serious disturbances of cardiac rhythm (for example so-called "torsade de pointes"). The potential of compounds to block the hERG channel can be determined by means of the displacement assay with radiolabelled dofetilide which is described in the literature (G. J. Diaz et al., Journal of Pharmacological and Toxicological Methods, 50 (2004), 187-199). A smaller IC50 in this dofetilide assay means a greater probability of potent hERG blockade. In addition, the blockade of the hERG channel can be measured by electrophysiological experiments on cells which have been transfected with the hERG channel, by so-called whole-cell patch clamping (G. J. Diaz et al., Journal of Pharmacological and Toxicological Methods, 50 (2004), 187-199).

vii. high free fraction in brain, i.e. the fraction of the compound bound to proteins should be low.

viii. low lipophilicity.

Brief Description of the Invention

The present ~~invention~~ disclosure is thus based on the object of providing compounds which inhibit PDE10A at low concentrations.

The compounds are further intended to display at least one of the properties i. to viii. mentioned above, in particular high selectivity with regard to inhibition of PDE10A, high selectivity vis-à-vis other phosphodiesterases such as , enhanced metabolic stability, in particular microsomal and/or cytosolic stability, low affinity to the HERG receptor, low inhibition of cytochrome P450 (CYP) enzymes, suitable solubility in water and suitable pharmacokinetics.

This object and further objects are achieved by the compounds of the general formula I described below, the N-oxides, the prodrugs, the hydrates and the tautomers thereof and the pharmaceutically suitable salts thereof:

1, 2 or 3 heteroatoms as ring members, which are selected from the group consisting of O, S and N, where the carbocyclic and the heterocyclic radical are unsubstituted or carry 1, 2, 3, 4 or 5 radicals $R^{C4}$;

$R^{C4}$ is selected from the group consisting of hydrogen, halogen, OH, CN, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, hydroxy-$C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy-$C_1$-$C_4$-alkyl, cyano-$C_1$-$C_4$-alkyl, $C_1$-$C_4$-fluoroalkyl, $C_1$-$C_4$-fluoroalkoxy, $C_2$-$C_6$-alkenyl, $C(O)R^a$, benzyl, Z-$C(O)OR^b$, Z-$C(O)NR^cR^d$, $S(O)_2NR^cR^d$ and Z-$NR^eR^f$, where, Z, $R^a$, $R^b$, $R^c$, $R^d$, $R^e$ and $R^f$ are as defined above or two radicals $R^{C4}$ which are bound at the same atom may form an oxygen atom.

The present ~~invention~~ disclosure therefore relates to the compounds of the general formula I, their tautomers, the hydrates thereof, the pharmaceutically suitable salts of the compounds of formula I, the prodrugs of the compounds of formula I and the pharmaceutically suitable salts of said prodrugs, tautomers or hydrates of the compounds of formula I.

The compounds of the formula I, their salts, their prodrugs, their hydrates and their tautomers effectively inhibit PDE10A even at low concentrations. They are additionally distinguished by a high selectivity in relation to the inhibition of the PDE10A vis-à-vis inhibition of other phosphodiesterease, such as PDE3 or PDE4. The compounds of the invention may additionally have one or more of the properties ii. to viii. mentioned above.

The compounds of the formula I, their salts, their prodrugs, their hydrates and their tautomers are therefore particularly suitable for treating disorders and conditions in creatures, especially human creatures, which can be treated or controlled by inhibition of phosphodiesterase type 10A.

The disclosure therefore also relates to a pharmaceutical composition which comprises at least one compound as disclosed herein and at least one excipient.

The ~~invention~~ disclosure ~~therefore~~ also relates to the use of carboxamide compounds of the formula I, their tautomers, their hydrates and their pharmaceutically suitable salts for the manufacture of a medicament, in particular of a medicament which is suitable for the treatment of a disorder or a condition which can be treated by inhibition of phosphodiesterase type 10A.

The ~~invention~~ disclosure further relates to a medicament, in particular a medicament which is suitable for the treatment of a disorder or a condition which can be treated by inhibition of phosphodiesterase type 10A. The medicament comprises at least one compound of the formula I, as described herein, or a tautomer, or a hydrate or a prodrug of said compound I, or a pharmaceutically suitable salt of the compound of the formula I or a pharmaceutically suitable salt of the tautomer, the hydrate or the prodrug of compound of the formula I.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating a medical disorder, selected from the group consisting of neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating CNS disorders in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating schizophrenia in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating cognitive dysfunction associated with schizophrenia in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating bipolar disorders in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating depression in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating cognitive dysfunction associated with Alzheimer's disease in a mammalian.

