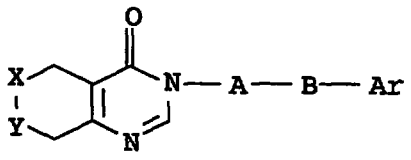
Use of compounds of the formula I for the prophylaxis and therapy of cerebral ischemia

The invention relates to the use of compounds of the formula I for the prophylaxis and therapy of cerebral ischemia.

DE 19747063.7 describes 3-substituted tetrahydropyridopyrimidinone derivatives of the formula I



(I),

in which

one of the two radicals X, Y is CH_2 and the other is NR^1,

R^1 is hydrogen, (C_{1-6})-alkyl, branched or unbranched, $CO-(C_{1-4})$-alkyl, CO_2tBu, CO-aryl or a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

A is branched or unbranched (C_{1-10})-alkylene or straight-chain or branched (C_{2-10})-alkylene which comprises at least one group Z selected from the group consisting of O, S, NR^2, cyclopropyl, CHOH, a double and a triple bond,

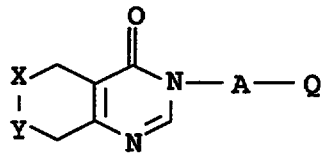
R^2 is hydrogen or C_1-C_4-alkyl,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by (C_{1-6})-alkyl, branched or unbranched, $O-(C_{1-6})$-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, NR^2_2, CO_2R^2, cyano or phenyl, is tetralin, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by (C_{1-4})-alkyl or $O-(C_{1-4})$-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from

the group consisting of O and N, and which may be fused with other aromatic radicals.

These compounds of the formula I can be prepared by reacting a compound of the formula II

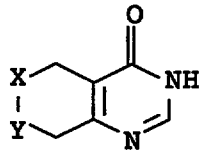


(II),

in which A, X and Y are as defined above and Q is a group that can be cleaved off (for example Cl, Br, I, alkanesulfonyloxy or arylsulfonyloxy), with a compound of the formula III

H-B-Ar (III),

in which B and Ar are as defined above, in a manner known per se and converting the resulting compound, if appropriate, into the acid addition salt of a physiologically acceptable acid. It is also possible to react a compound of the formula IV



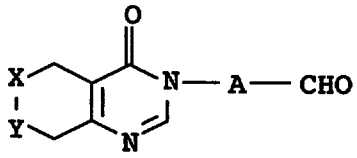
(IV)

with a compound of the formula V

Q-A-B-Ar (V)

in a manner known per se.

A further synthesis variant is the attachment of a compound of the formula VI



(VI)

to a compound of the formula III by a reductive amination, which is known per se.

The compounds of the formula III can be synthesized by

1. attaching compounds of the formula VII

$$W\text{-}B^1 \qquad \text{(VII)},$$

where B^1 is piperazine or homopiperazine and W is hydrogen or one of the customary amino protective groups (such as, for example, Boc or Cbz), to a compound of the formula VIII

$$P\text{-}Ar \qquad \text{(VIII)},$$

where P is $B(OH)_2$, SnR_3, OTf, Br, Cl or I and R is C_1-C_4-alkyl, is reacted [sic] in a manner known per se; or

2. attaching compounds of the formula IX

$$W\text{-}B^2\text{-}P^1 \qquad \text{(IX)},$$

where B^2 is 4-tetrahydro-1,2,3,6-pyridine or the corresponding cyclic compounds which are enlarged by a methylene group and P^1 is Cl, Br, I, SnR_3 - where R is C_1-C_4-alkyl - , OTf, to a compound of the formula X

$$P\text{-}Ar \qquad \text{(X)},$$

where W, P and Ar are each as defined above, and where the reactions are carried out by known processes, such as, for example, those described in

S.L. Buchwald et al. *J. Am. Chem. Soc.* **1996**, *118*, 7215,
J.F. Hartwig et al. *Tetrahedron Lett.* **1995**, *36*, 3604,
J.K. Stille et al. *Angew. Chem.* **1986**, *98*, 504,
S.L. Buchwald et al. *Angew. Chem.* **1995**, *107*, 1456 or
J.F. Hartwig et al. *J. Am. Chem. Soc* **1996**, *118*, 7217 or
J.F. Hartwig et al. *J. Org. Chem.* **1997**, *62*, 1268,
S.L. Buchwald et al. *J. Org. Chem.* **1997**, *62*, 1264 and literature cited therein or
S.L. Buchwald et al *J. Am. Chem. Soc* **1997**, *119*, 6054,
J.K. Stille, *Angew. Chem.* **1986**, *98*, 504 or
J.K. Stille et al. *J. Org. Chem.* **1990**, *55*, 3014,
M. Pereyre et al. "Tin in Organic Synthesis", Butterworth 1987; or

3. reducing compounds of the formula (XI)

$$W\text{-}B^2\text{-}Ar \qquad (XI),$$

where B^2 is as defined above, to give compounds of the formula XII

$$W\text{-}B^3\text{-}Ar \qquad (XII),$$

in which B^3 is a piperidine which is attached in 1,4 position or the corresponding cyclic compounds which are enlarged by a methylene group; or

4. cyclizing compounds of the formula XIII

$$W\text{-}N\text{-}(C_2H_4Q)_2 \qquad (XIII),$$

where W and Q are as defined above, with a compound of the formula XIV

$$NH_2\text{-}Ar \qquad (XIV),$$

where Ar is as defined above, to give compounds of the formula XV

$$W\text{-}B^1\text{-}Ar \qquad (XV).$$

The substances of the formulae III and V required as starting materials for synthesizing the novel compounds are known or can be prepared according to known processes (for example *Organikum* Barth Dt. Verl. der Wiss. **1993** or A. R. Katritzky, C. W. Rees (ed.) *Comprehensive Heterocyclic Chemistry* Pergamon Press) from analogous starting materials.

The further reaction of the compounds

$$H\text{-}B\text{-}Ar \qquad (III)$$

prepared in this manner according to 1. to 4. with subsequent removal of any protective groups to give the compounds of the formula V is carried out by attachment to compounds of the formula XVI

$$Q\text{-}A\text{-}Q' \qquad (XVI),$$

where Q and Q' are leaving groups, under conditions known per se.

The substances of the formulae II, IV, VI and of the formulae P-Ar, NH_2-Ar, W-B^1 or W-B^2-P^1 required as starting materials for synthesizing the novel compounds are known or can be prepared according to the preparation processes described in the literature from analogous starting materials (for example B. Dumaitre, N. Dodic *J. Med. Chem.* **1996**, *39*, 1635 or A. Yokoo et al. *Bull. Chem. Soc. Jpn.* **1956**, *29*, 631 or L. Börjeson et al. *Acta Chem. Chem.* **1991**, *45*, 621 or *Organikum* Barth Dt. Verl. der Wiss. **1993** or A. R. Katritzky, C. W. Rees (ed.) *Comprehensive Heterocyclic Chemistry* Pergamon Press or *The Chemistry of Heterocyclic Compounds* J. Wiley & Sons Inc. NY and the literature cited therein in each case).

Example 1:

3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one

Preparation of the starting materials

a) 5,6,7,8-Tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one

4.7 g of sodium were, a little at a time, allowed to react in 250 ml of ethanol, and a suspension of 14.2 g (0.05 mol) of methyl N-benzyl-4-piperidone-3-carboxylate in ethanol was then added dropwise at 5-10°C. The mixture was stirred for 30 minutes, after which 6 g (0.075 mol) of formamidine hydrochloride were added slowly, and the reaction mixture was heated under reflux for 10 h. The solvent was removed under reduced pressure and the residue was taken up in 100 ml of water and adjusted to pH = 6.5 - 7 using 2N of hydrochloric acid, so that the product precipitated out. The crystals were filtered off with suction and dried in a vacuum drying cabinet, giving 8 g (66%). m.p.: 88°C.

5,6,7,8-Tetrahydro-7-benzylpyrido-[3,4-d]pyrimidin-4(3H)-one (m.p.: 199°C) and methyl 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4(3H)-one-6-carboxylate (m.p.: 160°C) were obtained similarly.

b) 1-(2-Methoxyphenyl)-4-(2-chloroeth-1-yl)piperazine

At room temperature, a solution of 19.2 g (0.1 mol) of o-methoxyphenylpiperazine and 13.8 g (0.1 mol) of potassium carbonate in 200 ml of DMF was initially charged and, after

30 min, 30 ml (0.36 mol) of 1-bromo-2-chloroethane were added. The mixture was stirred at room temperature for 2 h. The mixture was poured into ice-water and then extracted with methyl tert-butyl ether, and the organic phases were washed with water, dried with sodium sulfate and subsequently concentrated. The residue was dissolved in ethyl acetate and the hydrochloride was precipitated out by addition of 30% strength isopropanol/HCl solution, filtered off with suction and then dried at 40°C in a vacuum drying cabinet. This gave 17 g (67%) of substance. m.p.: 200°C.

1-(2-Methoxyphenyl)-4-(3-chloroprop-1-yl)piperazine (m.p.: 217°C, hydrochloride), 1-(3,4-methylphenyl)-4-(2-chloroeth-1-yl)-piperazine (m.p.: 260°C, hydrochloride), 1-(2-pyrimidyl)-4-(2-chloroeth-1-yl)piperazine (m.p.: 270°C, hydrochloride), 1-(naphth-1-yl)-4-(3-chloroprop-1-yl)piperazine (m.p.: 217°C, hydrochloride), were obtained in a similar manner.

Two exemplary syntheses for preparing the piperazines are shown below.

1-Tetralin-5-yl-piperazine

14.7 g (0.1 mol) of 5-aminotetralin and 18 g (0.11 mol) of bis(β-chloroethyl)amine hydrochloride in 300 ml of n-butanol were refluxed for 48 h, 5.4 g of sodium carbonate were added after cooling and the mixture was once more refluxed for 20 h. The precipitate which was formed by cooling was filtered off with suction, taken up in water and admixed with 2N sodium hydroxide solution. The aqueous phase was extracted with ethyl acetate, and the extract was washed with water, dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 10.7 g (50%) of the product as an oil.

4-Piperazin-1-ylisoquinoline

4.51 g (21.7 mmol) of 4-bromoisoquinoline, 4.65 g (25.0 mmol) of t-butyl piperazine-N-carboxylate, 0.1 g (0.11 mmol) of tris-(dibenzylideneacetone)dipalladium, 0.11 g (0.18 mmol) of 2,2'-bis(diphenylphosphino)-1,1'-dinaphthyl and 2.92 g (30.4 mmol) of sodium t-butoxide were admixed in 50 ml of toluene and stirred at 75°C for 2 h. The reaction mixture was poured onto ice/sodium chloride and extracted with ethyl acetate, the organic phase was dried over sodium sulfate and the solvent was removed using a rotary evaporator. The product crystallized out, and it was filtered off with suction and washed with pentane. This gave

5.5 g (81%) of the Boc-protected piperazine (m.p.: 111°C). 5.2 g (16.6 mmol) of this substance were taken up in 17 ml of dichloromethane and, at 0°C, slowly admixed with 17 ml (0.22 mol) of trifluoroacetic acid. The mixture was stirred at 0°C for 4 h, poured onto ice-water and extracted with dichloromethane. The aqueous phase was filtered, made alkaline and extracted with dichloromethane. After drying over sodium sulfate and substantial removal of the solvent, the residue was diluted with diethyl ether and the hydrochloride was precipitated out using ethereal hydrochloric acid. This gave 3.2 g (67%) of the product. (m.p.: 293°C).

The following compounds were prepared similarly to the two processes described: 1-naphth-1-ylazepane (85°C, hydrochloride), 1-naphth-1-ylmethylpiperazine (oil), 4-piperazin-1-yl-indane (oil), 1-naphth-1-ylpiperazine (82°C), 4-chloro-1-piperazin-1-ylphthalazine (205°C, decomp.) and 4-piperazin-1-ylquinazoline (320°C, hydrochloride). Other derivatives were commercially available.

Preparation of the end product

2.9 g (10 mmol) of chloroethylpiperazine [b)] and 2.8 g (20 mmol) of potassium carbonate were added to a solution of 2.4 g (10 mmol) of tetrahydropyridopyrimidine [a)] in 40 ml of DMF. The reaction mixture was reacted at 90°C for two hours and then poured onto ice-water and extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution and dried over sodium sulfate, and the solvent was removed under reduced pressure. The oil that remained was taken up in acetone, and the hydrochloride was precipitated out using isopropanol/HCl. This gave 4 g (75%) of the product (m.p.: 205°C).

NMR: $CDCl_3$ δ 8.0 (s, 1H), 7.4 - 7.2 (m, 5H), 7.1 - 6.8 (m, 4H), 4.0 (t, 2H), 3.8 (s, 3H), 3.7 (s, 2H), 3.5 (s, 2H), 3.1 (brd. s, 4H), 2.8 - 2.6 (m, 10H) ppm.

The following compounds were obtained in a similar manner:

Example 2:

3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-benzylpyrido[3,4-d]pyrimidin-4(3H)-one (m.p.: 181°C, hydrochloride).

Example 3:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one (m.p.: 198°C, hydrochloride).

Example 4:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-5,6,7,8-tetrahydro-7-benzylpyrido[3,4-d]pyrimidin-4(3H)-one (m.p.: 190°C, hydrochloride).

Example 5:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]2-hydroxypropyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one.

Example 6:

t-butyl 3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-(3H)-one-6-carboxylate (m.p.: 170°C, hydrochloride).

Example 7:

3-[2-[4-(isoquinolin-4-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 268°C, hydrochloride).

