Summary of the invention

The present inventors have found that including a step in the synthesis of 1-[2-(2,4-dimethylphenylsulfanyl)-phenyl]piperazine and pharmaceutically acceptable salts thereof in which step 1-[2-(2,4-dimethylphenylsulfanyl)-phenyl]piperazine-HBr isopropanol solvate is prepared from 1-[2-(2,4-dimethylphenylsulfanyl)-phenyl]piperazine-HBr removes or reduces impurities and thus provides purified 1-[2-(2,4-dimethylphenylsulfanyl)-phenyl]piperazine and pharmaceutically acceptable salts thereof, e.g. the β-form of the HBr salt.

Hence, in one embodiment, the ~~invention~~disclosure provides a process for the manufacture of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine or a pharmaceutically acceptable salt thereof comprising the step of achieving a solution by dissolving 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr salt in a solvent comprising more than 65 %(v/v) isopropanol.

In one aspect~~embodiment~~, there ~~invention~~ is provided a process for the manufacture of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine or a pharmaceutically acceptable salt thereof comprising the step of precipitating 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr isopropanol solvate from a solvent comprising more than 65 %(v/v) isopropanol.

In one embodiment, the ~~invention~~disclosure relates to a process for the manufacture of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine or a pharmaceutically acceptable salt thereof comprising the step of dissolving 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr isopropanol solvate in a solvent that does not form stable solvates with the compound.

In another aspect, there is provided a process for the manufacture of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine or a pharmaceutically acceptable salt thereof comprising the step of dissolving 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr isopropanol solvate, in a non-solvate forming solvent, followed by precipitation of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr.

In yet another aspect, there is provided a process for removing or reducing an impurity from solid 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr or from a solution of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr, the process comprising the steps of

a) mixing a solvent comprising more than 65 %(v/v) isopropanol with solid 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr or with a solution of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr to achieve a solution of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr; and

b) cooling said achieved solution to precipitate 1-[2-(2,4-dimethylphenylsulfanyl)-phenyl]piperazine-HBr isopropanol solvate;

c) dissolving 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr, isopropanol solvate in a non-solvate forming solvent; and

d) precipitating 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr from the solution obtained in step c).

In one aspect~~embodiment~~, there ~~invention~~ is provided a compound which is 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr isopropanol solvate.

Figures

Figure 1: XRPD of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr, β-form

Figure 2: XRPD of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]piperazine-HBr, isopropanol solvate

Figure 3: TGA and DSC thermograms of 1-[2-(2,4-dimethylphenylsulfanyl)phenyl]-piperazine-HBr isopropanol solvate