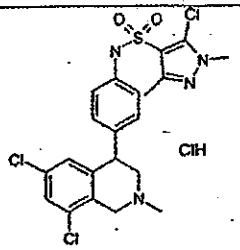
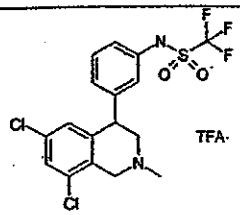
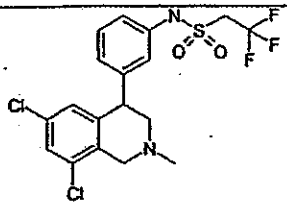
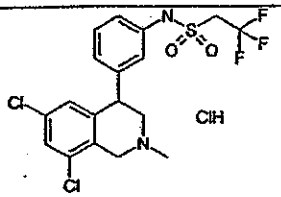
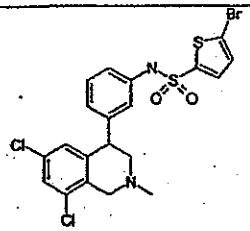
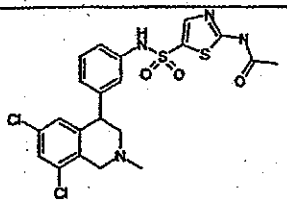
75	 TFA	2,41	C	385,3/387,3	ESI	
76	 TFA	2,49	C	399,3/401,3	ESI	
77	 TFA	2,55	C	414,4/416,4	ESI	
78		1,72	B	378,3/380,3	ESI	
79	 TFA	1,74	B	380,3/382,3	ESI	
80		1,75	B	378,3/380,3	ESI	
81	 TFA	1,68	B	380,3/382,3	ESI	

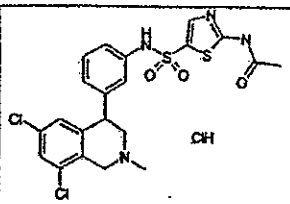
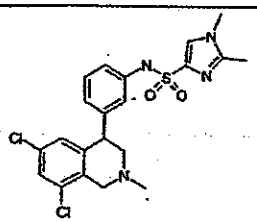
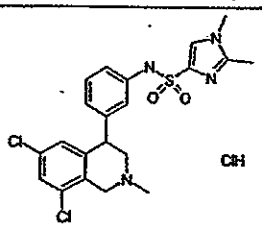
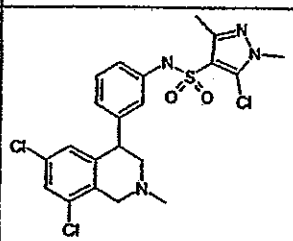
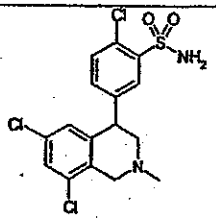
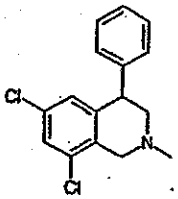
82		1,71	B	399,0/400,0/ 401,0/402,0/ 403,0	ESI	
83		1,66	B	385,0/386,0/ 387,0	ESI	
84		1,69	B	399,0/400,0/ 401,0/402,0	ESI	
85		1,64	B	385,0/386,0/ 387,0/388,0	ESI	
86a		1,64	B	349,3/351,3	ESI	(-) Enantiomer
86b		1,63	B	349,3/351,3	ESI	(+) Enantiomer

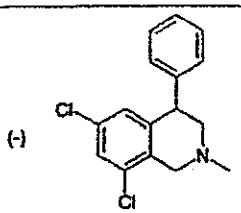
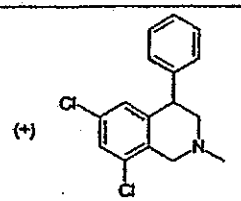
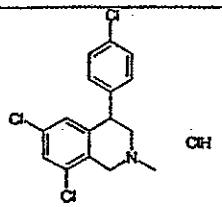
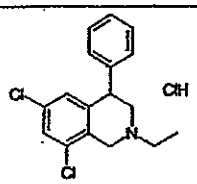
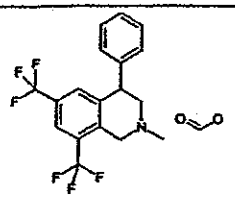
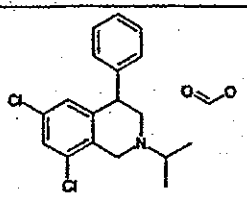
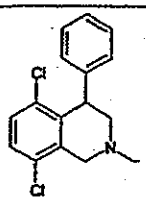
87	 TFA	1,97	B	439,0/441,1	ESI	
88		1,83	B	453,0/455,0	ESI	
88a	 ClH	1,83	B	453,0/455,0	ESI	
89		2,01	B	531,0/533,0/ 534,9	ESI	
89a	 ClH	2,02	B	531,0/533,0/ 534,9	ESI	

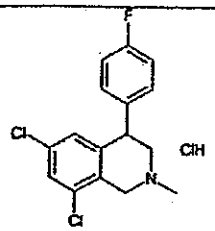
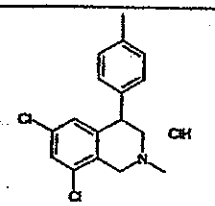
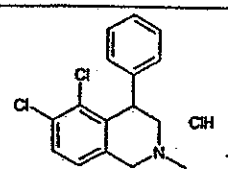
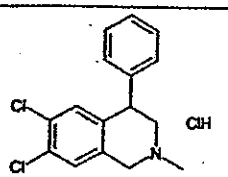
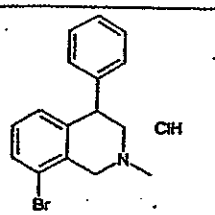
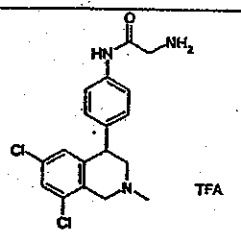
90		1,78	B	525,1/527,1	ESI	
90a		1,79	B	525,1/527,1	ESI	
91		1,63	B	465,1/467,1	ESI	
91a		1,64	B	465,1/467,1	ESI	
92		1,81	B	499,1/501,1/ 503,1	ESI	

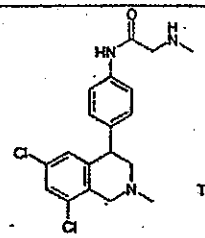
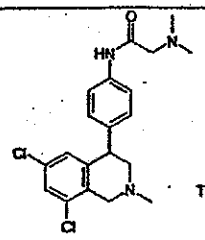
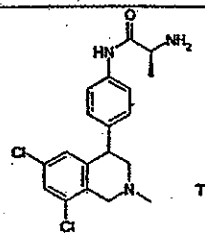
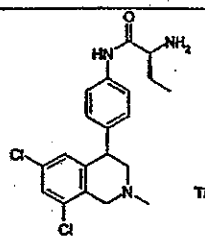
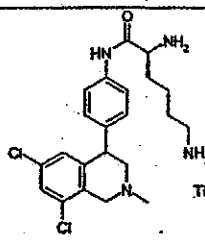
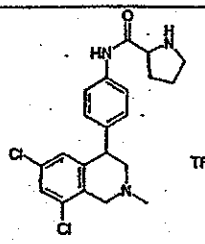
191

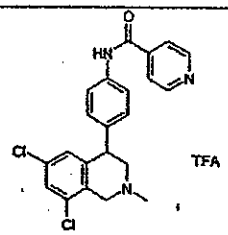
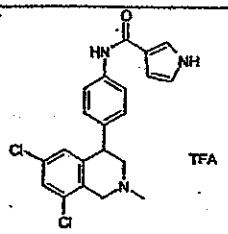
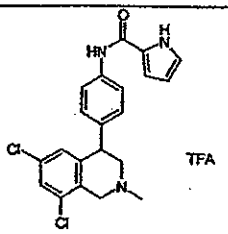
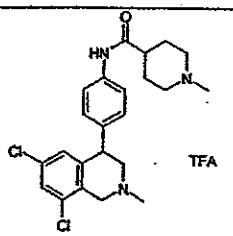
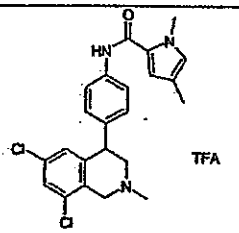
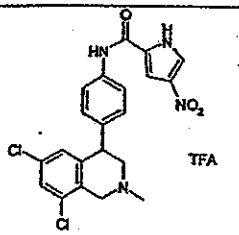
92a	 ClH	1,82	B	499,1/501,1/ 503,1	ESI	
93	 TFA	1,99	B	439,0/441,1	ESI	
94		1,87	B	453,0/455,0	ESI	
94a	 ClH	1,87	B	453,0/455,0	ESI	
95		2,01	B	531,0/533,0/ 535,0	ESI	
96		1,75	B	525,0/527,0	ESI	