Example 8:

3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 272°C, hydrochloride).

Example 9:

3-[2-[4-(quinazolin-4-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 258°C, hydrochloride).

Example 10:

3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 227°C, hydrochloride).

Example 11:

3-[2-[4-(naphth-1-yl)-tetrahydro-1,2,3,6-pyridin-1-yl]eth-1-yl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 216°C, hydrochloride).

Synthesis of the starting materials

a) N-Boc-4-(trifluoromethanesulfonyloxy)-tetrahydro-1,2,3,6-pyridine

At -78°C, a solution of 13.2 g (0.13 mol) of diisopropylamine in 200 ml of THF was deprotonated using 100 ml of nBuLi (1.6M in hexane), and, after 30 minutes at this temperature, 20.0 g (0.1 mol) of N-Boc-piperid-4-one dissolved in 50 ml of THF were added dropwise. After a further three hours at -78°C, a solution of 39.3 g (0.11 mol) of N,N-bistrifluoromethanesulfonylaniline in 50 ml of THF was added, and the mixture was allowed to warm to room temperature overnight. For work-up, the mixture was admixed with water and extracted with ether, the organic phases were washed with $NaHCO_3$ solution and water and dried over sodium sulfate, and the solvent was concentrated. The crude product was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 3/1).

Yield: 20.2 g (60% of theory)

1H NMR:(270 MHz,$CDCl_3$) δ = 1.4 (s, 9H); 2.4 (m, 2H); 3.6 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H) ppm

b) N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine

22 ml of 2M sodium carbonate solution, 7.63 g (44.4 mmol) of naphthyl-1-boronic acid, 4.13 g (97.6 mmol) of lithium chloride, 0.85 g (4.44 mmol) of copper(I) iodide and 2.1 g (1.77 mmol) of tetrakistriphenylpalladium were added successively to 14.7 g (44.4 mmol) of the compound described above dissolved in 115 ml of dimethoxyethane, and the mixture was heated at the boil for 4 h. For work-up, aqueous ammonia solution was added and the mixture was extracted with water and ethyl acetate, the extract was dried over sodium sulfate and the residue which was obtained after evaporation of the solvent was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 4/1).

Yield: 8.2 g (57% of theory)

1H-NMR (270 MHz, $CDCl_3$): δ = 1.4 (s, 9H); 2.5 (m, 2H); 3.7 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H); 7.2-7.5(m, 3H); 7.3-8.0 (m, 3H) ppm.

c) 4-Naphth-1-yltetrahydro-1,2,3,6-pyridine

7.84 g (25.3 mmol) of N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine were stirred overnight at room temperature with 200 ml of ethereal hydrochloric acid, and the precipitated product was filtered off and dried.

Yield: 5.5 g (88% of theory).

d) Preparation of the end product

0.51 g (2 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine dissolved in 30 ml of dry DMF was admixed with 0.61 g (2 mmol) of 3-(2-chloroeth-1-yl)-3,5,7,8-tetrahydro-4-oxo-6-benzylpyrido[4,3-d]pyrimidine and with 2 ml (17 mmol) of triethylamine, and the mixture was stirred at 120°C for 5 h. The organic phase was diluted with ether, washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure. The resulting crude product was purified chromatographically, giving a white solid by precipitating the salt using ethereal hydrochloric acid solution.

Yield: 0.2 g (20% of theory)

m.p.: 237°C.

Example 12

3-[2-[4-(Naphth-1-yl)piperidin-1-yl]eth-1-yl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one

4-Naphth-1-ylpiperidine

3.7 g (15.3 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine, dissolved in methanol, were hydrogenated at room temperature with hydrogen for 48 h, with addition of 0.8 g of palladium on carbon. The catalyst was filtered off and the solvent was concentrated.

Yield: 1.8 g (56% of theory)

1H NMR (270 MHz, $CDCl_3$) δ = 1.6-1.8 (m, 2H); 2.0 (m, 2H); 2.9 (dt, 2H); 3.3 (d, 2H); 3.5 (tt, 1H); 7.4-7.6 (m, 4H); 7.7 (d, 1H); 7.9 (d, 1H); 8.1 (d, 1H) ppm.

Preparation of the end product

0.42 g (2 mmol) of 4-naphth-1-ylpiperidine, dissolved in 30 ml of dry DMF, was admixed with 0.61 g (2 mmol) of 3-(2-chloroeth-1-yl)-3,5,7,8-tetrahydro-4-oxo-6-benzylpyrido[4,3-d]pyrimidine and with 2 ml (17 mmol) of triethylamine, and the mixture was stirred at 120°C for 5 h. The organic phase was diluted with ether, washed with water and dried over sodium ulfate [sic], and the solvent was removed under reduced pressure. The resulting crude product was purified chromatographically, giving a white solid by precipitating the salt using ethereal hydrochloric acid solution.

Yield: 0.24 g (27% of theory)

1H NMR (270 MHz, $CDCl_3$) δ = 8.3 (s, 1H), 8.0 (d, 1H), 7.8 (d, 1H), 7.7 (t, 1H), 7.5 - 7.2 (m, 9H), 4.5 (s, 2H), 4.0 (s, 2H), 3.7 - 2.3 (m, 15H), 2.1 (d, 2H) ppm.

Other preferred compounds of the formula I according to the invention are listed in the table below.

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
13.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	1-naphthalene	235°C
14.	NR^1	CH_2	CH_3-C=O	C_2		4-piperazine-1-yl	1-naphthalene	236°C
15.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	1-naphthalene	245°C
16.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	4-quinazoline	270°C
17.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-quinazoline	260°C
18.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	4-isoquinoline	286°C
19.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-isoquinoline	290°C
20.	NR^1	CH_2	Ph-CH_2	C_4		4-piperazine-1-yl	2-pyrimidine	265°C
21.	NR^1	CH_2	Ph-CH_2	C_3		4-piperazine-1-yl	4-indane	281°C
22.	NR^1	CH_2	Ph-CH_2	C_2		4-piperazine-1-yl	2-Cl-Ph	225°C
23.	NR^1	CH_2	Ph-CH_2	C_2		4-piperazine-1-yl	2-pyrimidine	250°C
24.	NR^1	CH_2	Ph-CH_2	C_2		4-piperazine-1-yl	6-CF_3-2-pyrimidine	145°C (free base)
25.	NR^1	CH_2	CH_2-Ph	C_3		4-piperazine-1-yl	3-CF_3-Ph	217°C
26.	NR^1	CH_2	CH_3C=O	C_2		4-piperazine-1-yl	6-CH_3-2-pyridine	132°C
27.	NR^1	CH_2	CH_3C=O	C_2		4-piperazine-1-yl	4-CF_3-2-pyridine	130°C
28.	NR^1	CH_2	CH_3C=O	C_2		4-piperazine-1-yl	3-CF_3-Ph	158°C
29.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-CF_3-Ph	196°C