The disclosure also relates to the use the compounds as disclosed herein in the manufacture of a medicament for treating diet-induced obesity in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating Huntington's disease in a mammalian.

The disclosure also relates to the use of the compounds as disclosed herein in the manufacture of a medicament for treating anxiety in a mammalian.

The disclosure also relates to the use at least one compound as disclosed herein in the manufacture of a medicament for treating a medical disorder, selected from

neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A to a subject in need thereof.

Detailed Description of the Invention

The terms "compound of the formula I" and "compounds I" are used as synonyms.

The term "prodrugs" means compounds which are metabolized in vivo to the compounds I of the invention. Typical examples of prodrugs are described in C.G. Wermuth (editor): The Practice of Medicinal Chemistry, Academic Press, San Diego, 1996, pages 671-715. These include for example phosphates, carbamates, amino acids, esters, amides, peptides, ureas and the like. Suitable prodrugs in the present case may be for example derivatives of those compounds I carrying an OH or $NH_2$-group, where the OH or $NH_2$-group forms an ester/amide/peptide linkage, i.e. where one of the hydrogen atoms of the OH or $NH_2$-group is substituted by a $C_1$-$C_4$-alkylcarbonyl group, e.g. by acetyl, propionyl, n-propylcarbonyl, isopropylcarbonyl, n-butylcarbonyl or tert-butylcarbonyl (pivaloyl), by benzoyl, or by an acyl group derived from an amino acid, e.g. glycine, alanine, serine, phenylalanine and the like, which is linked to the oxygen or nitrogen of the OH or $NH_2$-group via the carbonyl group of the amino acid. Further suitable prodrugs are alkylcarbonyloxyalkyl carbonates or carbamates of compounds I carrying an OH- or $NH_2$-group in which one of the hydrogen atoms of the OH- or $NH_2$-group has been replaced by a group of the formula $-C(=O)-O-CHR^p-O-C(=O)-R^q$ in which $R^p$ and $R^q$ are independently of one another $C_1$-$C_4$-alkyl. Such carbonates and carbamates are described for example in J. Alexander, R. Cargill, S. R. Michelson, H. Schwam, J. Medicinal Chem. 1988, 31(2), 318-322. These groups can then be eliminated under metabolic conditions and result in compounds I. Therefore, said prodrugs and their pharmaceutically acceptable salts are also part of the invention.

3,7-di(pyridin-4-yl)-5-[2-(pyrrolidin-1-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(dimethylamino)ethyl]-3,7-di(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(morpholin-4-yl)ethyl]-3,7-di(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-ethyl-7-(pyridin-4-yl)-3-(pyrimidin-5-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-(cyclopropylmethyl)-7-(pyridin-4-yl)-3-(pyrimidin-5-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-methyl-3-(pyridin-4-yl)-7-(pyridin-3-ylmethoxy)thieno[2,3-d]pyridazin-4(5H)-one;
and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

24. The compound selected from the group consisting of
3-bromo-5-methyl-7-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
7-chloro-5-methyl-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
3-bromo-7-(pyridin-4-yl)-5-(2,2,2-trifluoroethyl)-thieno[2,3-d]pyridazin-4(5H)-one;
7-hydroxy-5-methyl-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

25. The compound as claimed in any one of the preceding claims for use in therapy.

26. Pharmaceutical composition which comprises at least one compound as claimed in any one of claims 1 to 24 and at least one excipient.

27. Use of ~~The~~the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating a medical disorder, selected from the group consisting of neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A.

28. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating CNS disorders in a mammalian.

29. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating schizophrenia in a mammalian.

30. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating cognitive dysfunction associated with schizophrenia in a mammalian.

31. Use of the ~~The~~ compounds of any of claims 1 to 24 in the manufacture of a medicament for treating bipolar disorders in a mammalian.

32. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating depression in a mammalian.

33. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating cognitive dysfunction associated with Alzheimer's disease in a mammalian.

34. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating diet-induced obesity in a mammalian.

35. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating Huntington's disease in a mammalian.

36. ~~The~~ Use of the compounds of any of claims 1 to 24 in the manufacture of a medicament for treating anxiety in a mammalian.

37. ~~A method for treating a medical disorder, selected from neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A, said method comprising administering an effective amount of~~Use at least one compound of any of claims 1 to 24 in the manufacture of a medicament for treating a medical disorder, selected from neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A~~to a subject in need thereof~~.