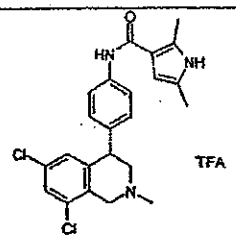
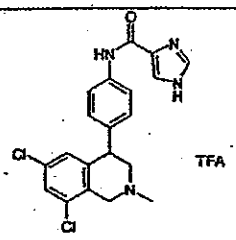
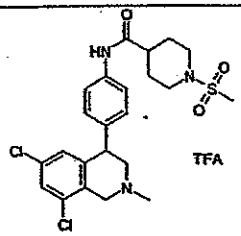
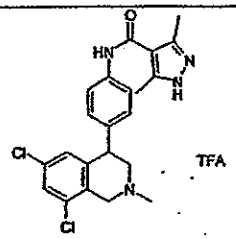
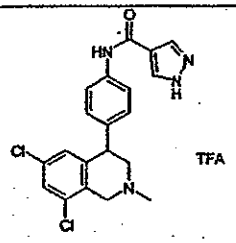
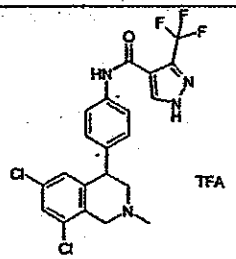
96a		1,75	B	525,0/527,0	ESI	
97		1,66	B	465,0/467,0	ESI	
97a		1,66	B	465,0/467,0	ESI	
98		1,81	B	499,1/501,1/ 503,1	ESI	
99				405,1/407,1	ESI	m.p.: 122 °C
100		4,44	A	292,2/294,2	CI	see Ex. 2; intermediate 4

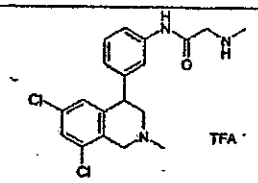
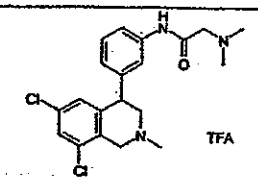
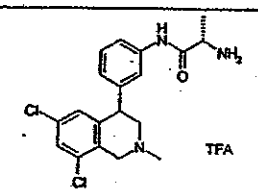
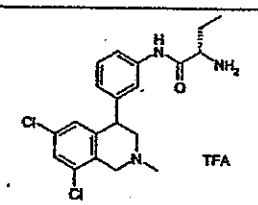
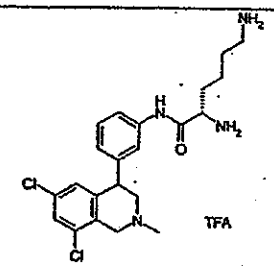
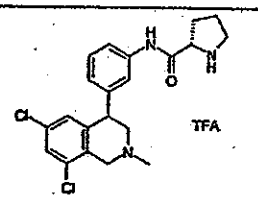
100a	 (-) TFA					see Ex. 2; intermediate 4a
100b	 (+) TFA					see Ex. 2; intermediate 4b
101	 ClH	4,43	A	326,0/328,0	ESI	
102	 ClH	4,23	A	306,1/308,0	ESI	
103		2,84	C	360,0	ESI	
104		2,79	C	320,0/322,0	ESI	
105		2,64	C	291,9/293,9	ESI	

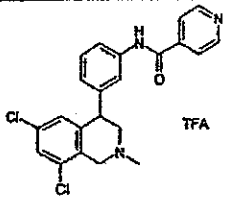
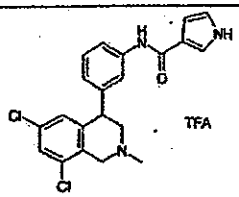
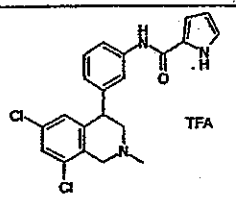
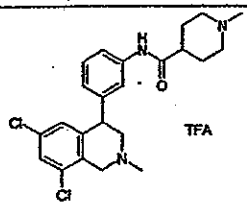
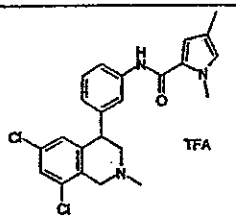
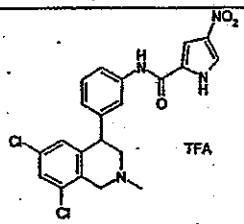
106		4,26	A	310,0/312,0	ESI	
107		4,43	A	306,1/308,1	ESI	
108		4,11	A	292,0/294,0	ESI	
109		4,28	A	292,0/294,0	ESI	
110		4,05	A	302,0/304	ESI	
111		1,37	D	364,4/366,4	ESI	

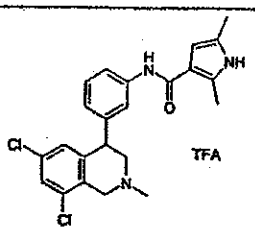
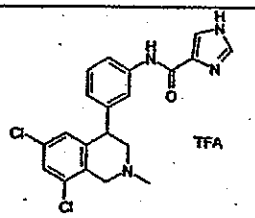
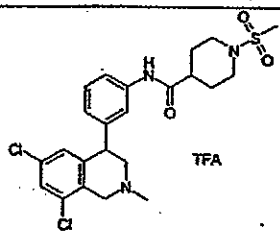
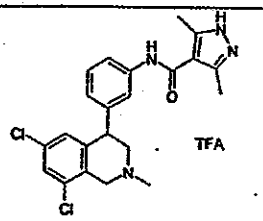
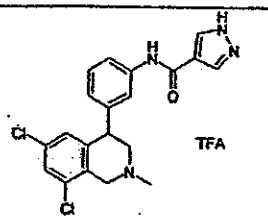
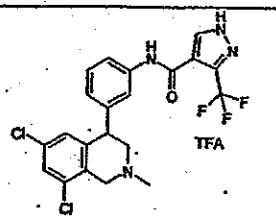
112		1,44	D	378,4/380,4	ESI	
113		1,51	D	392,4/394,4	ESI	
114		1,51	D	378,3/380,3	ESI	
115		1,58	D	392,4/394,4	ESI	
116		1,04	D	435,5/437,5	ESI	
117		1,67	D	404,4/406,4	ESI	

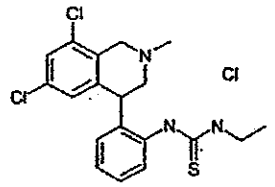
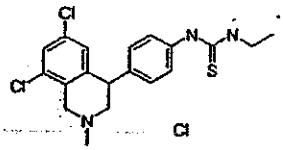
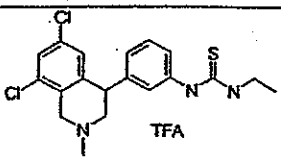
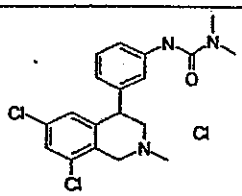
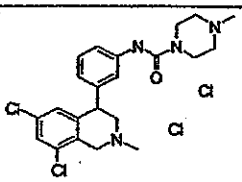
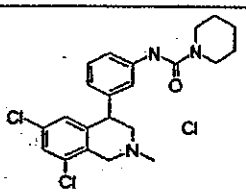
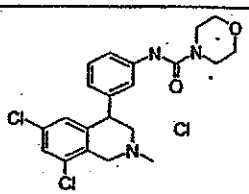
118		2,08	D	412,3/414,3	ESI	
119		2,27	D	400,4/402,4	ESI	
120		2,37	D	400,4/402,4	ESI	
121		1,54	D	432,5/434,5	ESI	
122		1,70	D	428,5/430,5	ESI	
123		2,55	D	445,4/447,4	ESI	