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
30.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	5-tetraline	235°C
31.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-CF_3-2-pyridine	253°C
32.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-CF_3-Ph	168°C
33.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	Ph	
34.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-OH-Ph	
35.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-OMe-Ph	
36.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Me-Ph	
37.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-CN-Ph	
38.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Cl-Ph	
39.	NR^1	CH_2	H	C_2	Me	4-piperazine-1-yl	3-NR^2_2-Ph	
40.	NR^1	CH_2	H	C_2	Me	4-piperazine-1-yl	3-CO_2R^2-Ph	
41.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-NO_2-Ph	
42.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-F-Ph	
43.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-iC_3-Ph	
44.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-I-Ph	
45.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-Br-Ph	
46.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-O(n-C_4)-Ph	
47.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-t-Bn-Ph	
48.	NR^1	CH_2	H	C_2	H	4-piperazine-1-yl	4-CO_2R^2-Ph	
49.	NR^1	CH_2	H	C_2	n-C_3	4-piperazine-1-yl	4-NR^2_2-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydrochloride
50.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-Me,4-Me-Ph	
51.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Cl,4-NO_2-Ph	
52.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-tBu,5-CF_3-Ph	
53.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-OMe,5-Ph-Ph	
54.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-OMe,4-Cl,5-Me-Ph	
55.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	5-tetraline	
56.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-indane	
57.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
58.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
59.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	8-OMe-1-naphthalene	
60.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-Indol	
61.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-quinazoline	
62.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-quinoxaline	
63.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	1-phthalazine	
64.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	4-quinoline	
65.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	1-isoquinoline	
66.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-pyrimidine	
67.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-6-pyrimidine	
68.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-pyridine	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
69.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Ph-4-quinazoline	
70.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	5-chromane	
71.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	3-isoxazole	
72.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	7-OMe-1-naphthalene	
73.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	1-tetraline	
74.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-Et-naphthalene	
75.	NR^1	CH_2	H	C_2		4-piperazine-1-yl	2-quinoline	
76.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	Ph	
77.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-OH-Ph	
78.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-Me-Ph	
79.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-CN-Ph	
80.	NR^1	CH_2	CH_2-Ph	C_2	Me	4-piperazine-1-yl	3-NR^2_2-Ph	
81.	NR^1	CH_2	CH_2-Ph	C_2	Me	4-piperazine-1-yl	3-CO_2R^2-Ph	
82.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-CF_3-Ph	
83.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-NO_2-Ph	
84.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-F-Ph	
85.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-iC_3-Ph	
86.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-I-Ph	
87.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-Br-Ph	
88.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-O(n-C_4)-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
89.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-tBu-Ph	
90.	NR^1	CH_2	CH_2-Ph	C_2	H	4-piperazine-1-yl	4-CO_2R^2-Ph	
91.	NR^1	CH_2	CH_2-Ph	C_2	n-C_3	4-piperazine-1-yl	4-$NR^2{}_2$-Ph	
92.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-Me,4-Me-Ph	
93.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-Cl,4-NO_2-Ph	
94.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-tBu,5-CF_3-Ph	
95.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-OMe,5-Ph-Ph	
96.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-OMe,4-Cl,5-MePh	
97.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-indane	
98.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
99.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
100.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	8-OMe-1-Naphtalin	
101.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-Indol	
102.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-quinazoline	
103.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-quinoxaline	
104.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	1-phthalazine	
105.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	4-quinoline	
106.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	1-isoquinoline	
107.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	7-benzofuran	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
108.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-6-pyrimidine	
109.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-pyridine	
110.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-Ph-4-quinazoline	
111.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	5-chromane	
112.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	3-isoxazole	
113.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	7-OMe-1-naphthalene	
114.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	1-tetraline	
115.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-Et-naphthalene	
116.	NR^1	CH_2	CH_2-Ph	C_2		4-piperazine-1-yl	2-quinoline	
117.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	Ph	
118.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-OH-Ph	
119.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-OMe-Ph	
120.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Me-Ph	
121.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-CN-Ph	
122.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Cl-Ph	
123.	NR^1	CH_2	Me	C_2	Me	4-piperazine-1-yl	3-NR^2_2-Ph	
124.	NR^1	CH_2	Me	C_2	Me	4-piperazine-1-yl	3-CO_2R^2-Ph	
125.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-NO_2-Ph	
126.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-F-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
127.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-iC_3-Ph	
128.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-I-Ph	
129.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-Br-Ph	
130.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-O(n-C_4)-Ph	
131.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-tBu-Ph	
132.	NR^1	CH_2	Me	C_2	H	4-piperazine-1-yl	4-CO_2R^2-Ph	
133.	NR^1	CH_2	Me	C_2	n-C_3	4-piperazine-1-yl	4-NR^2_2-Ph	
134.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-Me,4-Me-Ph	
135.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Cl,4-NO_2-Ph	
136.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-tBn,5-CF_3-Ph	
137.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-OMe,5-Ph-Ph	
138.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-OMe,4-Cl,5-MePh	
139.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	5-tetraline	
140.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-indane	
141.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
142.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
143.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	8-OMe-1-naphthalene	
144.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-Indol	
145.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-quinazoline	
146.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-quinazoline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
147.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-quinoxaline	
148.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	1-phthalazine	
149.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-quinoline	
150.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	1-isoquinoline	
151.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	4-isoquinoline	
152.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	7-benzofuran	
153.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-pyrimidine	
154.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-6-pyrimidine	
155.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-pyridine	
156.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Ph-4-quinazoline	
157.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	5-chromane	
158.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	3-isoxazole	
159.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	7-OMe-1-naphthalene	
160.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	1-tetraline	
161.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-Et-naphthalene	
162.	NR^1	CH_2	Me	C_2		4-piperazine-1-yl	2-quinoline	
163.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	Ph	
164.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-OMe-Ph	
165.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-Me-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
166.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-Cl-Ph	
167.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	3-CN-Ph	
168.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	4-F-Ph	
169.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	5-tetraline	
170.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	4-indane	
171.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-Me-naphthalene	
172.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	8-OMe-naphthalene	
173.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-quinazoline	
174.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	1-phthalazine	
175.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	4-quinoline	
176.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-pyrimidine	
177.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-6-pyrimidine	
178.	NR^1	CH_2	Boc	C_2		4-piperazine-1-yl	2-pyridine	
179.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	Ph	
180.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-OMe-Ph	
181.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-Me-Ph	
182.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-Cl-Ph	
183.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	3-CN-Ph	
184.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	3-tBu,5-CF_3-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
185.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	5-tetraline	
186.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	4-indane	
187.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-OMe-naphthalene	
188.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
189.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	8-OMe-1-naphthalene	
190.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	4-quinazoline	
191.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	4-quinoline	
192.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	4-isoquinoline	
193.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-pyrimidine	
194.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-6-pyrimidine	
195.	NR^1	CH_2	$CH_3C=O$	C_2		4-piperazine-1-yl	2-pyridine	
196.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	Ph	
197.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-OMe-Ph	
198.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-Me-Ph	
199.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-Cl-Ph	
200.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	3-CN-Ph	
201.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	4-F-Ph	
202.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	3-tBu, 5-CF_3-Ph	
203.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	5-tetraline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydrochloride
204.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	4-indane	
205.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
206.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
207.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	8-OMe-1-naphthalene	
208.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	4-quinazoline	
209.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-quinazoline	
210.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	1-phthalazine	
211.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	4-quinoline	
212.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	4-isoquinoline	
213.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-pyrimidine	
214.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-tBu,4-CF_3-pyrimidine	
215.	NR^1	CH_2	Ph-C=O	C_2		4-piperazine-1-yl	2-pyridine	
216.	NR^1	CH_2	i-C_3	C_2		4-piperazine-1-yl	1-naphthalene	
217.	NR^1	CH_2	C_2-Ph	C_2		4-piperazine-1-yl	1-naphthalene	
218.	NR^1	CH_2	C_2-(2-OMe)-Ph	C_2		4-piperazine-1-yl	1-naphthalene	
219.	NR^1	CH_2	C_3-(4-Cl)Ph	C_2		4-piperazine-1-yl	1-naphthalene	
220.	NR^1	CH_2	C_2-(2-CF_3)-Ph	C_2		4-piperazine-1-yl	1-naphthalene	
221.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	5-tetraline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
222.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	1-naphthalene	
223.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	2-OMe-Ph	
224.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	4-isoquinoline	
225.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	2-pyrimidine	
226.	NR^1	CH_2	H	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
227.	NR^1	CH_2	CH_2-Ph	C_3		4-piperazine-1-yl	5-tetraline	
228.	NR^1	CH_2	CH_2-Ph	C_3		4-piperazine-1-yl	1-naphthalene	
229.	NR^1	CH_2	CH_2-Ph	C_3		4-piperazine-1-yl	4-isoquinoline	
230.	NR^1	CH_2	CH_2-Ph	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
231.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	5-tetraline	
232.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	1-naphthalene	
233.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	2-OMe-Ph	
234.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	4-isoquinoline	
235.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	2-pyrimidine	
236.	NR^1	CH_2	Me	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
237.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	5-tetraline	
238.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	1-Napthalin	
239.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	2-OMe-Ph	
240.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	4-isoquinoline	
241.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	2-pyrimidine	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
242.	NR^1	CH_2	Boc	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
243.	NR^1	CH_2	CH_3-C=O	C_3		4-piperazine-1-yl	5-tetraline	
244.	NR^1	CH_2	CH_3-C=O	C_3		4-piperazine-1-yl	1-naphthalene	
245.	NR^1	CH_2	CH_3-C=O	C_3		4-piperazine-1-yl	2-OMe-Ph	
246.	NR^1	CH_2	CH_3-C=O	C_3		4-piperazine-1-yl	4-isoquinoline	
247.	NR^1	CH_2	CH_3-C=O	C_3		4-piperazine-1-yl	2-pyrimidine	
248.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
249.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	5-tetraline	
250.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	1-Napthalin	
251.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	2-OMe-Ph	
252.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	4-isoquinoline	
253.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	2-pyrimidine	
254.	NR^1	CH_2	Ph-C=O	C_3		4-piperazine-1-yl	2-OMe-naphthalene	
255.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	5-tetraline	
256.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	1-naphthalene	
257.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	2-OMe-Ph	
258.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	4-isoquinoline	
259.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	2-pyrimidine	
260.	NR^1	CH_2	H	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
261.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	5-tetraline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
262.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	1-naphthalene	
263.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	2-OMe-Ph	
264.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	4-isoquinoline	
265.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	2-pyrimidine	
266.	NR^1	CH_2	Me	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
267.	NR^1	CH_2	CH_2-Ph	C_2		4-piperidine-1-yl	5-tetraline	
268.	NR^1	CH_2	CH_2-Ph	C_2		4-piperidine-1-yl	2-OMe-Ph	
269.	NR^1	CH_2	CH_2-Ph	C_2		4-piperidine-1-yl	4-isoquinoline	
270.	NR^1	CH_2	CH_2-Ph	C_2		4-piperidine-1-yl	2-pyrimidine	
271.	NR^1	CH_2	CH_2-Ph	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
272.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	5-tetraline	
273.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	1-naphthalene	
274.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	2-OMe-Ph	
275.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	4-isoquinoline	
276.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	2-pyrimidine	
277.	NR^1	CH_2	CH_3C=O	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
278.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	5-tetraline	
279.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	1-naphthalene	
280.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	2-OMe-Ph	
281.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	4-isoquinoline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
282.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	2-pyrimidine	
283.	NR^1	CH_2	Boc	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
284.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	5-tetraline	
285.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	1-naphthalene	
286.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	2-OMe-Ph	
287.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	4-isoquinoline	
288.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	2-pyrimidine	
289.	NR^1	CH_2	Ph-C=O	C_2		4-piperidine-1-yl	2-OMe-naphthalene	
290.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	5-tetraline	
291.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
292.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
293.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
294.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
295.	NR^1	CH_2	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
296.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	5-tetraline	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
297.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
298.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
299.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
300.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
301.	NR^1	CH_2	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
302.	NR^1	CH_2	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	tetraline	
303.	NR^1	CH_2	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
304.	NR^1	CH_2	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
305.	NR^1	CH_2	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
306.	NR^1	CH_2	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
307.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	tetraline	
308.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
309.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
310.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
311.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
312.	NR^1	CH_2	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
313.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	tetraline	
314.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
315.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
316.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
317.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
318.	NR^1	CH_2	$CH_3C=O$	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
319.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	tetraline	
320.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
321.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
322.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
323.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
324.	NR^1	CH_2	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
325.	NR^1	CH_2	H	C_2		4-homopiperazine-1-yl	1-naphthalene	
326.	NR^1	CH_2	H	C_2		4-homopiperazine-1-yl	2-OMe-Ph	
327.	NR^1	CH_2	H	C_2		4-homopiperazine-1-yl	2-OMe-1-naphthalene	
328.	NR^1	CH_2	H	C_3		4-homopiperazine-1-yl	2-pyrimidine	
329.	NR^1	CH_2	Me	C_2		4-homopiperazine-1-yl	1-naphthalene	
330.	NR^1	CH_2	Me	C_2		4-homopiperazine-1-yl	2-OMe-Ph	
331.	NR^1	CH_2	CH_2-Ph	C_2		4-homopiperazine-1-yl	1-naphthalene	
332.	NR^1	CH_2	CH_2-Ph	C_3		4-homopiperazine-1-yl	2-OMe-Ph	
333.	NR^1	CH_2	Boc	C_2		4-homopiperazine-1-yl	1-naphthalene	
334.	NR^1	CH_2	Boc	C_2		4-homopiperazine-1-yl	2-OMe-Ph	
335.	NR^1	CH_2	Boc	C_3		4-homopiperazine-1-yl	2-OMe-1-naphthalene	
336.	NR^1	CH_2	CH_3-C=O	C_2		4-homopiperazine-1-yl	1-naphthalene	
337.	NR^1	CH_2	CH_3-C=O	C_2		4-homopiperazine-1-yl	2-OMe-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
338.	NR^1	CH_2	Ph-C=O	C_2		4-homopiperazine-1-yl	1-naphthalene	
339.	NR^1	CH_2	Ph-C=O	C_2		4-homopiperazine-1-yl	1-OMe-Ph	
340.	NR^1	CH_2	Ph-C=O	C_2		4-homopiperazine-1-yl	2-pyrimidine	
341.	NR^1	CH_2	H	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
342.	NR^1	CH_2	H	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
343.	NR^1	CH_2	H	CH_2-C(CH_2)-CH_2		4-piperidine-1-yl	1-naphthalene	
344.	NR^1	CH_2	Me	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
345.	NR^1	CH_2	Me	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
346.	NR^1	CH_2	Me	CH_2-C(CH_2)-CH_2		4-homopiperazine-1-yl	1-naphthalene	
347.	NR^1	CH_2	CH_2-Ph	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
348.	NR^1	CH_2	CH_2-Ph	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
349.	NR^1	CH_2	CH_2-Ph	CH_2-C(CH_2)-CH_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
350.	NR^1	CH_2	Boc	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
351.	NR^1	CH_2	Boc	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
352.	NR^1	CH_2	Boc	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-pyrimidine	
353.	NR^1	CH_2	CH_3-C=O	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
354.	NR^1	CH_2	CH_3-C=O	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
355.	NR^1	CH_2	Ph-C=O	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
356.	NR^1	CH_2	Ph-C=O	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
357.	NR^1	CH_2	H	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
358.	NR^1	CH_2	H	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
359.	NR^1	CH_2	H	CH_2-C(OH)-CH_2		4-piperidine-1-yl	1-naphthalene	
360.	NR^1	CH_2	Me	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
361.	NR^1	CH_2	H	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
362.	NR^1	CH_2	H	CH_2-C(OH)-CH_2		4-homopiperazine-1-yl	1-naphthalene	
363.	NR^1	CH_2	CH_2-Ph	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
364.	NR^1	CH_2	CH_2-Ph	CH_2-C(OH)-CH_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
365.	NR^1	CH_2	Boc	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
366.	NR^1	CH_2	Boc	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
367.	NR^1	CH_2	Boc	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-pyrimidine	
368.	NR^1	CH_2	CH_3-C=O	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
369.	NR^1	CH_2	CH_3-C=O	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
370.	NR^1	CH_2	Ph-C=O	CH_2-C(OH)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
371.	NR^1	CH_2	Ph-C=O	CH_2-C(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
372.	NR^1	CH_2	H	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	
373.	NR^1	CH_2	H	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
374.	NR^1	CH_2	H	C_2-N(Me)-C_2		4-piperidine-1-yl	1-naphthalene	
375.	NR^1	CH_2	Me	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydrochloride
376.	NR^1	CH_2	Me	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
377.	NR^1	CH_2	Me	C_2-N(Me)-C_2		4-homopiperazine-1-yl	1-naphthalene	
378.	NR^1	CH_2	CH_2-Ph	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	
379.	NR^1	CH_2	CH_2-Ph	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
380.	NR^1	CH_2	CH_2-Ph	C_2-N(Me)-C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
381.	NR^1	CH_2	Boc	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	
382.	NR^1	CH_2	Boc	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
383.	NR^1	CH_2	Boc	C_2-N(Me)-C_2		4-piperazine-1-yl	2-pyrimidine	
384.	NR^1	CH_2	CH_3-C=O	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	
385.	NR^1	CH_2	CH_3-C=O	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
386.	NR^1	CH_2	Ph-C=O	C_2-N(Me)-C_2		4-piperazine-1-yl	2-OMe-Ph	
387.	NR^1	CH_2	Ph-C=O	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
388.	NR^1	CH_2	H	CH_2-$CH(CH_3)$-CH_2		4-piperazine-1-yl	2-OMe-Ph	
389.	NR^1	CH_2	H	CH_2-$CH(CH_3)$-CH_2		4-piperazine-1-yl	1-naphthalene	
390.	NR^1	CH_2	H	CH_2-$CH(CH_3)$-CH_2		4-piperidine-1-yl	1-naphthalene	
391.	NR^1	CH_2	Me	CH_2-$CH(CH_3)$-CH_2		4-piperazine-1-yl	2-OMe-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydrochloride
392.	NR^1	CH_2	Me	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	1-naphthalene	
393.	NR^1	CH_2	Me	CH_2-CH(CH_3)-CH_2		4-homopiperazine-1-yl	1-naphthalene	
394.	NR^1	CH_2	CH_2-Ph	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
395.	NR^1	CH_2	CH_2-Ph	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	1-naphthalene	
396.	NR^1	CH_2	CH_2-Ph	CH_2-CH(CH_3)-CH_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
397.	NR^1	CH_2	Boc	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
398.	NR^1	CH_2	Boc	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	1-naphthalene	
399.	NR^1	CH_2	Boc	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	2-pyrimidine	
400.	NR^1	CH_2	CH_3-C=O	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
401.	NR^1	CH_2	CH_3-C=O	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	1-naphthalene	
402.	NR^1	CH_2	Ph-C=O	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	2-OMe-Ph	
403.	NR^1	CH_2	Ph-C=O	CH_2-CH(CH_3)-CH_2		4-piperazine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
404.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	Ph	
405.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-Me-Ph	
406.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-CN-Ph	
407.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-Cl-Ph	
408.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	3-CF_3-Ph	
409.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	4-iC_3-Ph	
410.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	3-Me, 4-Me-Ph	
411.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	5-tetraline	
412.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	4-indane	
413.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	1-naphthalene	
414.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
415.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
416.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	8-OMe-1-naphthalene	
417.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-quinazoline	
418.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	1-phthalazine	
419.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	4-quinoline	
420.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	4-isoquinoline	
421.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-pyrimidine	
422.	CH_2	NR^1	CH_2-Ph	C_2		4-piperazine-1-yl	2-pyridine	
423.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	2-OMe-Ph	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
424.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	2-F-Ph	
425.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	3-tBu-Ph	
426.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	5-tetraline	
427.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	1-naphthalene	
428.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	2-OMe-1-naphthalene	
429.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
430.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	1-isoquinoline	
431.	CH_2	NR^1	H	C_2		4-piperazine-1-yl	2-Ph-4-quinazoline	
432.	CH_2	NR^1	Me	C_2		4-piperazine-1-yl	2-OMe-Ph	
433.	CH_2	NR^1	Me	C_2		4-piperazine-1-yl	1-naphthalene	
434.	CH_2	NR^1	Me	C_2		4-piperazine-1-yl	2-Me-1-naphthalene	
435.	CH_2	NR^1	Me	C_2		4-piperazine-1-yl	2-pyrimidine	
436.	CH_2	NR^1	$CH_3C=O$	C_2		4-piperazine-1-yl	2-OMe-Ph	
437.	CH_2	NR^1	$CH_3C=O$	C_2		4-piperazine-1-yl	1-naphthalene	
438.	CH_2	NR^1	PhC=O	C_2		4-piperazine-1-yl	2-OMe-Ph	
439.	CH_2	NR^1	PhC=O	C_2		4-piperazine-1-yl	1-naphthalene	
440.	CH_2	NR^1	Boc	C_2		4-piperazine-1-yl	2-OMe-Ph	
441.	CH_2	NR^1	Boc	C_2		4-piperazine-1-yl	1-naphthalene	
442.	CH_2	NR^1	CH_2-Ph	C_3		4-piperazine-1-yl	1-naphthalene	
443.	CH_2	NR^1	H	C_3		4-piperazine-1-yl	2-OMe-Ph	

