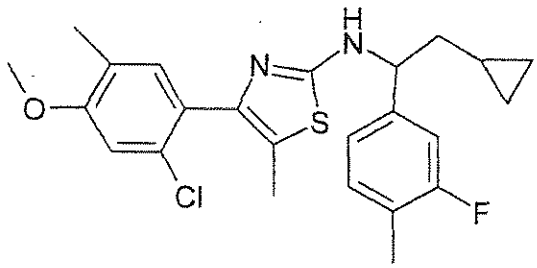
PROCESS FOR THE PREPARATION OF [4-(2-CHLORO-4-METHOXY-5-METHYLPHENYL)-5-METHYL-THIAZOLO-2-YL]-[2-CYCLOPROPYL-1-(3-FLUORO-4-METHYLPHENYL)-ETHYL]-AMINE

The subject of the present invention is novel process for the preparation of the [4-(2-chloro-4-methoxy-5-methylphenyl)-5-methyl-thiazolo-2-yl]-[2-cyclopropyl-1-(3-fluoro-4-methylphenyl)-ethyl]-amine of formula **(I)**

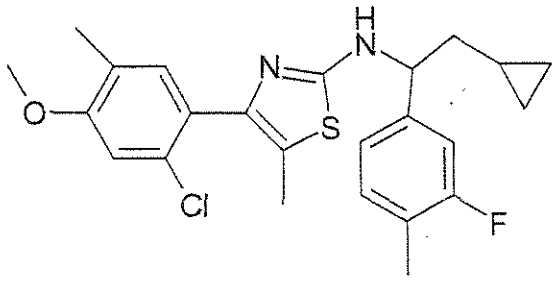


I

and the new intermediates of the preparation process.

SUMMARY

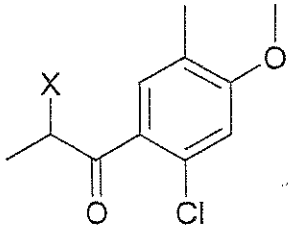
In a first aspect, there is provided a process for the preparation of the [4-(2-chloro-4-methoxy-5-methylphenyl)-5-methyl-thiazolo-2-yl]-[2-cyclopropyl-1-(3-fluoro-4-methylphenyl)-ethyl]-amine of formula (I)



I

characterized in that

a.) the compound of the general formula (II)

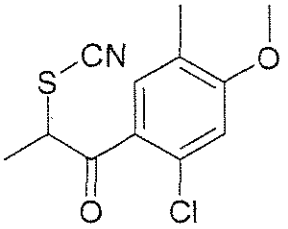


II

– where X means halogen – is reacted with an alkali metal-thiocyanate, in the presence of a phase transfer catalyst,

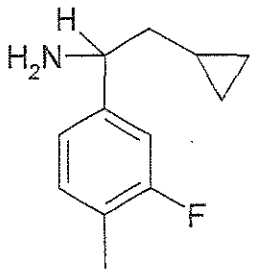
and

b.) the thus obtained 2-thioyanato-1-(2-chloro-4-metoxy-5-methylphenyl)-propan-1-one of formula (III)



III

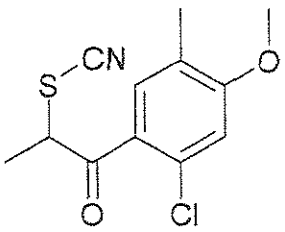
or a tautomeric form of it is reacted with the 2-cyclopropyl-1-(3-fluoro-4-methylphenyl)-ethyl-amine



IV

of formula **(IV)**.

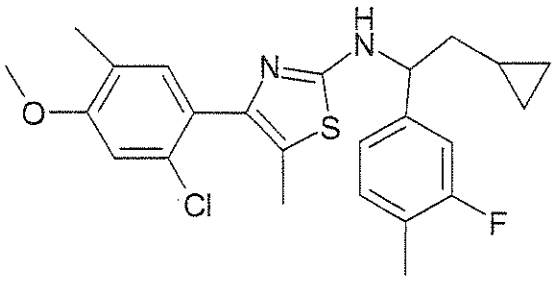
In a second aspect, there is provided the 2-thiocyanato-1-(2-chloro-4-methoxy-5-methylphenyl)-propan-1-one



III

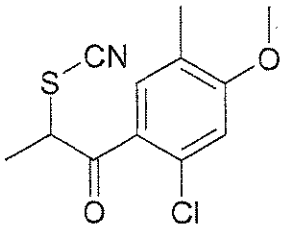
of formula **(III)** and its tautomers.

In a third aspect, there is provided a process for the preparation of the [4-(2-chloro-4-methoxy-5-methylphenyl)-5-methyl-thiazol-2-yl]-[2-cyclopropyl-1-(3-fluoro-4-methyl-phenyl)-ethyl]-amine of formula **(I)**



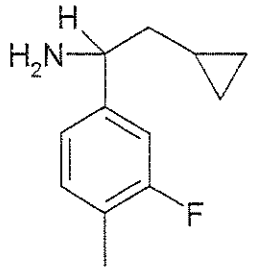
I

c h a r a c t e r i z e d b y that the 2-thiocyanato-1-(2-chloro-4-methoxy-5-methyl-phenyl)-propan-1-one of formula (III)



III

is reacted with the 2-cyclopropyl-1-(3-fluoro-4-methylphenyl)-ethyl-amine of formula (IV)

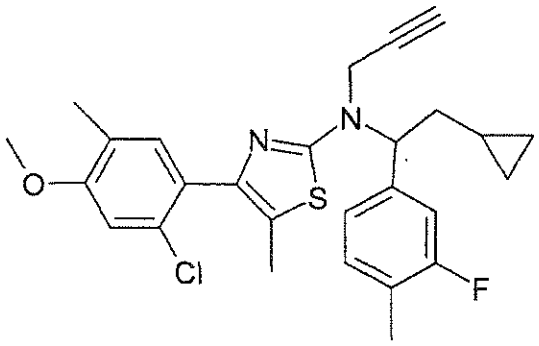


IV

in a way that the ketone of formula (III) is added to the amine of formula (IV).

DETAILED DESCRIPTION

The compound of formula **(I)** is the key intermediate to the preparation of the [4-(2-chloro-4-methoxy-5-methylphenyl)-*N*-propynyl-5-methyl-thiazolo-2-yl]-[2-cyclopropyl-1-(3-fluoro-4-methylphenyl)-ethyl]-amine of formula **(VI)**



VI

- which is a known CRF1 (corticrotropin releasing factor 1) receptor antagonist with potential antidepressant and / or anxiolytic effect.