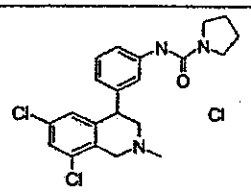
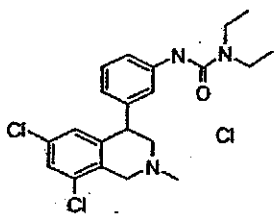
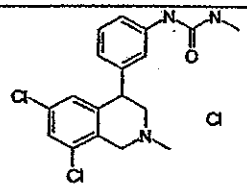
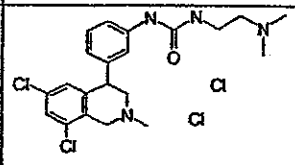
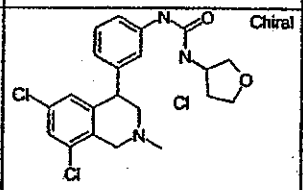
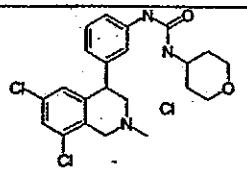
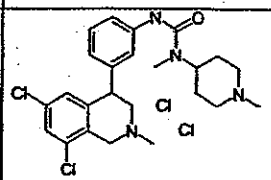
124		2,43	D	428,5/430,5	ESI	
125		1,88	D	401,4/403,4	ESI	
126		2,31	D	496,5/498,5	ESI	
127		2,14	D	429,4/431,4	ESI	
128		2,07	D	401,4/403,4	ESI	
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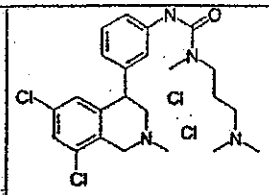
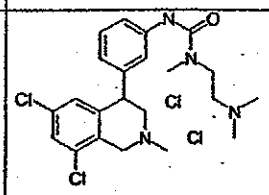
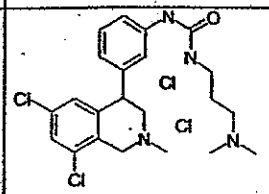
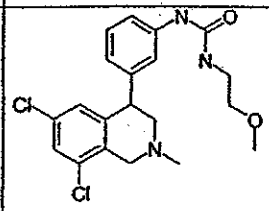
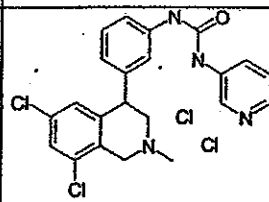
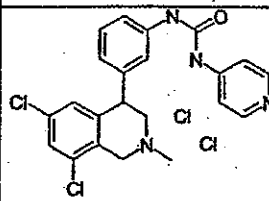
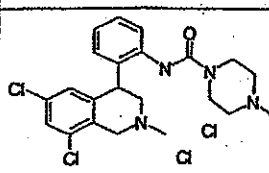
130		1,55	D	378,4/380,4	ESI	
131		1.52	D	392,4/394,4	ESI	
132		1,63	D	378,3/380,3	ESI	
133		1,64	D	392,4/394,4	ESI	
134		1,14	D	435,5/437,5	ESI	
135		1,62	D	404,4/406,4	ESI	

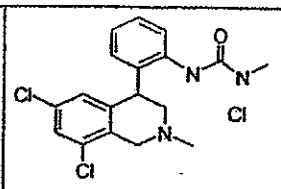
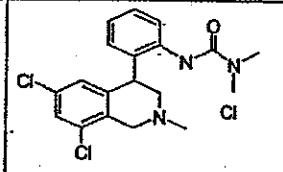
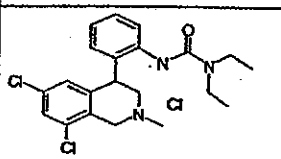
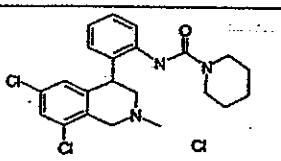
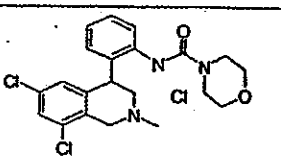
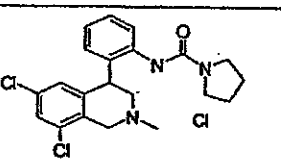
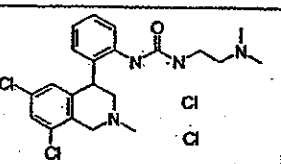
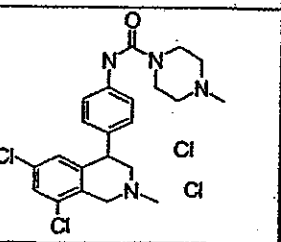
136		2,16	D	412,3/414,3	ESI	
137		2,31	D	400,4/402,4	ESI	
138		2,41	D	400,4/402,4	ESI	
139		1,62	D	432,5/434,5	ESI	
140		1,75	D	428,5/430,5	ESI	
141		2,54	D	445,4/447,4	ESI	

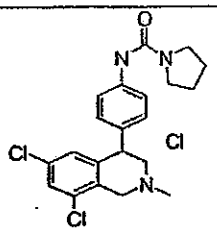
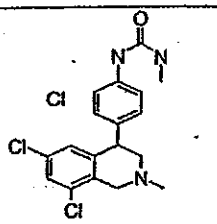
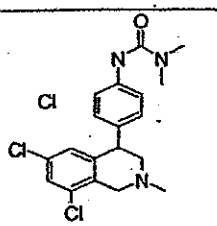
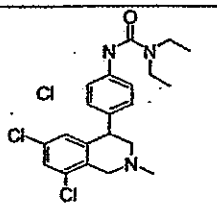
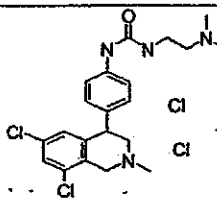
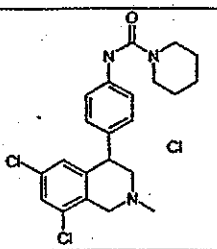
142		2,50	D	428,5/430,5	ESI	
143		1,95	D	401,4/403,4	ESI	
144		2,34	D	496,5/498,5	ESI	
145		2,31	D	429,4/431,4	ESI	
146		2,11	D	401,4/403,4	ESI	
147		2,48	D	469,4/471,4	ESI	

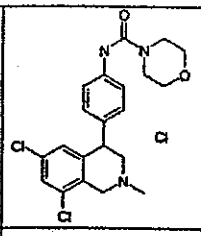
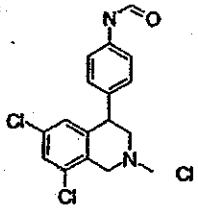
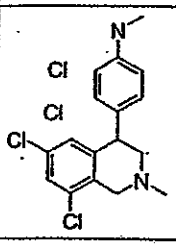
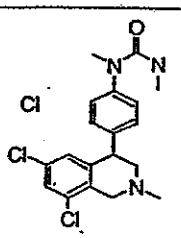
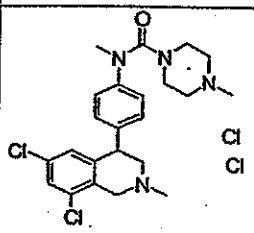
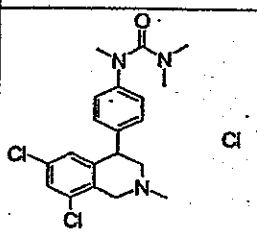
148		2,36	B	394,2	ESI	
149		2,35	B	394,2	ESI	
150		2,35	B	394,2	ESI	
151		2,15	B	378,2	ESI	
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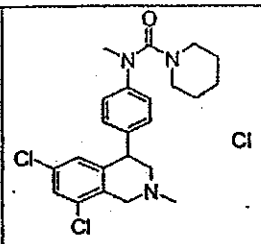
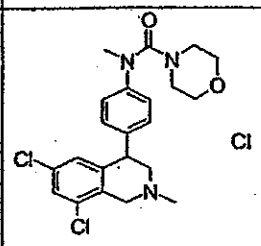
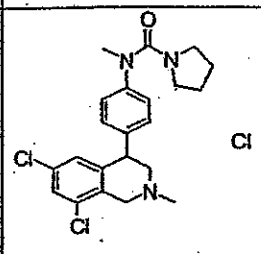
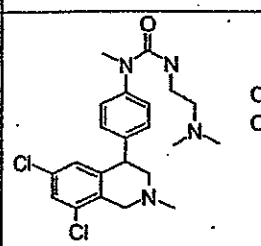
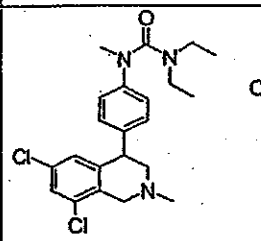
155		2,34	B	404,2	ESI	
156		2,43	B	406,2	ESI	
157		2,12	B	364,2	ESI	
158		1,65	B	421,2	ESI	
159		2,23	B	420,3	ESI	Chiral
160		2,25	B	434,3	ESI	
161		1,72	B	461,4	ESI	

