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CHIRAL SULPHOXIDES IN THE SYNTHESIS OF OPTICALLY PURE FLUOROSUBSTITUTED COMPOUNDS OF BIOLOGICAL INTEREST

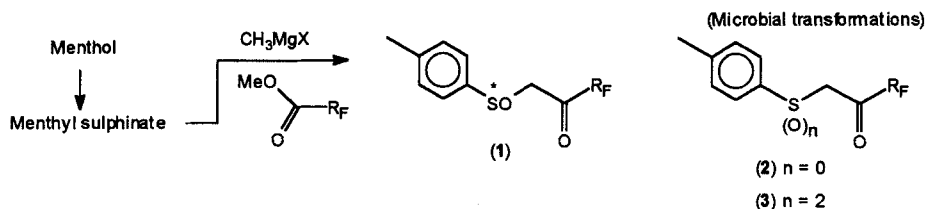
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Abstract The preparation of fluorosulphinyl chiral building blocks useful in the synthesis of biologically active compounds is described.

Fluorosubstituted molecules play an important role in the context of biological activity. A number of drugs in which fluorosubstitution is a key to the biological activity are in use or under intense study. There are essentially two ways to obtain selectively fluorinated complex organic molecules: a) fluorine atoms can be introduced at a later step of a synthetic plan to the target molecule by one of the known fluorinating reagents; b) a synthetic strategy to the target molecule from a simple and available fluoroorganic compound has to be studied. One of the inherent limitations of the second approach when the synthetic target is a chiral molecule lies in the limited number of chiral and optically pure fluorinated compounds now available. Nature does not provide to chemists the needed fluorocompounds¹.

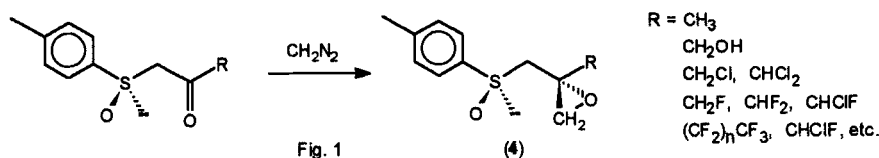
We have developed the synthesis of fluorosulphinyl chiral building blocks (**1**) from (+) or (-) menthol as source of chirality and of thio and sulphonyl analogs (**2**) and (**3**) by using biocatalysts. In both cases fluorinated carbons derive from esters of available fluorosubstituted carboxylic acids².



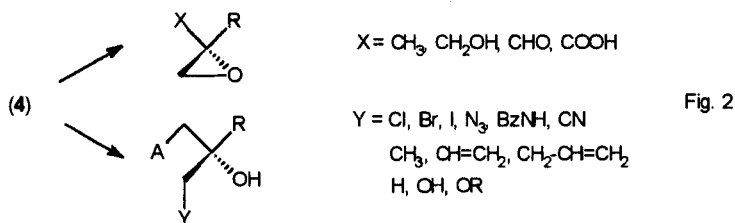
Chiral and optically pure fluoromuscarrine, fluorodideoxynojirimicin, fluoro-deoxyhexoses, fluorodeoxypentoses and corresponding fluoronucleoside analogs² have been prepared from synthon (1) ($R_F = -CH_2CH_2-CH=CH_2$). α -Trifluoromethyl-alanine and α -trifluoromethylserine have been obtained from trifluoropyruvic acid.

A new route to chiral and optically pure *gem*-difluoro-, *gem*-chlorofluoro- and fluoro-substituted cyclohexane derivatives, along with cyclopentane and tetrahydrofuran derivatives have been prepared from synthons bearing $R_F = CClF_2$, CCl_2F , $CHClF$ and an allyl or homoallyl group attached to α -carbon or to the β -hydroxyl, through radical mediated reactions.

Oxiranes (4) have been obtained through a high sito- and stereo-specific transfer of methylene from diazomethane³. (Fig. 1)



Independent elaborations of the oxirane ring and/or the methylene bearing the chiral auxiliary have been studied (Fig. 2).



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