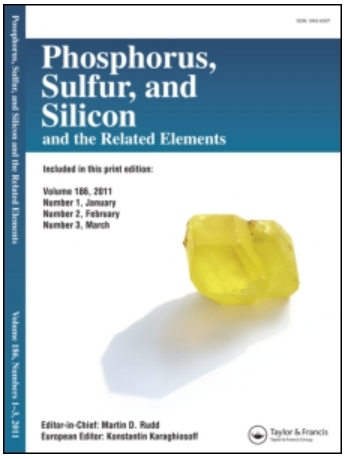

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Chiral Sulphoxides in the Synthesis of Optically Pure Fluorosubstituted Compounds of Biological Interest

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

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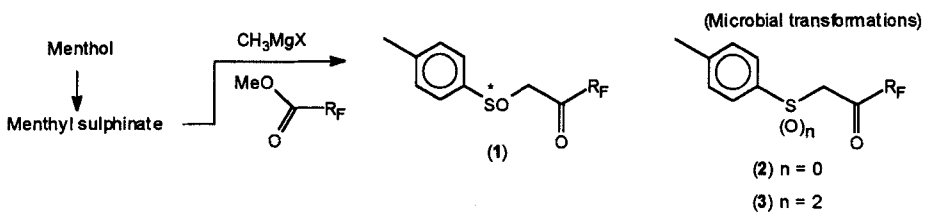
Abstract The preparation of fluorosulphinyl chiral building blocks useful in the synthesis of biologically active compounds is described.

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 fluorocompounds[1].

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 acids[2].



Chiral and optically pure fluoromuscarine, fluorodideoxynojirimicin, fluorodeoxyhexoses, fluorodeoxypentoses and corresponding fluoronucleoside analogs[2] have been prepared from synthon (1) (R_F = -$CHFCH_2$-CH=CH_2). α-Trifluoromethylalanine 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 tetrahydrofurane 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 diazomethane[3]. (Fig.1)

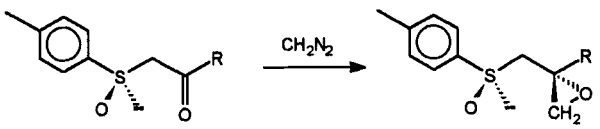
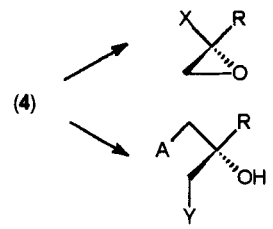


Fig. 1 (4)

R = CH_3
CH_2OH
CH_2Cl, $CHCl_2$
CH_2F, CHF_2, CHClF
$(CF_2)_nCF_3$, CHClF, etc.

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



X= CH_3, CH_2OH, CHO, COOH

Y = Cl, Br, I, N_3, BzNH, CN
CH_3, $CH=CH_2$, CH_2-$CH=CH_2$
H, OH, OR

Fig. 2

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3. P. Bravo *et al.*, Tetrahedron Lett., 33, 5609 (1992).