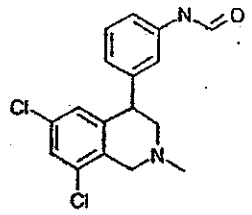
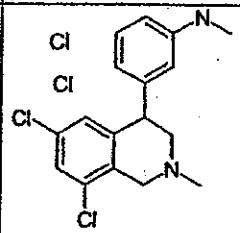
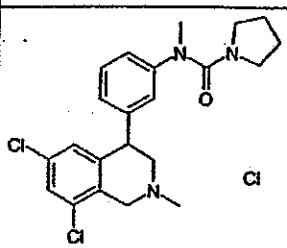
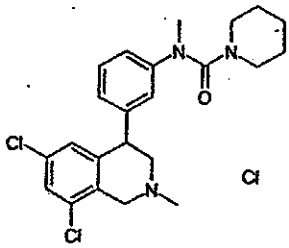
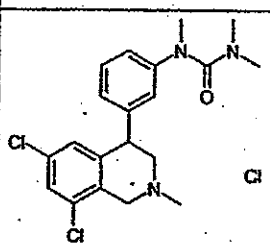
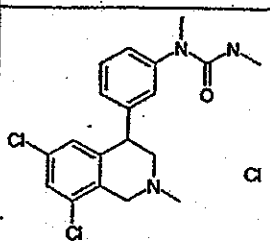
162		1,68	B	449,4	ESI	
163		1,62	B	435,3	ESI	
164		1,71	B	435,3	ESI	
165		2,21	B	408,3	ESI	
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168		1,59	B	433,3	ESI	

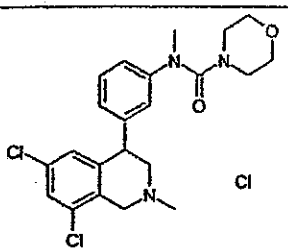
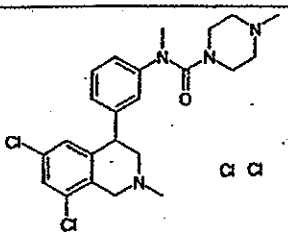
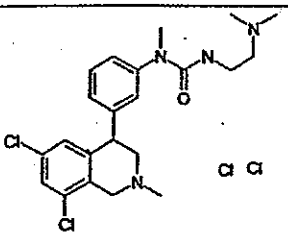
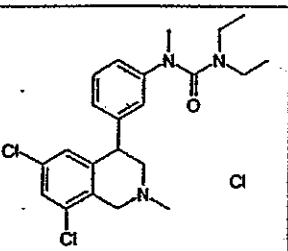
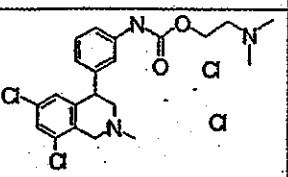
169		2,12	B	364,2	ESI	
170		2,12	B	378,2	ESI	
171		2,34	B	406,3	ESI	
172		2,44	B	418,3	ESI	
173		2,11	B	420,3	ESI	
174		2,25	B	404,3	ESI	
175		0,90	B	421,5	ESI	
176		1,52	B	433,3	ESI	

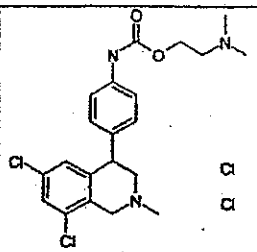
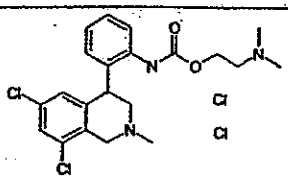
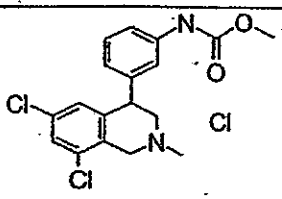
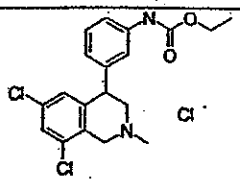
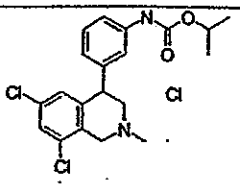
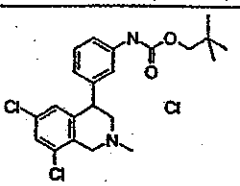
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178		2,11	B	364,2	ESI	
179		2,17	B	378,3	ESI	
180		2,51	B	406,3	ESI	
181		1,59	B	421,2	ESI	
182		2,47	B	418,2	ESI	

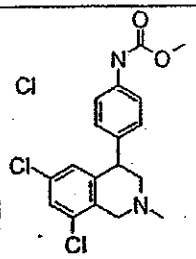
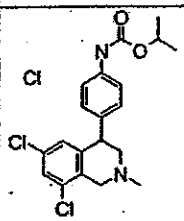
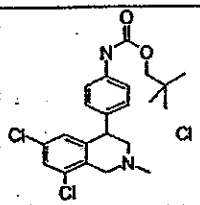
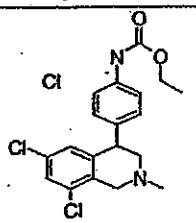
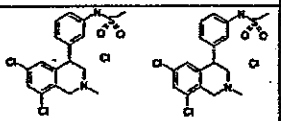
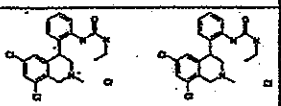
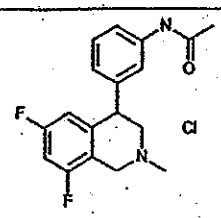
183		2,16	B	420,2	ESI	
184		2,02	B	335,2	ESI	
185		1,92	B	321,2	ESI	
186		1,05	C	378,4	ESI	
187		0,92	C	447,5	ESI	
188		1,10	C	392,5	ESI	

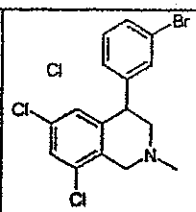
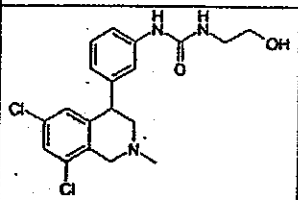
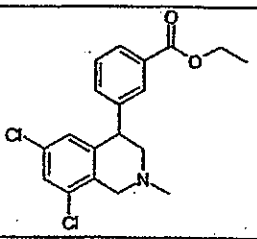
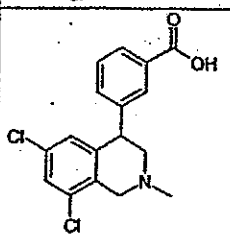
189	 Cl	1,24	C	432,5	ESI	
190	 Cl	1,10	C	434,5	ESI	
191	 Cl	1,15	C	418,4	ESI	
192	 ClH ClH	0,93	C	435,4	ESI	
193	 ClH	1,22	C	420,5	ESI	

194		2,04	C	335,4	ESI	
195		0,90	C	321,3	ESI	
196		2,48	B	418,3	ESI	
197		2,62	B	432,3	ESI	
198		2,32	B	392,3	ESI	
199		2,19	B	378,2	ESI	

200		2,16	B	434,3	ESI	
201		1,61	B	447,4	ESI	
202		1,59	B	435,3	ESI	
203		2,57	B	420,3	ESI	
204		1,71	B	422,2	ESI	

205		1,70	B	422,3	ESI	
206		1,68	B	422,3	ESI	
207		2,34	B	365,1	ESI	
208		1,18	C	379,4	ESI	
209		1,24	C	393,4	ESI	
210		1,38	C	421,5	ESI	

211		1,13	C	365,4	ESI	
212		1,26	C	393,4	ESI	
213		1,40	C	421,5	ESI	
214		1,20	C	379,4	ESI	
215a 215b				385,2	ESI	
216a 216b				378,1	ESI	
217		1,86	B	317,2	ESI	

218		1,27	C	370,2	ESI	
219		0,99	B1	394,1/396,2	ESI	
220		1,24	B1	364,1/366,1	ESI	
221		1,02	B1	336,1/338,1	ESI	

Pharmacological data:

Description of test:

In this test, the recovery in the intracellular pH (pH_i) after an acidification is ascertained, which is initiated if the NHE is capable of functioning, even under bicarbonate-free conditions. For this purpose, the pH_i was determined using the pH-sensitive fluorescent dye BCECF (Calbiochem, the precursor BCECF-AM is employed). The cells were initially loaded with BCECF. The BCECF fluorescence was determined in a "Ratio Fluorescence Spectrometer" (Photon Technology International, South Brunswick, N.J., USA) at excitation wavelengths of 505 and 440 nm and an emission wavelength of 535 nm and converted into the pH_i using calibration curves. The cells were incubated in NH_4Cl buffer (pH 7.4) (NH_4Cl buffer: 115 mM NaCl, 20 mM NH_4Cl, 5 mM KCl, 1 mM $CaCl_2$, 1 mM $MgSO_4$, 20 mM Hepes, 5 mM glucose, 1 mg/ml BSA; a pH of 7.4 is adjusted with 1 M NaOH) even during the BCECF loading.

