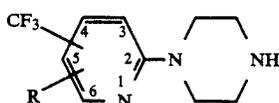


**PHARMACEUTICAL COMPOSITION
CONTAINING 1-(MONO- OR
BIS(TRIFLUOROMETHYL)-2-PYRIDINYL)PIPER-
AZINES**

The present invention relates to a pharmaceutical composition containing 1-[mono- or bis(trifluoromethyl)-2-pyridinyl]piperazines which is useful as a medicament, to new chemical compounds, and to the use of compounds for the preparation of a medicament which act on the central nervous system, in particular as anti-depressants, and against obsessive compulsive disorders, anxiety disorders, among which generalized anxiety, panic attacks and agoraphobia, obesity, aggression and alcohol addiction.

Such compounds correspond, more precisely, to the following general formula



in which the trifluoromethyl substituent is at the 4-position, at the 5-position, or at 4- and 5-positions of the pyridinyl ring, and the substituent R denotes either hydrogen or a halogen substituent, such as chlorine, at position(s) of the pyridinyl ring not occupied by CF₃.

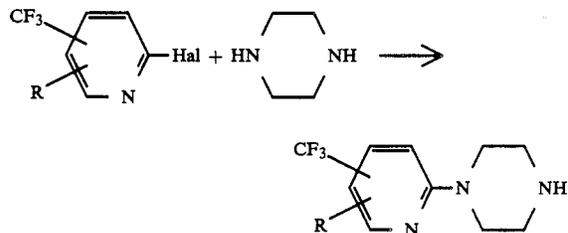
The invention also relates to pharmaceutical compositions containing pharmaceutically acceptable addition salts of the said compounds. These salts are usually obtained by combining the free base (I) with inorganic or organic acids such as hydrochloric, fumaric, maleic, citric or succinic acid, these acids being mentioned only by way of illustration and without implied limitation.

In the prior art, several pyridinylpiperazines containing one or two substituents on the pyridine ring are already known. There may be mentioned, for example, the publication by Walfred S. Saari which appeared in *J. Med. Chem.* 26 (12), 1696-1701, (1983). 1-(4-trifluoromethyl-2-pyridinyl)piperazine and 1-(5-trifluoromethyl-2-pyridinyl)piperazine, described in Ep 282,390 and Ep 220,873 respectively, are known chemical intermediates, albeit without any pharmaceutical utility. The subject of the invention is a pharmaceutical composition containing pyridinylpiperazines necessarily containing one or two trifluoromethyl substituents at the 4- and/or 5-positions of the pyridinyl ring which is useful as a medicament with activity for the treatment of disorders of the central nervous system. Such medicaments preferably contain 1-(4-trifluoromethyl-2-pyridinyl)piperazine or 1-(5-trifluoromethyl-2-pyridinyl)piperazine.

The compounds of formula I in which the trifluoromethyl substituent is at the 4-position, at the 5-position, or at 4- and 5-positions of the pyridinyl ring, and the substituent R denotes either hydrogen or a halogen substituent at position(s) of the pyridinyl ring not occupied by CF₃, and their pharmaceutically acceptable salts, with the proviso that R denotes a halogen when only one trifluoromethyl substituent is present, are new.

The compounds with formula I possess specific anti-depressant activity, resulting especially from their 5HT_{1B} type serotonergic agonist properties, and are prepared according to known processes for similar compounds.

According to one embodiment, an excess of piperazine is reacted with a suitably substituted 2-halopyridine in an organic solvent, heating to reflux of the solvent. Acetonitrile can be taken, for example, as a suitable solvent. This process corresponds to the following scheme:

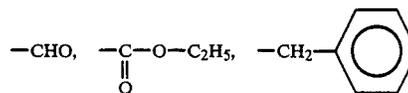


Hal denotes a halogen such as chlorine.

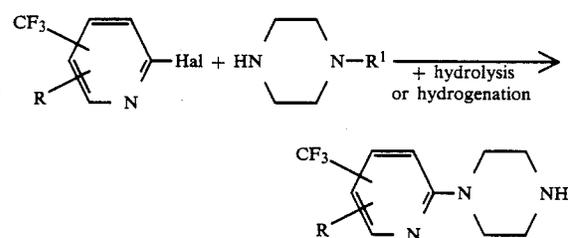
According to another embodiment, a suitably substituted 2-halopyridine is reacted in an organic solvent in the presence of a base with a piperazine in which one of the



groups is protected by a group R', and the protective group is then removed in the usual manner such as by hydrolysis or hydrogenation. By using an alcohol such as butanol as the organic solvent, the base may be a carbonate or a tertiary amine such as triethylamine. As a protective group R', the following will be used, for example:



This process corresponds to the following scheme:



Hal denotes a halogen such as chlorine.

The compounds of the invention and the processes for producing them are described in the examples below, without this constituting a limitation to the different embodiments.

EXAMPLE 1 :

1-(3-chloro-5-trifluoromethyl-2-pyridinyl)piperazine

A solution of 10.8 g (0.05 mol) of 2,3-dichloro-5-trifluoromethylpyridine and 12.9 g (0.15 mol) of anhydrous piperazine in 100 ml of acetonitrile was intro-