A PROCESS FOR THE PREPARATION OF OPTICALLY ACTIVE CYCLOPROPYLAMINES.

The Field of the Technology

This invention relates to a process for the production of optically active 2-(disubstituted aryl) cyclopropylamine derivatives and optically active 2-(disubstituted aryl) cyclopropane carboxamide derivative which are useful intermediates for the preparation of pharmaceutical agents, and in particular the compound [1*S*-(1α, 2α, 3β (1*S**,2*R**),5β)]-3-[7-[2-(3,4-difluorophenyl)-cyclopropyl]amino]-5-(propylthio)-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-3-yl)-5-(2-hydroxyethoxy)-cyclopentane-1,2-diol. This compound, and similar such compounds, are disclosed in WO 00/34283 and WO 99/05143. These compounds are disclosed as P_{2T} (which is now usually referred to as P_2Y_{12}) receptor antagonists. Such antagonists can be used as, *inter alia*, inhibitors of platelet activation, aggregation or degranulation.

Background Technology

Some processes are known for the production of optically active 2-cyclopropane carboxamide derivatives, optically active 2-aryl cyclopropylamine derivatives and optically active 2-arylcyclopropane-1-carboxylate ester derivatives.

Examples of processes for the production of optically active 2-arylcyclopropane carboxamide derivatives, are

(i) A process wherein excess thionyl chloride is reacted with optically active 2-phenylcyclopropane carboxylic acid in benzene solvent to form corresponding acid chloride, and after concentrating down excess thionyl chloride and benzene under reduced pressure, the acid chloride is isolated and purified by distillation, and, by causing ammonia water to act on this, 2-phenylcyclopropane carboxamide is obtained (J. Am. Chem. Soc. Vol.109, p.2311 (1987), Journal of Medicinal Chemistry Vol.20, p.771 (1977));

(ii) A Process to obtain optically active 3-aryl-2-dimethylcyclopropane-1-carboxamide by causing ammonia water to act on the corresponding acid chloride formed by reacting thionyl chloride with optically active 3-aryl-2-dimethylcyclopropane-1-carboxylic acid (J. Org. Chem. Vol.68, p.621 (2003));

A NOVEL OPTICALLY ACTIVE 2-(3,4-DIFLUOROPHENYL)CYCLOPROPANECARBOXAMIDE

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