The intracellular acidification was induced by adding 975 µl of an NH_4Cl-free buffer (see below) to 25 µl aliquots of the cells incubated in NH_4Cl buffer. The subsequent rate of pH recovery was recorded for two minutes with NHE1, five minutes with NHE2 and three minutes with NHE3. To calculate the inhibitory potency of the tested substances, the cells were initially investigated in buffers with which a complete or absolutely no pH recovery took place. For complete pH recovery (100%), the cells were incubated in Na^+-containing buffer (133.8 mM NaCl, 4.7 mM KCl, 1.25 mM $CaCl_2$, 1.25 mM $MgCl_2$, 0.97 mM Na_2HPO_4, 0.23 mM NaH_2PO_4, 5 mM Hepes, 5 mM glucose, a pH of 7.0 is adjusted with 1 M NaOH). To determine the 0% value, the cells were incubated in an Na^+-free buffer (133.8 mM choline chloride, 4.7 mM KCl, 1.25 mM $CaCl_2$, 1.25 mM $MgCl_2$, 0.97 mM K_2HPO_4, 0.23 mM KH_2PO_4, 5 mM Hepes, 5 mM glucose, a pH of 7.0 is adjusted with 1 M NaOH). The substances to be tested were made up in the Na^+-containing buffer. The recovery of the intracellular pH at each test concentration of a substance was expressed as a percentage of the maximum recovery. The IC_{50} value for the particular substance for the individual NHE subtypes was calculated from the pH recovery percentages using the Sigma-Plot program.

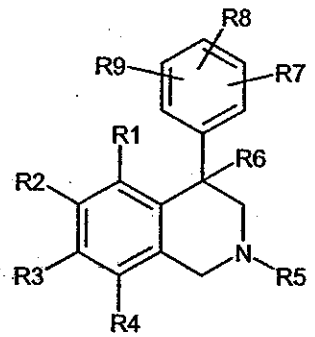
Results:

Table 14:

Example	IC_{50} [μM], (rNHE3)	Example	IC_{50} [μM], (rNHE3)
1a	0.075	119	0.0682
2a	0.082	144	0.695
2b	0.026	146	0.024
6	0.670	153	0.602
7	0.250	183	0.597
10	1.000	199	0.252
17	0.049	207	0.186
21	0.814		
23	1.507		
24	0.340		
29	0.318		
36	0.274		
48	0.349		
51	0.215		
60	0.202		
64	0.507		
81	0.730		
87	0.418		
97	0.308		
113	0.279		

Patent claims

1. A 4-phenyltetrahydroisoquinoline of the formula I



I

in which the meanings are:

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, $C_{qq}H_{2qq-1}$, OC_bH_{2b+1}, COOR10, OCOR10, COR10 or O_x-$(CH_2)_y$-phenyl;

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

qq 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms,

x zero or 1;

y zero, 1, 2, 3 or 4;

where the phenyl ring in the group O_x-$(CH_2)_y$-phenyl is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CN, NO_2, OH, NH_2 or C_dH_{2d+1};

d 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms,

or

R1, R2, R3 and R4

independently of one another heteroaryl, it being possible for zero, 1, 2, 3 or 4 N atoms, zero or 1 oxygen atom or zero or 1 S atom to be present as ring atoms;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3, 4, 5, 6, 7 or 8,

rr 3, 4, 5, 6, 7, or 8,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR13;

R13 H or C_fH_{2f+1};

f 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R13 and a CH_2 group of R11 or R12 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R11 and R12

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R11 and R12

independently of one another COR14, CSR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms, and it being

possible for one or more CH_2 groups to be replaced by O or NR13,

or

R1, R2, R3 and R4

independently of one another $-O_h-SO_j-R15$, with

h zero or 1;

j zero, 1 or 2;

R15 C_kH_{2k+1}, OH, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O, CO, CS or NR19;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R19 and a CH_2 group with R17 or R18 together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H,

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$, COR20 or SO_2R20;

p 1, 2, 3, 4, 5, 6, 7 or 8,

ss 3, 4, 5, 6, 7 or 8,

R20 C_qH_{2q+1};

q 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in the groups C_pH_{2p+1}, $C_{ss}H_{2ss-1}$ and C_qH_{2q+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR21;

R21 H or C_rH_{2r+1};

r 1, 2, 3 or 4;

it being possible for one or more H atoms in C_rH_{2r+1} to be replaced by F atoms;

R6 H, F, Cl, Br, I, C_sH_{2s+1}, $C_{dd}H_{2dd-1}$, OH, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

dd 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in C_sH_{2s+1}, $C_{dd}H_{2dd-1}$ and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another $-O_v-SO_w-R23$;

v zero or 1;

w zero, 1 or 2;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, OH, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8,

mm 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, $C_{zz}H_{2zz-1}$;

z 1, 2, 3, 4, 5, 6, 7 or 8;

zz 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms and,

in C_zH_{2z+1}, it being possible for one or more H atoms to be replaced by F atoms and it being possible for one or more CH_2 groups to be replaced by O, CO, CS or NR27;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_{bb}R30$;

R30 H, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

bb 2 or 3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6, 7 or 8;

h 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 forms together with a CH_2 group of R30 a 5-, 6- or 7-membered ring;

or

R30 a 5- or 6-membered heteroaryl with 1, 2, 3 or 4 N atoms, zero or 1 S atoms and zero or 1 O atoms,

which is unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71;

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ and COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

ww 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR44;

R44 H or $C_{gg}H_{2gg+1}$;

gg 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{gg}H_{2gg+1}$ to be replaced by F atoms, and it being possible for R44 together with a (CH_2) group of R40 or R41 and the N atom to which they are jointly bonded to form a 5- or 6-membered ring;

or

R40 and R41

with the N atom to which they are bonded a 5- or 6-membered ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$; and the pharmaceutically acceptable salts and trifluoroacetates thereof.

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

R1, R2, R3 and R4

independently of one another, H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1}, COOR10;

a and b

independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another 5- or 6-membered heteroaryl selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl and oxazolyl;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms

or

R11 and R12

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R11 and R12

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R_{15}, with

R15 C_kH_{2k+1}, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H, C_mH_{2m+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO and the second CH_2 group is replaced by NR19;

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H,

R5 H, C_pH_{2p+1};

p 1, 2, 3 or 4;

it being possible for one or more H atoms in C_pH_{2p+1} to be replaced by F atoms;

R6 H, C_sH_{2s+1}, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in C_sH_{2s+1} and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4 or 5,

mm 3, 4, 5 or 6,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6;

h 1, 2, 3 or 4;

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups

$C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 a 5- or 6-membered heteroaromatic system selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thienyl, thiazolyl and oxazolyl,

which are unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71,

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ or COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42;

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

to be selected independently of one another hydroxyethyl, , N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methyl-piperazine, piperazine and morpholine;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

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

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H;

R5 methyl or trifluoromethyl;

R6 H;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, methyl or CF_3;

cc 1, 2, 3, 4, 5 , 6, 7 or 8;

yy 3, 4, 5, 6;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3

substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3,

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of CONR40R41, $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$; and the pharmaceutically acceptable salts and trifluoroacetates thereof.

4. A compound of the formula I as claimed in claims 1-3 in which the meanings are:
R1, R2, R3 and R4

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

but where R2 must always not be equal to H;

R5 methyl or trifluoromethyl;

R6 H;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, methyl or CF_3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5 or 6;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a CH_2 group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3 substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$, or $C(NH)NH_2$;

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms;

but where two substituents from the group of R7, R8 and R9 may not simultaneously be OH or OCH_3,

and where at least one of the radicals R7, R8 or R9 must be selected from the group consisting of $-O_vSO_wR23$, NR32COR30, NR32CSR30 and $NR32SO_{bb}R30$;

and the pharmaceutically acceptable salts and trifluoroacetates thereof.