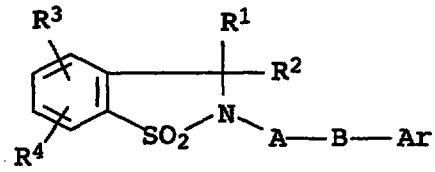
No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
444.	CH_2	NR^1	H	C_3		4-piperazine-1-yl	1-naphthalene	
445.	CH_2	NR^1	Me	C_3		4-piperazine-1-yl	2-OMe-Ph	
446.	CH_2	NR^1	Me	C_3		4-piperazine-1-yl	1-naphthalene	
447.	CH_2	NR^1	Boc	C_3		4-piperazine-1-yl	2-OMe-Ph	
448.	CH_2	NR^1	Boc	C_3		4-piperazine-1-yl	1-naphthalene	
449.	CH_2	NR^1	$CH_3C=O$	C_3		4-piperazine-1-yl	2-OMe-Ph	
450.	CH_2	NR^1	$CH_3C=O$	C_3		4-piperazine-1-yl	1-naphthalene	
451.	CH_2	NR^1	PhC=O	C_3		4-piperazine-1-yl	2-OMe-Ph	
452.	CH_2	NR^1	PhC=O	C_3		4-piperazine-1-yl	1-naphthalene	
453.	CH_2	NR^1	CH_2-Ph	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
454.	CH_2	NR^1	H	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
455.	CH_2	NR^1	Me	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
456.	CH_2	NR^1	Boc	C_2-N(Me)-C_2		4-piperazine-1-yl	1-naphthalene	
457.	CH_2	NR^1	CH_2-Ph	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
458.	CH_2	NR^1	H	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
459.	CH_2	NR^1	Me	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
460.	CH_2	NR^1	Boc	CH_2-C(CH_2)-CH_2		4-piperazine-1-yl	1-naphthalene	
461.	CH_2	NR^1	CH_2-Ph	CH_2-CH(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
462.	CH_2	NR^1	H	CH_2-CH(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
463.	CH_2	NR^1	Me	CH_2-CH(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
464.	CH_2	NR^1	Boc	CH_2-CH(OH)-CH_2		4-piperazine-1-yl	1-naphthalene	
465.	CH_2	NR^1	CH_2-Ph	CH_2-CH(CH_3)CH_2		4-piperazine-1-yl	1-naphthalene	
466.	CH_2	NR^1	H	CH_2-CH(CH_3)CH_2		4-piperazine-1-yl	1-naphthalene	
467.	CH_2	NR^1	Me	CH_2-CH(CH_3)CH_2		4-piperazine-1-yl	1-naphthalene	
468.	CH_2	NR^1	Boc	CH_2-CH(CH_3)CH_2		4-piperazine-1-yl	1-naphthalene	
469.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	5-tetraline	
470.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	1-naphthalene	
471.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	2-OMe-Ph	
472.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	4-isoquinoline	
473.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	2-pyrimidine	
474.	CH_2	NR^1	CH_2-Ph	C_2		4-piperidine-1-yl	2-OMe-Napthalin	
475.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	5-tetraline	
476.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	1-naphthalene	
477.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	2-OMe-Ph	
478.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	4-isoquinoline	
479.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	2-pyrimidine	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
480.	CH_2	NR^1	H	C_2		4-piperidine-1-yl	2-OMe-Napthalin	
481.	CH_2	NR^1	Me	C_2		4-piperidine-1-yl	2-OMe-Ph	
482.	CH_2	NR^1	Me	C_2		4-piperidine-1-yl	1-naphthalene	
483.	CH_2	NR^1	Me	C_3		4-piperidine-1-yl	2-pyrimidine	
484.	CH_2	NR^1	CH_3-C=O	C_2		4-piperidine-1-yl	2-OMe-Ph	
485.	CH_2	NR^1	CH_3-C=O	C_2		4-piperidine-1-yl	1-naphthalene	
486.	CH_2	NR^1	Ph-C=O	C_2		4-piperidine-1-yl	2-OMe-Ph	
487.	CH_2	NR^1	Ph-C=O	C_2		4-piperidine-1-yl	1-naphthalene	
488.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	5-tetraline	
489.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
490.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-Ph	
491.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	4-isoquinoline	
492.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-pyrimidine	
493.	CH_2	NR^1	CH_2-Ph	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	2-OMe-naphthalene	
494.	CH_2	NR^1	H	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	

No.	X	Y	R^1	A	R^2	B	Ar	m.p. hydro-chloride
495.	CH_2	NR^1	Me	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
496.	CH_2	NR^1	Boc	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
497.	CH_2	NR^1	CH_3-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
498.	CH_2	NR^1	Ph-C=O	C_2		4-tetrahydro-1,2,3,6-pyridine-1-yl	1-naphthalene	
499.	CH_2	NR^1	CH_2-Ph	C_2		4-homopiperazine-1-yl	1-naphthalene	
500.	CH_2	NR^1	H	C_2		4-homopiperazine-1-yl	1-naphthalene	
501.	CH_2	NR^1	Me	C_2		4-homopiperazine-1-yl	1-naphthalene	
502.	CH_2	NR^1	Boc	C_2		4-homopiperazine-1-yl	1-naphthalene	

DE 19746612.5 describes 2-substituted 1,2-benzisothiazole derivatives of the formula I



I

in which

R^1, R^2 independently of one another are (C_{1-6})-alkyl,

R^3, R^4 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, OH, O-(C_{1-6})-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, NR^5R^6, CO_2R^7, nitro, cyano, pyrrole, are a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

R^5, R^6 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, COPh, CO_2tBu, CO-(C_{1-4})-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

R^7 is hydrogen or (C_{1-6})-alkyl, branched or unbranched,

A is branched or unbranched (C_{1-10})-alkylene or straight-chain or branched (C_{2-10})-alkylene which comprises at least one group Z selected from the group consisting of O, S, NR^7, cyclopropyl, CHOH, a double and a triple bond,

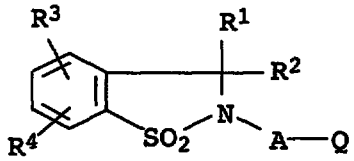
B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine and the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by (C_{1-6})-alkyl, branched or unbranched, O-(C_{1-6})-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, NR^5R^6, CO_2R^7, cyano or phenyl, is tetraline, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by (C_{1-4})-alkyl or O(C_{1-4})-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals, for example

quinoline, isoquinoline, phthalazine, indole and quinazoline, which for its part may be substituted again by phenyl,

and their salts with physiologically acceptable acids.

These compounds of the formula I can be prepared by reacting a compound of the formula II

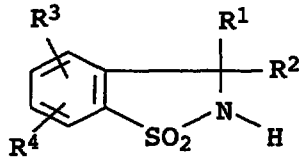


II,

in which R^1 to R^4 and A are as defined above and Q is a group that can be cleaved off (for example Cl, Br, I, alkanesulfonyloxy or arylsulfonyloxy), with a secondary amine of the formula III

$$H\text{-}B\text{-}Ar \qquad III,$$

in which B and Ar are as defined above, in a manner known per se and converting the resulting compound, if appropriate, into the acid addition salt of a physiologically acceptable acid. It is also possible to react a compound of the formula IV

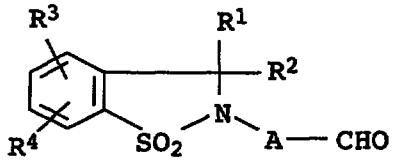


IV

with a compound of the formula V

$$Q\text{-}A\text{-}B\text{-}Ar \qquad V$$

in a manner known per se. A further synthesis variant is the attachment of a compound of the formula VI



VI

to a compound of the formula III by a reductive amination known per se.

The compounds of the formula III can be synthesized by

5. attaching compounds of the formula VII

$$W\text{-}B^1 \qquad \text{(VII)},$$

where B^1 is piperazine or homopiperazine and W is hydrogen or one of the customary amino protective groups (such as, for example, Boc or Cbz), to a compound of the formula VIII

$$P\text{-}Ar \qquad \text{(VIII)},$$

where P is $B(OH)_2$, SnR_3, OTf, Br, Cl or I and R is C_1-C_4-alkyl, in a manner known per se; or

6. attaching compounds of the formula IX

$$W\text{-}B^2\text{-}P^1 \qquad \text{(IX)},$$

where B^2 is 4-tetrahydro-1,2,3,6-pyridine or the corresponding cyclic compounds which are enlarged by a methylene group and P^1 is Cl, Br, I, SnR_3 - where R is C_1-C_4-alkyl - , OTf, to a compound of the formula X

$$P\text{-}Ar \qquad \text{(X)},$$

where W, P and Ar are each as defined above, and where the reactions are carried out by known processes, such as, for example, those described in
S.L. Buchwald et al. J. Am. Chem. Soc. 1996, 118, 7215
J.F. Hartwig et al. Tetrahedron Lett. 1995, 36, 3604
J.K. Stille et al. Angew. Chem. 1986, 98, 504
S.L. Buchwald et al. Angew. Chem. 1995, 107, 1456 or
J.F. Hartwig et al. J. Am. Chem. Soc 1996, 118, 7217 or
J.F. Hartwig et al. J. Org. Chem. 1997, 62, 1268
S.L. Buchwald et al. J. Org. Chem. 1997, 62, 1264 and literature cited therein or
S.L. Buchwald et al. J. Am. Chem. Soc 1997, 119, 6054
J.K. Stille, Angew. Chem. 1986, 98, 504 or
J.K. Stille et al. J. Org. Chem. 1990, 55, 3014.
M. Pereyre et al. "Tin in Organic Synthesis", Butterworth 1987; or

7. reducing compounds of the formula (XI)

$$W\text{-}B^2\text{-}Ar \qquad \text{(XI)},$$

where B^2 is as defined above, to give compounds of the formula XII

$$W\text{-}B^3\text{-}Ar \qquad (XII),$$

in which B^3 is a piperidine which is attached in 1,4-position or the corresponding cyclic compounds which are enlarged by a methylene group; or

8. cyclizing compounds of the formula XIII

$$W\text{-}N\text{-}(C_2H_4Q)_2 \qquad (XIII),$$

where W and Q are as defined above, with a compound of the formula XIV

$$NH_2\text{-}Ar \qquad (XIV),$$

where Ar is as defined above, to give compounds of the formula XV

$$W\text{-}B^1\text{-}Ar \qquad (XV).$$

The substances of the formulae III and V required as starting materials for synthesizing the novel compounds are known or can be prepared according to known processes (for example Organikum Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) Comprehensive Heterocyclic Chemistry Pergamon Press) from analogous starting materials.

The further reaction of the compounds

$$H\text{-}B\text{-}Ar \qquad (III)$$

prepared in this manner according to 1. to 4. with subsequent removal of any protective groups to give the compounds of the formula V is carried out by attachment to compounds of the formula XVI

$$Q\text{-}A\text{-}Q' \qquad (XVI),$$

where Q and Q' are leaving groups, under conditions known per se.

The substances of the formulae II, IV, VI and of the formulae P-Ar, NH_2-Ar, W-B^1 or W-B^2-P^1 required as starting materials for synthesizing the novel compounds are known or can be prepared according to the preparation processes described in the

literature from analogous starting materials (for example B. Schulze, K. Illgen J. prakt. Chem. 1997, 339, 1 or K. Auer, E. Hungerbühler, R. W. Lang Chimia 1990, 44, 120 or A. Yokoo et al. Bull. Chem. Soc. Jpn. 1956, 29, 631 or L. Börjeson et al. Acta Chem. Chem. 1991, 45, 621 or Organikum Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) Comprehensive Heterocyclic Chemistry Pergamon Press or The Chemistry of Heterocyclic Compounds J. Wiley & Sons Inc. NY and literature cited therein).

Example 1

3,3-Dimethyl-2-[3-(4-tetralin-5-yl-piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Preparation of the starting materials

a) 3,3-Dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

The preparation of this compound was carried out in a manner known from the literature (K. Auer, E. Hungerbühler, R. W. Lang Chimia 1990, 44, 120). 3,3-Diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 174°C) and 3,3-dimethyl-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 187°C) were obtained in a similar manner.

b) 2-(3-Chloroprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benziso-thiazole 1,1-dioxide

A solution of 5.9 g (3 mmol) of 3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide in 150 ml of DMF was initially charged at room temperature and, after addition of 3.7 g (3.3 mmol) of potassium t-butoxide, heated under nitrogen to 80°C. 14.2 g (9 mmol) of 1-bromo-3-chloropropane were then added quickly, and the mixture was stirred at 100°C for 30 min. The mixture was poured into ice-water and extracted with ether, and the organic phases were washed with water, dried with sodium sulfate and subsequently concentrated, so that the product precipitated out in crystalline form and could be filtered off with suction. This gave 6.7 g (82%) of substance. M.p.: 107°C.

