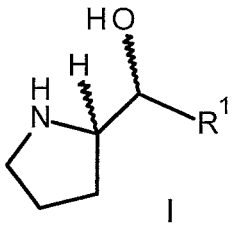
Process for the preparation of chiral pyrollidine-2-yl- methanol derivatives

The invention relates to a novel process for the preparation of a chiral pyrollidine-2-yl-methanol derivative or a salt thereof of the formula I



I

wherein R^1 is aryl or heteroaryl and both aryl or heteroaryl are optionally substituted by C_{1-4}-alkyl, halo-C_{1-4}-alkyl, C_{1-4}-alkoxy or halogen.

Chiral pyrollidine-2-yl- methanol derivatives of the formula I are versatile building blocks in the synthesis of pharmacologically active compounds, such as for the stereospecific synthesis of oligonucleotides carrying chiral phosphonate moieties (see e.g. Int. PCT Publication WO 2010/064146).

A process for the preparation of chiral pyrollidine-2-yl- methanol derivatives of the formula I has been described in Soai et al.; J.Chem.Soc., Chem.Commun. 1986, 412-413. The three step process starts from S-proline and is characterized by the reduction of a chiral benzoyl pyrrolidine with various reducing agents which affords, depending on the reducing agent, erythro/threo mixtures of the chiral pyrollidine-2-yl-methanol.

There is a need for a scalable process which affords the desired chiral building block in good yields and high enantiomeric purity. Object of the embodiments disclosed herein accordingly was to overcome the flaws of the state of the art processes.

The object could be achieved with the new process as described below.

In one aspect, there is provided a process for the preparation of a chiral pyrollidine-2-yl-methanol derivative or a salt thereof of the formula I