5. A compound of the formula I characterized in that it is selected from the group consisting of:

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N,N-dimethyl-benzenesulfonamide;
5) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
8) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
10) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
11) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-phenyl]-diethyl-amine
12) 6,8-dichloro-2-methyl-4-(4-piperidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
13) 6,8-dichloro-2-methyl-4-(4-pyrrolidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
14) 6,8-dichloro-2-methyl-4-[4-(4-methyl-piperazin-1-yl)-phenyl]-1,2,3,4-tetrahydro-isoquinoline;
15) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
16) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

17) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propylurea;

18) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

19) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

20) N-[4-(6-methanesulfonyl-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

21) N-[4-(2,6,8-trimethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

22) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

23) N-[4-(8-chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

24) N-[4-(8-chloro-2-methyl-6-morpholin-4-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

25) N-{4-[8-chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

26) N-{4-[8-chloro-6-(cyclopropylmethyl-amino)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

27) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;

28) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-N-methyl-benzamide;

29) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-ethyl-2-hydroxy-benzamide;

30) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;

31) N-[5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoyl]-guanidine;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

33) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

34) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
36) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;
37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]pentanamide;
38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;
39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;
40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;
41) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;
42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;
43) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;
44) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;
45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;
46) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;
47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;
48) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;
49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

61) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

62) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

63) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

64) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

65) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

66) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

67) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]cyclopropanecarbox-amide;

69) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-cyclobutanecarboxamide;

70) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

71) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

72) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

73) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

74) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

75) N',N'-dimethylamino-N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

78) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

80) N-{5-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

81) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

82) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

83) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

84) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

85) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

87) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

88) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

90) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoroethanesulfonamide;

91) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-ethanesulfonamide;

92) N-ethyl-N'-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

93) 2-chloro-5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

94) 2-methyl-4-phenyl-6,8-bis-trifluoromethyl-1,2,3,4-tetrahydro-isoquinoline;

95) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

96) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

97) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

98) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

99) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

100) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

101) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

102) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

103) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

104) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

105) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

106) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

107) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

108) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

109) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

110) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

111) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

112) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

113) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

114) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

115) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

116) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

117) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

118) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

119) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

120) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

121) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

122) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

123) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

124) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

125) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

126) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

127) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

128) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

129) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

130) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

131) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

132) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

133) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

134) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

135) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

136) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

137) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

138) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

139) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

140) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

141) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

142) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

143) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

144) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

145) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

146) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

147) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

148) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

149) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

150) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

151) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

152) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

153) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

154) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

155) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

156) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

157) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

158) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

159) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

160) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

161) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

162) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

163) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

164) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

165) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

166) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

167) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

168) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

169) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

170) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

171) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

172) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

173) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

174) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

175) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

176) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

177) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

178) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

179) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

180) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

181) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

182) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

183) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

184) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

185) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

186) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

187) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

188) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

189) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

190) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

191) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

192) ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

193) isopropyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

194) 2,2-dimethyl-propyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

195) methyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

196) isopropyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

197) 2,2-dimethyl-propyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

198) ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

199) (R)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

200) (S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

201) (R)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

202) (S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

203) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

204) 4-(3-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline;

205) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

206) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;

207) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.

and the pharmaceutically acceptable salts thereof.

and from the pharmaceutically acceptable salts thereof.

6. A compound of the formula I as claimed in claim 1, selected from the group consisting of:

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;
5) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;
6) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
7) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
8) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
9) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;
10) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;
11) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;
12) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;
13) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
14) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;
15) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;
16) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;
17) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;
18) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

19) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

20) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

21) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

22) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;

23) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

24) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

25) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

26) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

27) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

28) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

29) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

30) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

31) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

32) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

33) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

34) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

36) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-carboxamide;

41) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

42) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

43) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

44) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

45) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

46) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

47) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

48) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-carboxamide;

51) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

52) N-[3-(6,8-dichloro-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

56) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

57) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

58) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

59) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

60) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

61) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

62) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

63) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

64) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-diethylamino-propyl)-urea;

65) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

66) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl)-urea;

67) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

69) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

70) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

71) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

72) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

73) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

74) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

75) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

76) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

77) N-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

78) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

79) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

80) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

81) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

82) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

83) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

84) 2-dimethylamine-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

85) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

86) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

87) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

88) (R or S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

89) (R or S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

90) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

and from the pharmaceutically acceptable salts thereof.

7. The use of a compound of the formula I and of the pharmaceutically acceptable salts thereof for producing a medicament for the treatment of disorders which can be influenced by inhibition of the sodium-proton exchanger of subtype III (NHE3), in which the meanings are:

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, $C_{qq}H_{2qq-1}$, OC_bH_{2b+1}, COOR10, OCOR10, COR10 or O_x-$(CH_2)_y$-phenyl;

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

qq 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms,

x zero or 1;

y zero, 1, 2, 3 or 4;

where the phenyl ring in the group O_x-$(CH_2)_y$-phenyl is unsubstituted or substituted by 1-3 substituents selected from the group consisting of F, Cl, Br, CN, NO_2, OH, NH_2 or C_dH_{2d+1};

d 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms,

or

R1, R2, R3 and R4

independently of one another heteroaryl, it being possible for zero, 1, 2, 3 or 4 N atoms, zero or 1 oxygen atom or zero or 1 S atom to be present as ring atoms;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3, 4, 5, 6, 7 or 8,

rr 3, 4, 5, 6, 7, or 8,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR13;

R13 H or C_fH_{2f+1};

f 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R13 and a CH_2 group of R11 or R12 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R11 and R12

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R11 and R12

independently of one another COR14, CSR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms, and it being possible for one or more CH_2 groups to be replaced by O or NR13,

or

R1, R2, R3 and R4

independently of one another $-O_h-SO_j-R15$, with

h zero or 1;

j zero, 1 or 2;

R15 C_kH_{2k+1}, OH, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O, CO, CS or NR19;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring;

or

R19 and a CH_2 group of R17 or R18 together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$, COR20 or SO_2R20;

p 1, 2, 3, 4, 5, 6, 7 or 8,

ss 3, 4, 5, 6, 7 or 8, is being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms,

R20 C_qH_{2q+1};

q 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_qH_{2q+1} to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR21;

R21 H or C_rH_{2r+1};

r 1, 2, 3 or 4;

it being possible for one or more H atoms in C_rH_{2r+1} to be replaced by F atoms;

R6 H, F, Cl, Br, I, C_sH_{2s+1}, $C_{dd}H_{2dd-1}$, OH, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

dd 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms in C_sH_{2s+1}, $C_{dd}H_{2dd-1}$ and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another $-O_v-SO_w-R23$;

v zero or 1;

w zero, 1 or 2;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, OH, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8,

mm 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, $C_{zz}H_{2zz-1}$;

z 1, 2, 3, 4, 5, 6, 7 or 8;

zz 3, 4, 5, 6, 7 or 8, it being possible for one or more H atoms to be replaced by F atoms and,

in C_zH_{2z+1}, it being possible for one or more H atoms to be replaced by F atoms and it being possible for one or more CH_2 groups to be replaced by O, CO, CS or NR27;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5-, 6- or 7-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_{bb}R30$;

R30 H, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

bb 2 or 3;

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5, 6, 7 or 8;

h 1, 2, 3, 4, 5, 6, 7 or 8,

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$, COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 forms together with a CH_2 group of R30 a 5-, 6- or 7-membered ring;

or

R30 a 5- or 6-membered heteroaryl with 1, 2, 3 or 4 N atoms, zero or 1 S atoms and zero or 1 O atoms,

which is unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71;

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ and COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3, 4, 5, 6, 7 or 8;

ww 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms and for one or more CH_2 groups to be replaced by O or NR44;

R44 H or $C_{gg}H_{2gg+1}$;

gg 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{gg}H_{2gg+1}$ to be replaced by F atoms, and it being possible for R44 together with a (CH_2) group of R40 or R41 and the N atom to which they are jointly bonded to form a 5- or 6-membered ring,

or

R40 and R41

with the N atom to which they are bonded a 5- or 6-membered ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms.

8. The use as claimed in claim 7, characterized in that compounds of the formula I are used, in which the meanings are:

R1, R2, R3 and R4

independently of one another, H, F, Cl, Br, I, CN, NO_2, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1}, COOR10;

a and b

independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R10 H or C_cH_{2c+1};

c 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another 5- or 6-membered heteroaryl selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl and oxazolyl;

or

R1, R2, R3 and R4

independently of one another CONR11R12 or NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms

or

R11 and R12

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R11 and R12

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R_{15}, or

R15 C_kH_{2k+1}, OC_lH_{2l+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

l 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H, C_mH_{2m+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO and the second CH_2 group is replaced by NR19;

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

R19 H or C_nH_{2n+1};

n 1, 2, 3 or 4;

it being possible for one or more H atoms in C_nH_{2n+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}; $C_{ss}H_{2ss-1}$;

p 1, 2, 3 or 4;

ss 3, 4, 5 or 6, it being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms;

R6 H, C_sH_{2s+1}, OC_tH_{2t+1} or OCOR22;

s and t

independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in C_sH_{2s+1} and OC_tH_{2t+1} to be replaced by F atoms;

R22 C_uH_{2u+1};

u 1, 2, 3 or 4;

it being possible for one or more H atoms in C_uH_{2u+1} to be replaced by F atoms;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$, $OC_{pp}H_{2pp+1}$ or NR25R26;

nn and pp

independently of one another 1, 2, 3, 4 or 5,

mm 3, 4, 5 or 6,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$, $C_{mm}H_{2mm-1}$ and $OC_{pp}H_{2pp+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_ZH_{2Z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_ZH_{2Z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 independently of one another H or C_hH_{2h+1};

cc 1, 2, 3, 4, 5, 6, 7 or 8;

yy 3, 4, 5 or 6;

h 1, 2, 3 or 4;

it being possible for one or more H atoms in C_hH_{2h+1} to be replaced by F atoms, and it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more (CH_2) groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, $C_{kk}H_{2kk+1}$,COR65 or SO_2R65;

kk 1, 2, 3, or 4;

it being possible for one or more H atoms to be replaced by F atoms,

R65 H, $C_{xx}H_{2xx+1}$;

xx 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R31 together with a CH_2 group or R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 a 5- or 6-membered heteroaromatic system selected from the group consisting of pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thienyl, thiazolyl and oxazolyl,

which are unsubstituted or substituted by up to three substituents selected from the group consisting of F, Cl, Br, I, $C_{oo}H_{2oo+1}$, NR70R71,