2-(3-Chloroprop-1-yl)-3,3-diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 70°C), 2-(3-chloroprop-1-yl)-3,3-dimethyl-6-nitro-2,3-dihydro-1,2- benzisothiazole 1,1-dioxide (m.p.: 146°C), 2-(2-chloroethyl)-3,3-diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (oil), 2-(2-chloroethyl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

(oil), 2-(3-chloro-2-methyleneprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 115°C) and 2-(3-chloroprop-1-yl)-3,3-dimethyl-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 146°C) were obtained in a similar manner.

c) 1-Tetralin-5-yl-piperazine

14.7 g (0.1 mol) of 5-aminotetraline and 18 g (0.11 mol) of bis(β-chloroethyl)amine hydrochloride in 300 ml of n-butanol were refluxed for 48 h, 5.4 g of sodium carbonate were added after cooling and the mixture was once more refluxed for 20 h. The precipitate which was formed by cooling was filtered off with suction, taken up in water and admixed with 2N sodium hydroxide solution. The aqueous phase was extracted with ethyl acetate, and the extract was washed with water, dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 10.7 g (50%) of the product as an oil.

4-Piperazin-1-ylisoquinoline

4.51 g (21.7 mmol) of 4-bromoisoquinoline, 4.65 g (25.0 mmol) of t-butyl piperazine-N-carboxylate, 0.1 g (0.11 mmol) of tris-(dibenzylideneacetone)dipalladium, 0.11 g (0.18 mmol) of 2,2'-bis(diphenylphosphino)-1,1'-dinaphthyl and 2.92 g (30.4 mmol) of sodium t-butoxide were admixed in 50 ml of toluene and stirred at 75°C for 2 h. The reaction mixture was poured onto ice/sodium chloride and extracted with ethyl acetate, the organic phase was dried over sodium sulfate and the solvent was removed using a rotary evaporator. The product crystallized out, and it was filtered off with suction and washed with pentane. This gave 5.5 g (81%) of the Boc-protected piperazine (m.p.: 111°C). 5.2 g (16.6 mmol) of this substance were taken up in 17 ml of dichloromethane and, at 0°C, slowly admixed with 17 ml (0.22 mol) of trifluoroacetic acid. The mixture was stirred at 0°C for 4 h, poured onto ice-water and extracted with dichloromethane. The aqueous phase was filtered, made alkaline and extracted with dichloromethane. After drying over sodium sulfate and substantial removal of the solvent, the residue was diluted with diethyl ether and the hydrochloride was precipitated out using ethereal hydrochloric acid. This gave 3.2 g (67%) of the product. (m.p.: 293°C).

The following compounds were prepared similarly to the two processes described: 1-naphth-1-yldiazepane (85°C, hydrochloride), 1-naphth-1-ylmethylpiperazine (oil), 4-piperazin-1-yl-indane (oil), 1-naphth-1-ylpiperazine (82°C), 4-chloro-1-piperazin-

1-ylphthalazine (205°C, decomp.) and 4-piperazin-1-ylquinazoline (320°C, hydrochloride). Other derivatives were commercially available.

Preparation of the end product

1.1 g (5.2 mmol) of 1-tetralin-5-ylpiperazine, 1.5 ml of triethylamine and a trace of potassium iodide were added to a solution of 1.64 g (6.0 mmol) of 2-(3-chloroprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide in 40 ml of DMF. The reaction mixture was allowed to react at 100°C for four hours and then poured onto ice-water, and the resulting precipitate was filtered off with suction. Purification was carried out by recrystallization from isopropanol, giving 1 g (43%) of the product (m.p.: 140°C).

NMR: $CDCl_3$ δ 7.8 (d, 1H), 7.6 (dd, 1H), 7.5 (dd, 1H), 7.4 (d, 1H), 7.1 (dd, 1H), 6.9 (d, 1H), 6.8 (d, 1H), 3.4 (t, 2H), 3.0-2.5 (m, 14H), 2.1 (tt, 2H), 1.8-1.7 (m, 4H), 1.5 (s, 6H) ppm.

The following compounds were obtained in a similar manner:

Example 2:
3,3-dimethyl-2-[3-(4-(2-phenylquinazolin-4-yl)piperazin-1-yl)-prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 269°C, hydrochloride).

Example 3:
3,3-dimethyl-2-[3-(4-quinolin-2-yl-piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 63°C).

Example 4:
3,3-dimethyl-2-[3-(4-naphth-1-yl-1,4-diazepan-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 126°C, hydrochloride).

Example 5:
3,3-dimethyl-2-[3-(4-(4-chlorophthalazin-1-yl)piperazin-1-yl)-eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 190°C).

Example 6:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)-2-methyleneprop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 193°C).

Example 7:
3,3-dimethyl-2-[2-(4-quinazolin-4-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 178°C, hydrochloride).

Example 8:
3,3-dimethyl-2-[2-(4-naphth-1-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 282°C, hydrochloride).

Example 9:
3,3-dimethyl-2-[2-(4-isoquinolin-4-yl)piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 243°C, hydrochloride).

Example 10:
3,3-diethyl-2-[2-(4-naphth-1-yl-piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (oil).

Example 11:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-pyrrol-1-yl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 269°C, hydrochloride).

The pyrrole ring was constructed by reacting 3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-amino-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide with 2,5-dimethoxytetrahydrofuran in glacial acetic acid at 100°C (1h), in a yield of 86%.

Example 12:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-benzoylamido-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 127°C).

Example 13:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 203°C).

Example 14:
3,3-dimethyl-2-[2-(4-(2,3-dimethylphenyl)piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 291°C, hydrochloride).

Example 15:
3,3-dimethyl-2-[2-(4-indan-4-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 271°C, hydrochloride).

Example 16:
3,3-dimethyl-2-[3-(4-(4-chloronaphth-1-yl)piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 151°C).

Example 17:
3,3-dimethyl-2-[3-(4-pyrimidin-2-ylpiperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 263°C, hydrochloride).

Example 18:
3,3-dimethyl-2-[2-(4-(4-methoxyphenyl)-piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 207°C, hydrochloride).

Example 19:
3,3-dimethyl-2-[3-(4-(2-methoxyphenyl)piperazin-1-yl)-2-hydroxy-prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 160°C).

Example 20:
3,3-diethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 179°C).

Example 21:
3,3-dimethyl-2-[3-(4-(2,5-dimethylphenyl)piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 218°C, hydrochloride).

Example 22:
3,3-dimethyl-2-[2-(4-(2-cyanophenyl)piperazin-1-yl)-eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 228°C, hydrochloride).

Example 23:
3,3-dimethyl-2-[2-(4-naphth-1-ylpiperazin-1-yl)eth-1-yl]-4-chloro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Preparation of the starting materials

a) 4-Chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide. This compound was prepared similarly to Example 1 a). Yield 7.8 g (70%). (m.p. 121°C)

b) 2-(2,2-Diethoxyeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

7.7 g (33 mmol) of 4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide, 8.25 ml (55 mmol) of bromoacetaldehyde diethyl acetal and 7.0 g of potassium carbonate were taken up in 100 ml of dry DMF and stirred at 120°C for 5 h. The reaction mixture was poured into ice-water and then extracted with ethyl acetate, and the organic phase was washed with water and dried over sodium sulfate. The solvent was removed under reduced pressure and the crude product was purified by column chromatography. This gave 7.5 g (65%) of the product as an oil.

c) 2-(2-Oxoeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

7.5 g (21.5 mmol) of 2-(2,2-diethoxyeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide and 25 ml of conc. hydrochloric acid were taken up in 25 ml of water and 150 ml of THF and stirred at 40°C for 1.5 h. The reaction mixture was neutralized using aqueous sodium hydroxide solution and extracted with ether, and the organic phase was dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 5.8 g (98%) of the product as an oil.

Preparation of the end product

1.5 g (5.5 mmol) of the aldehyde 24 c), 1.06 g (5 mmol) of naphthylpiperazine (prepared analogously to Example 1 c)) and 0.42 g (7 mmol) of glacial acetic acid were initially charged in 50 ml of ethanol, the mixture was stirred at room temperature for 30 minutes and 0.5 g (8 mmol) of sodium cyanoborohydride were then added slowly. The reaction mixture was stirred at room temperature for 2 h and then poured onto an ice/sodium chloride mixture and extracted with dichloromethane. The extract was dried with sodium sulfate, the solvent was distilled off and the residue was subsequently recrystallized from ethanol, giving 0.9 g (39%) of colorless crystals (m.p. 156°C).

NMR:$CDCl_3$ δ = 8.3 (m, 1H), 7.8 (m, 1H), 7.7 (d, 1H), 7.6 - 7.3 (m, 6H), 7.1 (d, 1H), 3.5 (t, 2H), 3.2 (m, 4H), 3.0 - 2.8 (m, 6H), 1.8 (s, 6H) ppm.

Example 24

Preparation of 3,3-dimethyl-2-[2-(4-naphth-1-yltetrahydro-1,2,3,6-pyridin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Synthesis of the starting materials

a) N-Boc-4-(trifluoromethanesulfonyloxy)tetrahydro-1,2,3,6-pyridine

At -78°C, a solution of 13.2 g (0.13 mol) of diisopropylamine in 200 ml of THF was deprotonated with 100 ml of nBuLi (1.6M in hexane), and, after 30 minutes at this temperature, 20.0 g (0.1 mol) of N-Boc-piperidone, dissolved in 50 ml of THF, were added dropwise. After a further three hours at -78°C, a solution of 39.3 g (0.11 mol) of N,N-bistrifluoromethanesulfonylaniline in 50 ml of THF was added, and the reaction mixture was allowed to warm to room temperature overnight. For work-up, the mixture was admixed with water and extracted with ether, the organic phases were washed with $NaHCO_3$ solution and water and dried over sodium sulfate, and the solvent was concentrated. The crude product was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 3/1).
Yield: 20.2 g (60% of theory)
^1H NMR:(270 MHz, $CDCl_3$) δ = 1.4 (s, 9H); 2.4 (m, 2H); 3.6 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H) ppm.

b) N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine

14.7 g (44.4 mmol) of the compound described above, dissolved in 115 ml of dimethoxyethane, were admixed successively with 22 ml of 2M sodium carbonate solution, 7.63 g (44.4 mmol) of naphthyl-1-boronic acid, 4.13 g (97.6 mmol) of lithium chloride, 0.85 g (4.44 mmol) of copper(I) iodide and 2.1 g (1.77 mmol) of tetrakistriphenylpalladium, and the mixture was heated at the boil for 4 h. For work-up, aqueous ammonia solution was added to the mixture, which was then extracted with water and ethyl acetate, the extract was dried over sodium sulfate and the residue which was obtained after evaporation of the solvent was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 4/1).
Yield: 8.2 g (57% of theory)

^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.4 (s, 9H); 2.5 (m, 2H); 3.7 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H); 7.2-7.5 (m, 3H); 7.3-8.0 (m, 3H) ppm.

c) 4-Naphth-1-yltetrahydro-1,2,3,6-pyridine

7.84 g (25.3 mmol) of N-Boc-4-naphth-1-yl-3,6-dihydro-2H-pyridine were stirred overnight at room temperature with 200 ml of ethereal hydrochloric acid, and the precipitated product was filtered off and dried.
Yield: 5.5 g (88% of theory).

d) Preparation of the end product

1.0 g (4.1 mmol) of the compound 24c described above, dissolved in 20 ml of methanol, was, in the presence of 2.22 g (16.8 mmol) of zinc(II) chloride, admixed first with 1.27 g (5.3 mmol) of the aldehyde described under Example 23c and then with 0.5 g (8.14 mmol) of sodium cyanoborohydride. After 16 h at room temperature, the mixture was worked up as described and the resulting crude product was purified by chromatography (silica gel, mobile phase dichloromethane/methanol = 97/3). Precipitation of the salt using ethereal hydrochloric acid solution gave a white solid.
Yield: 0.9 g (47% of theory)
^{1}H NMR (270 MHz, DMSO-d6): δ = 1.6 (m, 6H); 2.6 (m, 1H); 3.1 (m, 1H); 3.4-3.6 (m, 6H); 4.0-4.2 (m, 2H); 5.8 (brd. s, 1H); 7.6-8.0 (m, 7H); 8.2 (d, 1H); 12.0 (s, 1H) ppm.

Example 25

Preparation of 3,3-dimethyl-2-[2-(4-naphth-1-ylpiperidin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

a) 4-Naphth-1-ylpiperidine

3.7 g (15.3 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine, dissolved in methanol, were hydrogenated with hydrogen for 48 h at room temperature, with addition of 0.8 g of palladium on carbon. The catalyst was filtered off and the solvent was concentrated.
Yield: 1.8 g (56% of theory)
^{1}H NMR (270 MHz, $CDCl_3$) δ = 1.6-1.8 (m, 2H); 2.0 (m, 2H); 2.9 (dt, 2H); 3.3 (d, 2H); 3.5 (tt, 1H); 7.4-7.6 (m, 4H); 7.7 (d, 1H); 7.9 (d, 1H); 8.1 (d, 1H) ppm.

