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(54) Title: A PROCESS FOR THE PREPARATION OF RACEMIC CITALOPRAM DIOL AND/OR S- OR R- CITALOPRAM DIOLS AND THE USE OF SUCH DIOLS FOR THE PREPARATION OF RACEMIC CITALOPRAM, R-CITALOPRAM AND/OR S-CITALOPRAM

(57) Abstract: In the following, citalopram diol means 4-(4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl)-3-(hydroxymethyl)-benzonitrile, as free base and/or acid addition salt. The invention relates to a process for the preparation of racemic citalopram diol and/or R- or S-citalopram diol, comprising the separation of a non-racemic mixture of R- and S-citalopram diol with more than 50% of one of the enantiomers into a fraction being enriched with S- or R-citalopram diol and a fraction comprising RS-citalopram diol wherein the ratio of R-citalopram diol:S-citalopram diol is equal to 1:1 or closer to 1:1 than in the initial mixture. The method is characterized in that (i) RS-citalopram diol is precipitated from a solution of the initial non-racemic mixture, or R- or S-citalopram diol is dissolved into a solvent from the initial non-racemic mixture, leaving a residue of RS-citalopram diol, and in that (ii) the residue/precipitate formed is separated from the final solution phase, followed by optional steps of repetition, recrystallisation, purification, isolation and conversion between free base and salts. The invention also relates to a process for the preparation of RS-citalopram, S-citalopram or R-citalopram (all as free base and/or acid addition salt) comprising the method described above followed by ring closure.



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