R70 and R71

independently of one another H, $C_{uu}H_{2uu+1}$ or COR72;

R72 H, $C_{vv}H_{2vv+1}$;

oo, uu and vv independently of one another 1, 2, 3 or 4;

it being possible for one or more H atoms in the groups $C_{oo}H_{2oo+1}$, $C_{uu}H_{2uu+1}$ or $C_{vv}H_{2vv+1}$ to be replaced by F atoms;

or

R7, R8 and R9

independently of one another H, F, Cl, Br, I, NO_2, CN, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42, COR42 or OCOR42;

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

to be selected independently of one another hydroxyethyl, , N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methyl-piperazine, piperazine and morpholine;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms.

9. The use as claimed in claim 7, characterized in that the meanings in formula I are:

R1, R2, R3 and R4

independently of one another H, F, Cl, Br, OH, NH_2, C_aH_{2a+1}, cycloalkyl with 3, 4, 5 or 6 C atoms, OC_bH_{2b+1};

a and b

in the groups C_aH_{2a+1} and OC_bH_{2b+1} independently of one another 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another NR11R12;

R11 and R12

independently of one another H, C_eH_{2e+1}, $C_{rr}H_{2rr-1}$;

e 1, 2, 3 or 4,

rr 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups C_eH_{2e+1} and $C_{rr}H_{2rr-1}$ to be replaced by F atoms;

or

R11 and R12

together with the N atom to which they are bonded form a ring selected from the group consisting of pyrrolidine, piperidine, N-methylpiperazine, piperazine and morpholine;

or

R11 and R12

independently of one another COR14, CSR14, CONHR14, CSNHR14 or SO_2R14;

R14 C_gH_{2g+1};

g 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

or

R1, R2, R3 and R4

independently of one another OSO_3H, SO_3H, SO_2R15;

R15 C_kH_{2k+1} or NR17R18;

k 1, 2, 3 or 4, it being possible for one or more H atoms to be replaced by F atoms;

R17 and R18

independently of one another H or C_mH_{2m+1};

m 1, 2, 3, 4 or 5, it being possible for one or more H atoms in the group C_mH_{2m+1} to be replaced by F atoms;

or

R17 and R18

together with the N atom to which they are bonded a 5- or 6-membered ring;

R5 H, C_pH_{2p+1}, $C_{ss}H_{2ss-1}$;

p 1, 2, 3 or 4;

ss 3, 4, 5 or 6, it being possible for one or more H atoms in C_pH_{2p+1} and $C_{ss}H_{2ss-1}$ to be replaced by F atoms;

R6 H, CH_3;

R7, R8 and R9

independently of one another OSO_3H, SO_3H or SO_2R23;

R23 $C_{nn}H_{2nn+1}$ or NR25R26;

nn 1, 2, 3, 4 or 5,

it being possible for one or more H atoms in $C_{nn}H_{2nn+1}$ to be replaced by F atoms;

R25 and R26

independently of one another H, CN or C_zH_{2z+1}, in which the first CH_2 group bonded to the nitrogen is replaced by CO or CS and the second CH_2 is replaced by NR27;

z 1, 2, 3, 4, 5 or 6;

it being possible for one or more H atoms in C_zH_{2z+1} to be replaced by F atoms;

R27 H or $C_{aa}H_{2aa+1}$;

aa 1, 2, 3 or 4;

it being possible for one or more H atoms in $C_{aa}H_{2aa+1}$ to be replaced by F atoms;

or

R25 and R26

together with the N atom to which they are bonded a 5- or 6-membered ring,

or

R27 and a CH_2 group of R25 or R26 together with the N atom to which they are bonded a 5- or 6-membered ring;

or

R7, R8 and R9

independently of one another NR32COR30, NR32CSR30 or $NR32SO_2R30$;

R30 H, OH, $C_{cc}H_{2cc+1}$, $C_{yy}H_{2yy-1}$, pyrrolidinyl or piperidinyl, in which rings a CH_2 group may be replaced by O or NR33;

R32 and R33 H, CH_3 or CF_3;

cc 1, 2, 3, 4, 5 or 6;

yy 3, 4, 5, 6, 7 or 8;

it being possible for one or more H atoms in the groups $C_{cc}H_{2cc+1}$ and $C_{yy}H_{2yy-1}$ to be replaced by F atoms and for one or more (CH_2) groups to be replaced by NR31 and for a (CH_2) group to be replaced by O;

R31 H, methyl, ethyl, CF_3, CH_2CF_3, acetyl, propionyl, methanesulfonyl or ethanesulfonyl;

or

R31 together with a CH_2 group of R30 and the N atom to which they are jointly bonded form a 5- or 6-membered ring;

or

R30 pyridyl, imidazolyl, pyrazolyl, pyrrolyl, triazolyl, tetrazolyl, thiazolyl or oxazolyl, which are unsubstituted or substituted by a maximum of 3 substituents selected from the group consisting of F, Cl, methyl, ethyl, trifluoromethyl, NH_2, NHacetyl;

or

R7, R8 and R9

independently of one another H, F, Cl, OH, NH_2, $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$, $OC_{ff}H_{2ff+1}$, NR40R41, CONR40R41, COOR42 or OCOR42,

ee and ff

independently of one another 1, 2, 3 or 4;

ww 3, 4, 5 or 6,

it being possible for one or more H atoms in the groups $C_{ee}H_{2ee+1}$, $C_{ww}H_{2ww-1}$ and $OC_{ff}H_{2ff+1}$ to be replaced by F atoms;

R40 and R41

H, $C_{tt}H_{2tt+1}$ or $C(NH)NH_2$;

tt 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{tt}H_{2tt+1}$ to be replaced by F atoms;

or

R40 and R41

independently of one another hydroxyethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, pyrrolidinoethyl, N-methylpiperazinoethyl, piperazinoethyl, morpholinoethyl or piperidinoethyl;

or

R40 and R41

together with the N atom to which they are bonded a pyrrolidine, piperidine, N-methylpiperazine, piperazine or morpholine ring;

R42 H or $C_{hh}H_{2hh+1}$;

hh 1, 2, 3 or 4;

it being possible for one or more H atoms in the group $C_{hh}H_{2hh+1}$ to be replaced by F atoms.

10. The use as claimed in claim 7, characterized in that the compounds of the formula I are selected from the group consisting of:

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;
4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N,N-dimethyl-benzenesulfonamide;
5) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinoline;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
8) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
10) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
11) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-phenyl]-diethyl-amine
12) 6,8-dichloro-2-methyl-4-(4-piperidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
13) 6,8-dichloro-2-methyl-4-(4-pyrrolidin-1-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
14) 6,8-dichloro-2-methyl-4-[4-(4-methyl-piperazin-1-yl)-phenyl]-1,2,3,4-tetrahydro-isoquinoline;
15) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline;
16) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
17) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-propylurea;
18) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

19) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

20) N-[4-(6-methanesulfonyl-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

21) N-[4-(2,6,8-trimethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

22) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

23) N-[4-(8-chloro-2-methyl-6-pyrrolidin-1-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

24) N-[4-(8-chloro-2-methyl-6-morpholin-4-yl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

25) N-{4-[8-chloro-2-methyl-6-(4-methyl-piperazin-1-yl)-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

26) N-{4-[8-chloro-6-(cyclopropylmethyl-amino)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl]-phenyl}-acetamide;

27) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;

28) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-N-methyl-benzamide;

29) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-ethyl-2-hydroxy-benzamide;

30) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;

31) N-[5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoyl]-guanidine;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

33) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

34) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;

35) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

36) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

37) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]pentanamide;

38) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

39) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

40) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

41) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

43) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

44) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

46) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

48) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

49) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

50) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

53) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

54) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

55) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

61) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

62) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

63) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

64) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

65) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pentanamide;

66) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

67) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2-dimethyl-propionamide;

68) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

69) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-cyclobutanecarboxamide;

70) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopentanecarboxamide;

71) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

72) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetylpiperidine-4-carboxamide;

73) N-[2-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

74) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)- phenyl]-ethanesulfonamide;