Preparation of the end product

A solution of 1.5 g (7.1 mmol) of the amine 25a in 20 ml of methanol was admixed first with 3.8 g (28.4 mmol) of zinc chloride and then with 2.21 g (9.2 mmol) of the aldehyde described under Example 23 c, dissolved in 15 ml of methanol, and 0.89 g (14.2 mmol) of sodium cyanoborohydride was then added a little at a time. The mixture was stirred for six hours, undissolved particles were then filtered off, the mother liquor was concentrated and the residue was taken up in ethyl acetate. The organic phase was washed with water and saturated sodium chloride solution, dried over sodium sulfate and filtered, giving, on concentration, a yellowish oil.
Yield: 2.2 g (65% of theory)
^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.7-1.9 (m, 8H); 2.0 (m, 2H); 2.7-3.0 (m, 4H); 3.2 (m, 2H); 3.5 (m, 1H); 3,7 (t, 2H); 7.1 (d, 1H); 7.3-7.7 (m, 9H); 8.2 (d, 1H) ppm.

Other preferred compounds of the formula I according to the invention are listed in the table below.

These compounds are suitable for preparing medicaments for the prophylaxis and therapy of neurodegeneration, cerebral trauma and cerebral ischemia, in particular stroke, and of diseases which are caused by these disorders.

A use according to the invention also relates to neuroprotection.

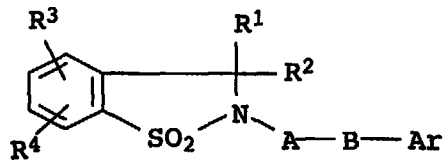
The preparation of these compounds is described in the patents mentioned at the outset.

The preparation as a medicament is carried out using a compound of the formula I or its pharmacologically acceptable acid addition salt as active compound, together with customary excipients and diluents.

The use according to the invention can be carried out in a customary manner, orally or parenterally, intravenously or intramuscularly.

The dosage depends on the age, on the state and the weight of the patient and on the type of administration. In general, the daily dose of active compound is between approximately 1 and 100 mg/kg of body weight in the case of oral administration and between 0.1 and 10 mg/kg of body weight in the case of parenteral administration.

The medicaments can be used in solid or liquid form in customary pharmaceutical administration forms, for example as tablets, film-coated tablets, capsules, powders, granules, sugar-coated tablets, suppositories, solutions, ointments, creams or sprays. These are prepared in a customary manner. Here, the active compounds can be processed with the customary pharmaceutical auxiliaries, such as tablet binders, fillers, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, sustained-release agents, antioxidants and/or propellants (cf. H. Sucker et al.: Pharmazeutische Technologie [Pharmaceutical Technology], Thieme-Verlag, Stuttgart, 1978). The resulting administration forms generally comprise the active compound in an amount of from 1 to 99% by weight.



I

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
26	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	9-anthracene	178°C (HCl)
27	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe-1-naphthaline	181°C (HCl)
28	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	1-naphthaline	>250°C (HCl)
29	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-pyridine	135°C (HCl)
30	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CH_3-2-pyridine	128°C
31	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Ph-4-quinazoline	172°C
32	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CF_3-2-pyridine	138°C
33	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-pyrimidine	124°C
34	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-Cl-1-Phthalazin	190°C (HCl)
35	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	5-tetra-lin	275°C (HCl)
36	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CF_3-Ph	265°C (HCl)

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
37	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-NO_2-Ph	152°C
38	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Me-Ph	
39	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OH-Ph	
40	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Br-Ph	
41	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-CF_3-Ph	
42	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OEt-Ph	
43	Me	H	H	Me	Me	/	C_2	4-piperazine-1-yl	2-NR^5R^6-Ph	
44	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-O(n-C_4)-Ph	
45	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-F-Ph	
46	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-Ph	
47	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Cl-Ph	
48	Me	H	H	/	/	H	C_2	4-piperazine-1-yl	2-CO_2R^7-Ph	
49	Me	H	H	/	/	Me	C_2	4-piperazine-1-yl	2-CO_2R^7-Ph	
50	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	2-NR^5R^6-Ph	
51	Me	H	H	n-C_3	n-C_3	/	C_2	4-piperazine-1-yl	2-NR^5R^6-Ph	
52	Me	H	H	i-C_3	i-C_3	/	C_2	4-piperazine-1-yl	2-NR^5R^6-Ph	
53	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-I-Ph	
54	Me	H	H	/	/	i-C_3	C_2	4-piperazine-1-yl	2-CO_2R^7-Ph	
55	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	Ph	
56	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Et-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
57	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-iC_3-Ph	
58	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Ph-Ph	
59	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-tBu-Ph	
60	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Et-Ph	
61	Me	H	H	/	/	Et	C_2	4-piperazine-1-yl	3-CO_2R^7-Ph	
62	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-I-Ph	
63	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Cl-Ph	
64	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Br-Ph	
65	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-F-Ph	
66	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-OH-Ph	
67	Me	H	H	/	/	H	C_2	4-piperazine-1-yl	3-CO_2R^7-Ph	
68	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	3-NR^5R^6-Ph	
69	Me	H	H	Me	Me	/	C_2	4-piperazine-1-yl	3-NR^5R^6-Ph	
70	Me	H	H	i-C_3	i-C_3	/	C_2	4-piperazine-1-yl	3-NR^5R^6-Ph	
71	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CN-Ph	
72	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-OMe-Ph	
73	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-NO_2-Ph	
74	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-OEt-Ph	
75	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-O(n-C_5)Ph	
76	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-Ph-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
77	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-iC_3-Ph	
78	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-nC_3-Ph	
79	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-nC_6-Ph	
80	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-I-Ph	
81	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-F-Ph	
82	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-Br-Ph	
83	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-Cl-Ph	
84	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-OH-Ph	
85	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-CN-Ph	
86	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-CF_3-Ph	
87	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-NO_2-Ph	
88	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	4-NR^5R^6-Ph	
89	Me	H	H	Me	Me	/	C_2	4-piperazine-1-yl	4-NR^5R^6-Ph	
90	Me	H	H	n-C_4	n-C_4	/	C_2	4-piperazine-1-yl	4-NR^5R^6-Ph	
91	Me	H	H	Me	Et	/	C_2	4-piperazine-1-yl	4-NR^5R^6-Ph	
92	Me	H	H	/	/	H	C_2	4-piperazine-1-yl	4-CO_2R^7-Ph	
93	Me	H	H	/	/	Me	C_2	4-piperazine-1-yl	4-CO_2R^7-Ph	
94	Me	H	H	/	/	n-C_5	C_2	4-piperazine-1-yl	4-CO_2R^7-Ph	
95	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-OEt-Ph	
96	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Cl,4-NO_2-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
97	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Cl,4-Me-Ph	
98	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-CN,6-CN-Ph	
99	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Me,6-Me-Ph	
100	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-NO_2,4-CF_3-Ph	
101	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Cl,4-Cl-Ph	
102	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Et,3-Et-Ph	
103	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	2-NR^5R^6,4-Cl-Ph	
104	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	2-NR^5R^6,4-Me-Ph	
105	Me	H	H	Me	Me	/	C_2	4-piperazine-1-yl	2-NR^5R^6,4-Cl-Ph	
106	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Me,4-Me-Ph	
107	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Cl,5-Cl-Ph	
108	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,4-OMe-Ph	
109	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-tBu,5-tBu-Ph	
110	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-tBu,5-CF_3-Ph	
111	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,5-Cl-Ph	
112	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,5-OMe-Ph	
113	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,5-Ph-Ph	
114	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,4-OMe-Ph	
115	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CF_3,4-Cl-Ph	
116	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-NO_2,4-CF_3,5-NO_2-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
117	Me	H	H	H	H	/	C_2	4-piperazine-1-yl	2-NR^5R^6,4-Me,5-Cl-Ph	
118	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,3-Cl,5-Cl-Ph	
119	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,4-NO_2,5-Me-Ph	
120	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe,4-Cl,5-Me-Ph	
121	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Me,4-Cl,5-CF_3-Ph	
122	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	1-tetra-lin	
123	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	1-Indan	
124	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-1-naphthaline	
125	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OEt-1-naphthaline	
126	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Me-1-naphthaline	
127	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Et-1-naphthaline	
128	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	8-OMe-1-naphthaline	
129	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	8-Me-1-naphthaline	
130	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	9-anthracene	
131	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Indol	
132	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-quinazoline	
133	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Chinoxalin	
134	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	1-Phthalazin	
135	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-quinoline	
136	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-quinoline	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
137	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	5-quinoline	
138	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	1-Isoquinoline	
139	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	8-Isoquinoline	
140	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	7-benzofuran	
141	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-2H-chromene	
142	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	5-chromane	
143	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	8-chromane	
144	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-pyrimidine	
145	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	4-pyrimidine	
146	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Pyrazin	
147	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-Isoxazol	
148	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	3-pyrrole	
149	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	6-iC_3-4-pyrimidine	
150	Me	H	H	/	/	/	C_2	4-piperazine-1-yl	7-OMe-1-naphthaline	
151	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Me-Ph	
152	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OH-Ph	
153	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Br-Ph	
154	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-CF_3-Ph	
155	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OEt-Ph	
156	Me	H	H	Me	Me	/	C_2	4-piperidine-1-yl	2-NR^5R^6-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
157	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-O(n-C_4)-Ph	
158	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-NO_2-Ph	
159	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-F-Ph	
160	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe-Ph	
161	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-CN-Ph	
162	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Cl-Ph	
163	Me	H	H	/	/	H	C_2	4-piperidine-1-yl	2-CO_2R^7-Ph	
164	Me	H	H	/	/	Me	C_2	4-piperidine-1-yl	2-CO_2R^7-Ph	
165	Me	H	H	H	H	/	C_2	4-piperidine-1-yl	2-NR^5R^6-Ph	
166	Me	H	H	n-C_3	n-C_3	/	C_2	4-piperidine-1-yl	2-NR^5R^6-Ph	
167	Me	H	H	i-C_3	i-C_3	/	C_2	4-piperidine-1-yl	2-NR^5R^6-Ph	
168	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-I-Ph	
169	Me	H	H	/	/	i-C_3	C_2	4-piperidine-1-yl	2-CO_2R^7-Ph	
170	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	Ph	
171	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Et-Ph	
172	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-iC_3-Ph	
173	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Ph-Ph	
174	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-tBu-Ph	
175	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Et-Ph	
176	Me	H	H	/	/	Et	C_2	4-piperidine-1-yl	3-CO_2R^7-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
177	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-I-Ph	
178	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Cl-Ph	
179	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Br-Ph	
180	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-F-Ph	
181	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-CF_3-Ph	
182	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-OH-Ph	
183	Me	H	H	/	/	H	C_2	4-piperidine-1-yl	3-CO_2R^7-Ph	
184	Me	H	H	H	H	/	C_2	4-piperidine-1-yl	3-NR^5R^6-Ph	
185	Me	H	H	Me	Me	/	C_2	4-piperidine-1-yl	3-NR^5R^6-Ph	
186	Me	H	H	i-C_3	i-C_3	/	C_2	4-piperidine-1-yl	3-NR^5R^6-Ph	
187	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-CN-Ph	
188	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-OMe-Ph	
189	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-NO_2-Ph	
190	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-OEt-Ph	
191	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-O(n-C_5)Ph	
192	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-Ph-Ph	
193	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-iC_3-Ph	
194	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-nC_3-Ph	
195	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-nC_6-Ph	
196	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-I-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
197	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-F-Ph	
198	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-Br-Ph	
199	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-Cl-Ph	
200	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-OH-Ph	
201	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-CN-Ph	
202	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-CF_3-Ph	
203	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-NO_2-Ph	
204	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-NR^5R^6-Ph	
205	Me	H	H	Me	Me	/	C_2	4-piperidine-1-yl	4-NR^5R^6-Ph	
206	Me	H	H	n-C_4	n-C_4	/	C_2	4-piperidine-1-yl	4-NR^5R^6-Ph	
207	Me	H	H	Me	Et	/	C_2	4-piperidine-1-yl	4-NR^5R^6-Ph	
208	Me	H	H	/	/	H	C_2	4-piperidine-1-yl	4-CO_2R^7-Ph	
209	Me	H	H	/	/	Me	C_2	4-piperidine-1-yl	4-CO_2R^7-Ph	
210	Me	H	H	/	/	n-C_5	C_2	4-piperidine-1-yl	4-CO_2R^7-Ph	
211	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-OMe-Ph	
212	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-OEt-Ph	
213	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Cl,4-NO_2-Ph	
214	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Cl,4-Me-Ph	
215	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-CN,6-CN-Ph	
216	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Me,6-Me-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
217	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-NO_2,4-CF_3-Ph	
218	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Cl,4-Cl-Ph	
219	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Me,3-Me-Ph	
220	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Et,3-Et-Ph	
221	Me	H	H	H	H	/	C_2	4-piperidine-1-yl	2-NR^5R^6,4-Cl-Ph	
222	Me	H	H	H	H	/	C_2	4-piperidine-1-yl	2-NR^5R^6,4-Cl-Ph	
223	Me	H	H	Me	Me	/	C_2	4-piperidine-1-yl	2-NR^5R^6,4-Cl-Ph	
224	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Me,4,Me-Ph	
225	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Cl,5-Cl-Ph	
226	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,4-OMe-Ph	
227	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-tBu,5-tBu-Ph	
228	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-tBu,5-CF_3-Ph	
229	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,5-Cl-Ph	
230	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,5-OMe-Ph	
231	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,5-Ph-Ph	
232	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-OMe,4-OMe-Ph	
233	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-CF_3,4-Cl-Ph	
234	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-NO_2,4-CF_3,5-NO_2-Ph	
235	Me	H	H	H	H	/	C_2	4-piperidine-1-yl	2-NR^5R^6,4-Me,5-Cl-Ph	
236	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,3-Cl,5-Cl-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
237	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,4-NO_2,5-Me-Ph	
238	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe,4-Cl,5-Me-Ph	
239	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Me,4-Cl,5-CF_3-Ph	
240	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	5-tetra-lin	
241	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-Indan	
242	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	1-tetra-lin	
243	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	1-Indan	
244	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OMe-1-naphthaline	
245	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-OEt-1-naphthaline	
246	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Me-1-naphthaline	
247	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Et-1-naphthaline	
248	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	8-OMe-1-naphthaline	
249	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	8-Me-1-naphthaline	
250	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	9-anthracene	
251	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Indol	
252	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-quinazoline	
253	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-quinazoline	
254	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Chinoxalin	
255	Me	H	H	/	/	(	C_2	4-piperidine-1-yl	1-Phthalazin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
256	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-quinoline	
257	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-quinoline	
258	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-quinoline	
259	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	5-quinoline	
260	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	1-Isoquinoline	
261	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-Isoquinoline	
262	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	8-Isoquinoline	
263	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	7-benzofuran	
264	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-2H-chromene	
265	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	5-chromane	
266	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	8-chromane	
267	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-pyrimidine	
268	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	pyrimidine	
269	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	5-OMe-4-pyrimidine	
270	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	4-pyrimidine	
271	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Pyrazin	
272	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-Isoxazol	
273	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-pyridine	
274	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-pyridine	
275	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	3-pyrrole	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
276	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	2-Ph-4-quinazoline	
277	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	6-iC_3-4-pyrimidine	
278	Me	H	H	/	/	/	C_2	4-piperidine-1-yl	7-OMe-1-naphthaline	
279	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine	2-Me-Ph	
280	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OH-Ph	
281	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Br-Ph	
282	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CF_3-Ph	
283	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OEt-Ph	
284	Me	H	H	Me	Me	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6-Ph	
285	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-O(n-C_4)-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
286	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NO_2-Ph	
287	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-F-Ph	
288	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe-Ph	
289	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CN-Ph	
290	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Cl-Ph	
291	Me	H	H	/	/	H	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CO_2R^7-Ph	
292	Me	H	H	/	/	Me	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CO_2R^7-Ph	
293	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
294	Me	H	H	n-C_3	n-C_3	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6-Ph	
295	Me	H	H	i-C_3	i-C_3	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6-Ph	
296	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-I-Ph	
297	Me	H	H	/	/	i-C_3	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CO_2R^7-Ph	
298	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	Ph	
299	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Et-Ph	
300	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-iC_3-Ph	
301	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Ph-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
302	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-tBu-Ph	
303	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Et-Ph	
304	Me	H	H	/	/	Et	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-CO_2R^7-Ph	
305	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-I-Ph	
306	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Cl-Ph	
307	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Br-Ph	
308	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-F-Ph	
309	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-CF_3-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
310	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-OH-Ph	
311	Me	H	H	/	/	H	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-CO_2R^7-Ph	
312	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-NR^5R^6-Ph	
313	Me	H	H	Me	Me	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-NR^5R^6-Ph	
314	Me	H	H	i-C_3	i-C_3	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-NR^5R^6-Ph	
315	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-CN-Ph	
316	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-OMe-Ph	
317	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-NO_2-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
318	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-OEt-Ph	
319	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-O(n-C_5)Ph	
320	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-Ph-Ph	
321	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-iC_3-Ph	
322	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-nC_3-Ph	
323	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-nC_6-Ph	
324	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-I-Ph	
325	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-F-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
326	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-Br-Ph	
327	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-Cl-Ph	
328	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-OH-Ph	
329	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-CN-Ph	
330	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-CF_3-Ph	
331	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-NO_2-Ph	
332	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-NR^5R^6-Ph	
333	Me	H	H	Me	Me	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-NR^5R^6-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
334	Me	H	H	n-C_4	n-C_4	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-NR^5R^6-Ph	
335	Me	H	H	Me	Me	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-NR^5R^6-Ph	
336	Me	H	H	/	/	H	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-CO_2R^7-Ph	
337	Me	H	H	/	/	Me	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-CO_2R^7-Ph	
338	Me	H	H	/	/	n-C_5	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-CO_2R^7-Ph	
339	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-OMe-Ph	
340	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-OEt-Ph	
341	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Cl,4-NO_2-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
342	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Cl,4-Me-Ph	
343	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-CN,6-CN-Ph	
344	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Me,6-Me-Ph	
345	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NO_2,4-CF_3-Ph	
346	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Cl,4-Cl-Ph	
347	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Me,3-Me-Ph	
348	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Et,3-Et-Ph	
349	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6,4-Cl-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
350	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6,4-Me-Ph	
351	Me	H	H	Me	Me	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6,4-Cl-Ph	
352	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Me,4-Me-Ph	
353	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Cl,5-Cl-Ph	
354	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,4-OMe-Ph	
355	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-tBu,5-tBu-Ph	
356	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-tBu,5-CF_3-Ph	
357	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,5-Cl-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
358	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,5-OMe-Ph	
359	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,5-Ph-Ph	
360	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,4-OMe-Ph	
361	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-CF_3,4-Cl-Ph	
362	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NO_2,4-CF_3,5-NO_2-Ph	
363	Me	H	H	H	H	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-NR^5R^6,4-Me,5-Cl-Ph	
364	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,3-Cl,5-Cl-Ph	
365	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,4-NO_2,5-Me-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
366	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OMe,4-Cl,5-Me-Ph	
367	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Me,4-Cl,5-CF_3-Ph	
368	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-tetra-lin	
369	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-Indan	
370	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	1-tetra-lin	
371	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	1-Indan	
372	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-OEt-1-naphthaline	
373	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Me-1-naphthaline	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
374	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Et-1-naphthaline	
375	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	8-OMe-1-naphthaline	
376	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	8-Me-1-naphthaline	
377	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Indol	
378	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-quinazoline	
379	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-quinazoline	
380	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Chinoxalin	
381	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	1-Phthalazin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
382	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-quinoline	
383	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-quinoline	
384	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-quinoline	
385	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	5-quinoline	
386	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	1-Isoquinoline	
387	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-Isoquinoline	
388	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	8-Isoquinoline	
389	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	7 Benzoferan	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
390	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-2H-chromene	
391	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	5-chromane	
392	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	8-chromane	
393	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-pyrimidine	
394	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	pyrimidine	
395	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	5-OMe-4-pyrimidine	
396	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	4-pyrimidine	
397	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Pyrazin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	m.p. MS ^{1}H-NMR
398	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-Isoxazol	
399	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-pyridine	
400	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-pyridine	
401	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	3-pyrrole	
402	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	2-Ph-4-quinazoline	
403	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	6-iC_3-4-pyrimidine	
404	Me	H	H	/	/	/	C_2	4-tetra-hydro-1,2,3,6 pyridine-1-yl	7-OMe-1-naphthaline	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
405	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-Me-Ph	137°C
406	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-OMe-Ph	233°C (HCl)
407	Me	H	H	H	H	/	C_3	4-piperazine-1-yl	4-OMe-Ph	237°C (HCl)
408	Me	H	H	/	/	Me	C_3	4-piperazine-1-yl	3-OMe, 4-OMe-Ph	224°C (HCl)
409	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-pyrimidine	> 265°C (HCl)
410	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	3-NO_2, 6-OCH_3-Ph	^{1}H-NMR (DMSO-d_6) δ= 1.5(6H,s), 3.3(3H,s)
411	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	3-NH_2, 6-OCH_3-Ph	^{1}H-NMR (DMSO-d_6) δ= 1.5(6H,s), 3.4(3H,s)
412	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	3-OCH_3_Ph	179°C (HCl)
413	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	quinazoline	271°C (HCl)
414	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	4-isoquinoline	138°C
415	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-thiazole	217°C (HCl)
416	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-Me, 5-Me-Ph	98°C (HCl)
417	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-Me,3-Me-Ph	132°C
418	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	3-Me, 4-Me-Ph	124°C

