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(54) Title: A PROCESS FOR THE PREPARATION OF IOPAMIDOL AND THE NEW INTERMEDIATES THEREIN

(57) Abstract: A process for the preparation of (S)-N,N'-bis[2-hydroxy-1-(hydroxymethyl)ethyl]-5-[(2-hydroxy-1-oxopropyl)amino]-2,4,6-triiodo-1,3-benzendicarboxamide (iopamidol) starting from 5-amino-N,N'-bis[2-hydroxy-1-(hydroxymethyl)ethyl]-2,4,6-triiodo-1,3-benzenedicarboxamide (II) which process comprises a) reacting the compound of formula (II) with a suitable protecting agent, to give a compound of formula (III) wherein R is a group of formula A or B wherein R₁ is a hydrogen atom, a C₁-C₄ straight or branched alkoxy group, R₂ is hydrogen, a C₁-C₄ straight or branched alkoxy group and R₃ is a C₁-C₄ straight or branched alkyl group, a trifluoromethyl or a trichloromethyl group; b) acylating the amino group in position 5 of the intermediate compound of formula (III), by reaction with a (S)-2-(acetyloxy)propanoyl chloride to give a compound of formula (IV) wherein R is as defined above; and c) removing all the acyl groups present in the compound of formula (IV) under basic conditions, with prior cleavage of the cyclic protections of the hydroxy groups in the carboxamido substituents under acidic conditions, when R is a group of formula A carboxamido hydroxy groups under acidic conditions. The invention also refers to the new intermediates of formula (III) and (IV) wherein -R is a group A.

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