75) N',N'-dimethylamino-N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

78) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

80) N-{5-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

81) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

82) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

83) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

84) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

85) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

87) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-5-bromo-thiophene-2-sulfonamide;

88) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

90) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoroethanesulfonamide;

91) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-ethanesulfonamide;

92) N-ethyl-N'-4-(6,8-Dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

93) 2-chloro-5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

94) 2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;

95) 6,8-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

96) 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;

97) 8-methoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

98) 2-(8-amino-2-ethyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;

99) 2-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenol;

100) 5-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-methoxy-phenol;

101) 2-methyl-8-nitro-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

102) 4-(8-amino-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzene-1,2-diol;

103) 2,8-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;

104) 4-(3,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;

105) 4-(3,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;

106) 4-(2,4-dichloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
107) 4-(3-chloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
108) 2,4-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
109) 2-butyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-ylamine;
110) N-(2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinolin-8-yl)-acetamide;
111) 7-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
112) 8-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
113) 2,6-dimethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
114) 6-chloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
115) 6-methoxy-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
116) 2-ethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
117) 2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
118) 6,8-dichloro-2-ethyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
119) 4-(4-bromo-phenyl)-6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
120) 2-methyl-4-phenyl-6,8-bis-trifluoromethyl-1,2,3,4-tetrahydro-isoquinoline;
121) 6,8-dichloro-2-isopropyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
122) 5,8-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
123) 6,8-dichloro-4-(4-fluoro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
124) 6,8-dichloro-2-methyl-4-p-tolyl-1,2,3,4-tetrahydro-isoquinoline;
125) 5,6-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
126) 6,7-dichloro-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
127) 8-bromo-2-methyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
128) 6,8-dichloro-4-(4-chloro-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
129) 6,8-dichloro-2-cyclopropyl-4-phenyl-1,2,3,4-tetrahydro-isoquinoline;
130) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
131) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;
132) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;
133) 2-amino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

134) 2-amino-N-[6-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

135) 2,6-diamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

136) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

137) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

138) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

139) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

140) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

141) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

142) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

143) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

144) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

145) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

146) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

147) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

148) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

149) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

150) N[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

151) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

152) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

153) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

154) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-2-carboxamide;

155) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isonicotinamide;

156) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

157) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-2-carboxamide;

158) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

159) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,4-dimethyl-1H-pyrrole-2-carboxamide;

160) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-nitro-1H-pyrrole-2-carboxamide;

161) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,5-dimethyl-1H-pyrrole-3-carboxamide;

162) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

163) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

164) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

165) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

166) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-trifluoromethyl-1H-pyrazole-4-carboxamide;

167) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

168) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

169) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-thiourea;

170) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

171) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

172) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

173) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

174) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

175) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

176) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

177) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

178) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

179) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

180) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

181) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

182) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

183) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

184) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

185) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

186) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

187) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

188) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

189) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

190) 3-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

191) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

192) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

193) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

194) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

195) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

196) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

197) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

198) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

199) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

200) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

201) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

202) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

203) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

204) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

205) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

206) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

207) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

208) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

209) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

210) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

211) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

212) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

213) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

214) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

215) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-pyrrolidine-1-carboxamide;

216) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-piperidine-1-carboxamide;

217) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

218) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

219) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-morpholine-4-carboxamide;

220) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

221) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

222) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,3-diethyl-1-methyl-urea;

223) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

224) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

225) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

226) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

227) ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

228) isopropyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

229) 2,2-dimethyl-propyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

230) methyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

231) isopropyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

232) 2,2-dimethyl-propyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

233) ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

234) (R)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

235) (S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

236) (R)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

237) (S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

238) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

239) 4-(3-bromo-phenyl)-6,8-dichloro-methyl-1,2,3,4-tetrahydro-isoquinoline;

240) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

241) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;

242) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.

and from the pharmaceutically acceptable salts thereof.

11. The use as claimed in claim 7, characterized in that the compounds of the formula I are selected from the group consisting of:

1) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;

2) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

3) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonamide;

4) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid;
5) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-ethyl-benzamide;
6) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydroisoquinolin-4-yl)-N-propyl-benzamide;
7) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-benzamide;
8) 6,8-dichloro-2-methyl-4-(4-morpholin-4-yl-phenyl)-1,2,3,4-tetrahydroisoquinoline;
9) 4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
10) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;
11) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;
12) N-[4-(6-bromo-8-chloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
13) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-2-hydroxy-benzoic acid;
14) 5-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-N-(2-dimethylamino-ethyl)-2-hydroxy-benzamide;
15) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-acetamide;
16) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
17) 2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylamine;
18) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;
19) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;
20) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;
21) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;
22) N',N'-dimethylamino-N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

23) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

24) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

25) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-isobutyramide;

26) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

27) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclobutanecarboxamide;

28) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2,2,2-trifluoro-acetamide;

29) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

30) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-nicotinamide;

31) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methane-sulfonamide;

32) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-ethanesulfonamide;

33) N',N'-dimethylamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-sulfamide;

34) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-cyclopropanecarboxamide;

35) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-acetyl-piperidine-4-carboxamide;

36) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

37) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

38) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

39) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-thiourea;

40) N-{5-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide;

41) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,2-dimethyl-1H-imidazole-4-sulfonamide;

42) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

43) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-C,C,C-trifluoro-methanesulfonamide;

44) N-ethyl-N'-4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzenesulfonylurea;

45) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

46) 2,6-diamino N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

47) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrrole-3-carboxamide;

48) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

49) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

50) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

51) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-methylamino-acetamide;

52) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-2-dimethylamino-acetamide;

53) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-propionamide;

54) 2-amino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-butyramide;

55) 2,6-diamino-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-hexanamide;

56) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-piperidine-4-carboxamide;

57) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-imidazole-4-carboxamide;

58) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methanesulfonyl-piperidine-4-carboxamide;

59) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3,5-dimethyl-1H-pyrazole-4-carboxamide;

60) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1H-pyrazole-4-carboxamide;

61) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

62) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

63) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-piperidine-1-carboxamide;

64) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

65) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-pyrrolidine-1-carboxamide;

66) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

67) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

68) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

69) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-furan-3-yl)-urea;

70) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(tetrahydro-pyran-4-yl)-urea;

71) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-methyl-1-(1-methyl-piperidin-4-yl)-urea;

72) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(3-dimethylamino-propyl)-1-methyl-urea;

73) 3-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1-(2-dimethylamino-ethyl)-1-methyl-urea;

74) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(3-dimethylamino-propyl)-urea;

75) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-methoxy-ethyl)-urea;

76) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-3-yl-urea;

77) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-pyridin-4-yl-urea;

78) N-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

79) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

80) 1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

81) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-4-methyl-piperazine-1-carboxamide;

82) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-methyl-urea;

83) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-dimethyl-urea;

84) 3-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,1-diethyl-urea;

85) 1-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-urea;

86) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

87) N-[4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

88) [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

89) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-formamide;

90) [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-amine;

91) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3,3-trimethyl-urea;

92) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-1,3-dimethyl-urea;

93) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-morpholine-4-carboxamide;

94) N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methyl-4-methyl-piperazine-1-carboxamide;

95) 1[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-dimethylamino-ethyl)-1-methyl-urea;

96) 2-dimethylamino-ethyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

97) 2-dimethylamino-ethyl [4-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

98) 2-dimethylamino-ethyl [2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

99) methyl [3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-carbamate;

100) (R or S)-N-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-methanesulfonamide;

101) (R or S)-1-[2-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-ethyl-urea;

102) 1-[3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-phenyl]-3-(2-hydroxy-ethyl)-urea;

103) ethyl 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoate;
104) 3-(6,8-dichloro-2-methyl-1,2,3,4-tetrahydro-isoquinolin-4-yl)-benzoic acid.
and from the pharmaceutically acceptable salts thereof.

12. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of disorders of respiratory drive.

13. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of respiratory disorders, in particular sleep-related respiratory disorders such as sleep apneas.

14. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of snoring.

15. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of acute and chronic renal disorders, particularly of acute renal failure and of chronic renal failure.

16. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of disorders of intestinal function.

17. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of disorders of biliary function.

18. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of ischemic states of the peripheral and central nervous system and of stroke.

19. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of ischemic states of peripheral organs and limbs.

20. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment of states of shock.

21. The use of a compound I as claimed in claim 7 for producing a medicament for use in surgical operations and organ transplantations.

22. The use of a compound I as claimed in claim 7 for producing a medicament for the preservation and storage of transplants for surgical procedures.

23. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment of disorders in which cell proliferation represents a primary or secondary cause.

24. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of disorders of lipid metabolism.

25. The use of a compound I as claimed in claim 7 for producing a medicament for the treatment or prophylaxis of infestation by ectoparasites.

26. A medicine comprising an effective amount of a compound I as claimed in claim 1.