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
419	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	1-naphthaline	178°C
420	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	4-Cl-1-naphthaline	152°C
421	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	2-pyrimidine3-CF_3_Ph	196°C (HCl)
422	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	1-isoquinoline	63°C
423	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	3-CF_3-Ph	184°C (HCl)
424	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	5-tetraline	CH_2-C(CH_2)-$CH_2$177°C
425	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	4-indane	CH_2-C(CH_2)-$CH_2$156°C
426	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-piperazine-1-yl	1-naphthaline	177°C
427	Me	H	H	/	/	/	CH_2_CH(OH)-CH_2	4-piperazine-1-yl	2-OCH_3_Ph	160°C
428	Me	H	H	/	/	/	CH_2-CH(CH_3)-CH_2	3-CF_3-Ph	5-Tetralin	155°C (HCl)
429	Me	H	H	/	/	/	C_4	4-piperazine-1-yl	2-pyrimidine	220°C (HCl)
430	Me	6-NR^5R^6	H	H	H	/	C_3	4-piperazine-1-yl	1-Naphthalin	183°C
431	Me	6-NR^5R^6	H	COPh	H	/	C_3	4-piperazine-1-yl	1-Naphthalin	127°C
432	Me	6-NR^5R^6	H	COMe	H	/	C_3	4-piperazine-1-yl	1-Naphthalin	197°C
433	Me	6-NR^5R^6	H	Pyrrol		/	C_3	4-piperazine-1-yl	1-Naphthalin	269°C (HCl)
434	Me	6-NO_2	H	/	/	/	C_3	4-piperazine-1-yl	1-Naphthalin	183°C

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
435	Et	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CF_3-Ph	277°C (HCl)
436	Et	H	H	/	/	/	C_3	4-piperazine-1-yl	1-Naphthalin	176°C
437	Prop	H	H	/	/	/	C_2	4-piperazine-1-yl	3-CF_3-Ph	107°C
438	Prop	H	H	/	/	/	C_3	4-piperazine-1-yl	3-CF_3-Ph	96°C (HCl)
439	Et	H	H	/	/	/	C_3	4-piperazine-1-yl	3-CF_3-Ph	235°C (HCl)
440	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Me-Ph	
441	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-OH-Ph	
442	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Br-Ph	
443	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-CF_3-Ph	
444	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-OMe-Ph	
445	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-CN-Ph	
446	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	Ph	
447	Me	H	H	H	H	/	C_2	4-Homopiperazine-1-yl	2-NR^5R^6-Ph	
448	Me	H	H	Me	Me	/	C_2	4-Homopiperazine-1-yl	2-NR^5R^6-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
449	Me	H	H	/	/	H	C_2	4-Homopiperazine-1-yl	2-CO_2R^7-Ph	
450	Me	H	H	/	/	Me	C_2	4-Homopiperazine-1-yl	2-CO_2R^7-Ph	
451	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-tBu-Ph	
452	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-Me-Ph	
453	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-CF_3-Ph	
454	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-Cl-Ph	
455	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-OMe-Ph	
456	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	4-NO_2-Ph	
457	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	4-Ph-Ph	
458	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	4-F-Ph	
459	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-Cl,4-Me-Ph	
460	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Me,6-Me-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
461	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Me,3-Me-Ph	
462	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Et,3,-Et-Ph	
463	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3t-Bu,5-CF_3-Ph	
464	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-OMe,5-Ph-Ph	
465	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-OMe,4-Cl,5-Me-Ph	
466	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Me,4-Cl,5-CF_3-Ph	
467	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	5-Tetralin	
468	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	4-Indan	
469	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	1-Naphthalin	
470	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-OMe-1Naphthalin	
471	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Me-1Naphthalin	
472	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	7-OMe-1-Naphthalin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
473	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	8-Me-1-Naphthalin	
474	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-quinazoline	
475	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-Indol	
476	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	1-Phthalazin	
477	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Chinolin	
478	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	1-Isoquinoline	
479	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-pyrimidine	
480	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	4-Isoquinoline	$[M+H]^+$=451
481	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	3-Isoquinoline ^1H-	NMR(DMSO-d_6) δ=1.5 (6H,s), 8.7 (1H,d)
482	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	pyrimidine	
483	Me	H	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Pyridin	
484	Me	H	H	/	/	/	C_3	4-piperazine-1-yl	4-Indan	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
485	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	2-Me-Ph	
486	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	2-OMe-Ph	
487	Me	H	H	H	H	/	C_3	4-Piperidin-1-yl	2-NR^5R^6-Ph	
488	Me	H	H	/	/	Me	C_3	4-Piperidin-1-yl	2-CO_2R^7-Ph	
489	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	3-tBu-Ph	
490	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	2-Me,3-Me-Ph	
491	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	5-Tetralin	
492	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	4-Indan	
493	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	1-Naphthalin	
494	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	2-Me-1-Naphtha-lin	
495	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	2-pyrimidine	
496	Me	H	H	/	/	/	C_3	4-Piperidin-1-yl	1-Phthalazin	
497	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-Me-Ph	
498	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-OMe-Ph	
499	Me	H	H	H	H	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-NR^5R^6-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
500	Me	H	H	/	/	Me	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-CO_2R^7-Ph	
501	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	3-tBu-Ph	
502	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-Me,3-Me-Ph	
503	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	5-Tetralin	
504	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	4-Indan	
505	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	1-Naphthalin	
506	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-Me-1-Naphthalin	
507	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	2-pyrimidine	
508	Me	H	H	/	/	/	C_3	4-Tetrahydro-1,2,3,6-pyridin-1-yl	1-Phthalazin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
509	Me	H	H	/	/	/	C_3	4-Homopiperazine-1-yl	2-Me-Ph	
510	Me	H	H	/	/	/	C_3	4-Homopiperazine-1-yl	2-Me,3-Me-Ph	
511	Me	H	H	/	/	/	C_3	4-Homopiperazine-1-yl	5-Tetralin	
512	Me	H	H	/	/	/	C_3	4-Homopiperazine-1-yl	2-Me-1-Naphtha-lin	
513	Me	H	H	/	/	/	C_3	4-Homopiperazine-1-yl	2-pyrimidine	
514	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	2-Me, 3-Me-Ph	
515	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	2-OMe-1-Naphtha-lin	
516	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-piperazine-1-yl	2-pyrimidine	
517	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	2-Me-Ph	
518	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	2-Me, 3-Me-Ph	
519	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	5-Tetralin	
520	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	1-Naphthalin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
521	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	2-OMe-1-Naphthalin	
522	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	2-pyrimidine	
523	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Piperidin-1-yl	2-Chinolin	
524	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	2-Me-Ph	
525	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	2-Me, 3-Me-Ph	
526	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	5-Tetralin	
527	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	1-Naphthalin	
528	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	2-OMe-1-Naphthalin	
529	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	2-pyrimidine	
530	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Tetrahydropyridin-1-yl	2-Chinolin	
531	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	2-Me-Ph	
532	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	2Me, 3-Me-Ph	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
533	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Hompoipera-zin-1-yl	5-Tetralin	
534	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	1-Naphthalin	
535	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	2-OMe-1-Naphtha-lin	
536	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	2-pyrimidine	
537	Me	H	H	/	/	/	CH_2-C(CH_2)-CH_2	4-Homopiperazine-1-yl	2-Chinolin	
538	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-piperazine-1-yl	2-Me-Ph	
539	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-piperazine-1-yl	2-Me, 3-Me-Ph	
540	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-piperazine-1-yl	5-Tetralin	
541	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-Piperidin-1-yl	2-OMe-1-Naphtha-lin	
542	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-Tetrahydropyi-din-1-yl	2-pyrimidine	
543	Me	H	H	/	/	/	CH_2-CH(OH)-CH_2	4-Homopiperazine-1-yl	2-Chinolin	
544	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-piperazine-1-yl	2-Me-Ph	
545	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-piperazine-1-yl	2-Me, 3-Me-Ph	
546	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-piperazine-1-yl	5-Tetralin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
547	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-piperazine-1-yl	1-Naphthalin	
548	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-Piperidin-1-yl	2-OMe-1-Naphthalin	
549	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-Tetrahydropyridin-1-yl	2-pyrimidine	
550	Me	H	H	/	/	/	C_2-N(Me)-C_2	4-Homopiperazine-1-yl	2-Chinolin	
551	Me	H	H	/	/	/	CH_2-CH(CH_3)-CH_2	4-piperazine-1-yl	1-Naphthalin	
552	Me	H	H	/	/	/	CH_2-CH(CH_3)-CH_2	4-Piperidin-1-yl	2-Me, 3-Me-Ph	
553	Me	H	H	/	/	/	CH_2-CH(CH_3)-CH_2	4-Tetrahydropyridin-1-yl	2-pyrimidine	
554	Me	H	H	/	/	/	CH_2-CH(CH_3)-CH_2	4-Homopiperazine-1-yl	2-OMe-Naphthalin	
555	Me	5-Me	H	/	/	/	C_2	4-piperazine-1-yl	5-Tetralin	
556	Me	5-Me	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
557	Me	5-Me	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-Ph	
558	Me	5-Me	H	/	/	/	C_2	4-piperazine-1-yl	2-pyrimidine	
559	Me	5-Me	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-Naphthalin	
560	Me	5-Me	H	/	/	/	C_2	4-Piperidin-1-yl	2-Me,3-Me-Ph	
561	Me	5-Me	H	/	/	/	C_2	4-Tetrahydropyridin-1-yl	2-Chinolin	

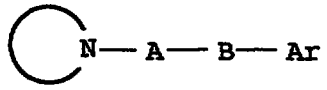
No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
562	Me	5-Me	H	/	/	/	C_2	4-Homopiperazine-1-yl	2-Cl-Ph	
563	Me	5-Me	H	/	/	/	C_3	4-piperazine-1-yl	5-Tetralin	
564	Me	5-Me	H	/	/	/	C_3	4-piperazine-1-yl	1-Naphthalin	
565	Me	5-Me	H	/	/	/	C_3	4-Piperidin-1-yl	2-pyrimidine	
566	Me	5-Me	H	/	/	/	C_3	4-Tetrahydropyridin-1-yl	2-Me,3Me Ph	
567	Me	5-Me	H	/	/	/	C_3	4-Homopiperazine-1-yl	2-OMe-Naphthalin	
568	Me	5-OH	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
569	Me	6-OMe	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
570	Me	4-F	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
571	Me	6-OMe	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
572	Me	4-CF_3	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
573	Me	6-CO_2R^7	H	/	/	H	C_2	4-piperazine-1-yl	1-Naphthalin	
574	Me	6-CO_2R^7	H	/	/	Me	C_2	4-piperazine-1-yl	1-Naphthalin	
575	Me	4-CN	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
576	Me	4(-C_2-Ph)	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
577	Me	4[-C_4-(4-Cl)-Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
578	Me	4[-C_2-(2-OMe)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
579	Me	4[C_2-(3-CF_3)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
580	Me	4[C_2-(2-Me)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
581	Me	4[C_2-(2-NH_2)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
582	Me	4[C_2-(4-NO_2)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
583	Me	4[C_2-(4-OH)Ph]	H	/	/	/	C_2	4-piperazine-1-yl	1-Naphthalin	
584	Me	6-NR^5R^6	H	Me	H	/	C_2	4-piperazine-1-yl	1-Naphthalin	
585	Me	6-NR^5R^6	H	CO Me	H	/	C_2	4-piperazine-1-yl	1-Naphthalin	
586	Me	6-NR^5R^6	H	CO_2tBu	H	/	C_2	4-piperazine-1-yl	1-Naphthalin	
587	Me	6-NR^5R^6	H	H	H	/	C_2	4-piperazine-1-yl	1-Naphthalin	
588	Me	6-NR^5R^6	H	piperazine		/	C_2	4-piperazine-1-yl	1-Naphthalin	
589	Me	6-NR^5R^6	H	Me	H	/	C_3	4-Piperidin-1-yl	5-Tetralin	
590	Me	6-NR^5R^6	H	CO Ph	H	/	C_3	4-Piperidin-1-yl	5-Tetralin	
591	Me	6-NR^5R^6	H	CO Me	H	/	C_3	4-Piperidin-1-yl	5-Tetralin	
592	Me	6-NR^5R^6	H	/	/	/	C_3	4-Piperidin-1-yl	5-Tetralin	
593	Me	6-Pyrrol	H	/	/	/	C_3	4-Piperidin-1-yl	5-Tetralin	
594	Et	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-Ph	
595	Et	H	H	/	/	/	C_2	4-piperazine-1-yl	2-pyrimidine	

No	R^1/R^2	R^3	R^4	R^5	R^6	R^7	A	B	Ar	
596	Et	H	H	/	/	/	C_2	4-piperazine-1-yl	2-OMe-1-Naphtha-lin	
597	Et	H	H	/	/	/	C_2	4-piperazine-1-yl	2-Me,3-Me-Ph	

These compounds are suitable for the treatment of mood disorders caused by the central nervous system, such as seasonal affective disorders and dysthymia. These also include anxieties, such as generalized anxiety disorder, panic attacks, sociophobia, compulsive neuroses and post-traumatic stress symptoms, memory disorders including dementia, amnesia and senile dementia, and also psychogenic eating disorders, such as anorexia nervosa and bulimia nervosa.

It has now been found that compounds of the formula I



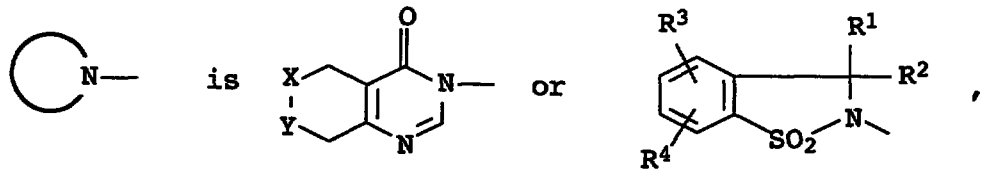
(I),

in which

A is branched or unbranched (C_{1-10})-alkylene or straight-chain or branched (C_{2-10})-alkylene which comprises at least one group Z selected from the group consisting of O, S, NR^8, cyclopropyl, CO_2, CHOH, a double and a triple bond,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by (C_{1-6})-alkyl, branched or unbranched, O-(C_{1-6})-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, NR^2_2, CO_2R^2, cyano or phenyl, is tetraline, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by (C_{1-4})-alkyl or O-(C_{1-4})-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals,



one of the two radicals X, Y being CH_2 and the other being NR^9,

R^1, R^2 independently of one another are C_1-C_6-alkyl,

R^3, R^4 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, OH, O-(C_{1-6})-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, NR^5R^6, CO_2R^7, nitro, cyano, pyrrole, are a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

R^5, R^6 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, COPh, CO_2tBu, CO-(C_{1-4})-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

R^7 is hydrogen or (C_{1-6})-alkyl, branched or unbranched,

R^8 is hydrogen or C_1-C_4-alkyl,

R^9 is hydrogen, (C_{1-6})-alkyl, branched or unbranched, CO-(C_{1-4})-alkyl, CO_2tBu, CO-aryl or a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

and salts thereof,

are suitable for preparing medicaments for the prophylaxis and therapy of neurodegeneration, cerebral trauma and cerebral ischemia, in particular stroke, and of diseases which are caused by these disorders.

A use according to the invention also relates to neuroprotection.

The preparation of these pyrimidine derivatives is described in the patents mentioned at the outset.

The preparation as a medicament is carried out using a compound of the formula I or its pharmacologically acceptable acid addition salt as active compound, together with customary excipients and diluents.

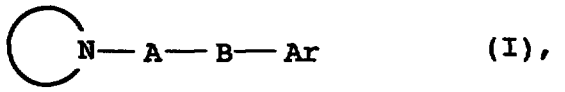
The use according to the invention can be carried out in a customary manner, orally or parenterally, intravenously or intramuscularly.

The dosage depends on the age, on the state and the weight of the patient and on the type of administration. In general, the daily dose of active compound is between approximately 1 and 100 mg/kg of body weight in the case of oral administration and between 0.1 and 10 mg/kg of body weight in the case of parenteral administration.

The medicaments can be used in solid or liquid form in customary pharmaceutical administration forms, for example as tablets, film-coated tablets, capsules, powders, granules, sugar-coated tablets, suppositories, solutions, ointments, creams or sprays. These are prepared in a customary manner. Here, the active compounds can be processed with the customary pharmaceutical auxiliaries, such as tablet binders, fillers, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, sustained-release agents, antioxidants and/or propellants (cf. H. Sucker et al.: Pharmazeutische Technologie [Pharmaceutical Technology], Thieme-Verlag, Stuttgart, 1978). The resulting administration forms generally comprise the active compound in an amount of from 1 to 99% by weight.

We claim:

1. The use of compounds of the formula I



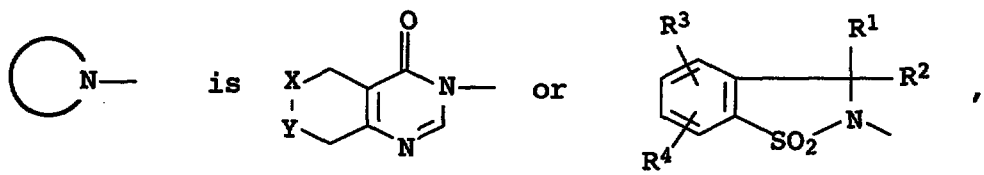
(I),

in which

A is branched or unbranched (C_{1-10})-alkylene or straight-chain or branched (C_{2-10})-alkylene which comprises at least one group Z selected from the group consisting of O, S, NR^8, cyclopropyl, CO_2, CHOH, a double and a triple bond,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by (C_{1-6})-alkyl, branched or unbranched, O-(C_{1-6})-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, NR^2_2, CO_2R^2, cyano or phenyl, is tetralin, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by (C_{1-4})-alkyl or O-(C_{1-4})-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals,



one of the two radicals X, Y being CH_2 and the other being NR^9,

* C L M S *

R^1, R^2 independently of one another are C_1-C_6-alkyl,

R^3, R^4 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, OH, O-(C_{1-6})-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, NR^5R^6, CO_2R^7, nitro, cyano, pyrrole, are a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

R^5, R^6 independently of one another are hydrogen, (C_{1-6})-alkyl, branched or unbranched, COPh, CO_2tBu, CO-(C_{1-4})-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

R^7 is hydrogen or (C_{1-6})-alkyl, branched or unbranched,

R^8 is hydrogen or C_1-C_4-alkyl,

R^9 is hydrogen, (C_{1-6})-alkyl, branched or unbranched, CO-(C_{1-4})-alkyl, CO_2tBu, CO-aryl or a phenyl-C_1-C_4-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, C_1-C_4-alkyl, C_1-C_4-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

and their salts with pharmacologically acceptable acids for preparing medicaments for the prophylaxis and therapy of cerebral ischemia and stroke.