Pergamon

Tetrahedron: Asymmetry Vol. 5, No. 6, pp. 987-1004, 1994
Elsevier Science Ltd
Printed in Great Britain
0957-4166/94 $7.00+0.00

0957-4166(94)00129-4

New Fluorinated Chiral Synthons

Pierfrancesco Bravo*, Alessandra Farina, Massimo Frigerio, Stefano Valdo Meille, and Fiorenza Viani.

C.N.R. - Centro di Studio per le Sostanze Organiche Naturali. Dipartimento di Chimica del Politecnico di Milano, via Mancinelli 7, I - 20131 Milano, Italy.

Vadim Soloshonok

Ukrainian Academy of Sciences - Institute of Bioorganic Chemistry and Petrochemistry, 1, Murmanskaya str. Kiev - 94, 252660 Ukraine.

Abstract: the syntheses of new optically pure poly-halo and poly-fluoro oxiranes **5b-e** by addition of diazomethane on the corresponding β-keto-γ-fluorosubstituted sulphoxide intermediates, both in keto **3**, hydrate **4** or in keto/ hydrate form are described. Syntheses of sulphur-free fluorinated oxiranes **18b-e**, β-hydroxy-β-trifluoromethyl amine **21d**, α-hydroxy-α-trifluoromethyl-β-amino acid **24d**, α-trifluoromethyl-α,β-dihydroxy acid **25d** and β,γ-dihydroxy-β-trifluoro- and -chlorodifluoromethyl amines **26c** and **26d** are shown as examples of their chemical versatility

The implication of chirality on molecular recognition and therefore on biological activity is one of the major forces at present for the developement of syntheses of single enantiomers[1]. The use of fluorine and of fluoromethyl groups as isosteric and isopolar substituents for hydrogen and oxygen respectively in molecules of potential biological significance is increasing as a consequence of the continuing search for better activity profiles of the molecules. For these reasons, there has been recently a growing interest in the synthesis of enantiomerically pure and selectively fluorinated organic molecules[2]. Because Nature does not provide small fluorosubstituted chiral molecules [3] to be used as chiral building blocks in asymmetric synthesis, the search for routes providing fluorinated chirons from easily available fluoro compounds is mandatory[4].

In that context, we are developing strategies to chiral and optically pure small fluorinated molecules from fluorosubstituted esters as the source of fluorine atoms and sulphoxides as chiral auxiliaries[5].

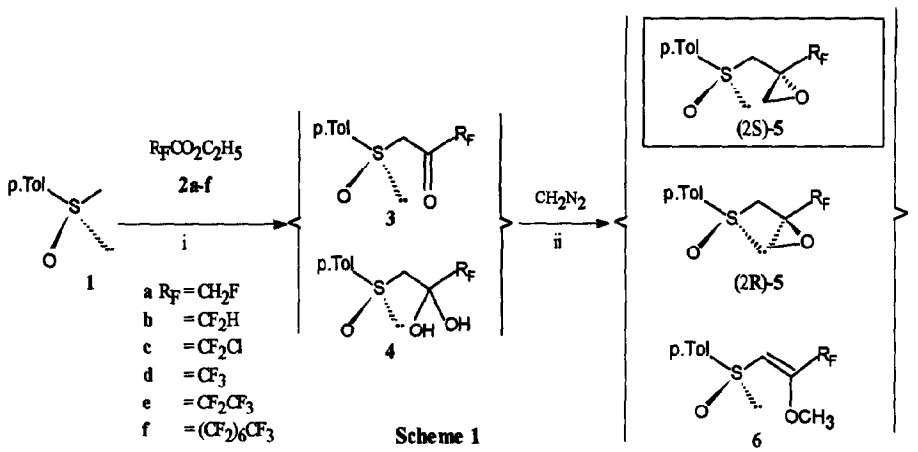
The transfer of chirality from sulphur to carbon in β-keto-γ-fluorosubstituted sulphoxide intermediates could be well accomplished, as well as for all other β-keto sulphoxides, through hydride reduction of the carbonyl by diisobutyl aluminium hydride[6]. On the contrary, diastereoselection in the addition of carbon nucleophiles to the same carbonyl group is a process unlikely to be controlled. Only a methyl or a cyano group have been introduced from trimethyl aluminium and trichloromethyltitanium or potassium cyanide respectively with marked diastereoselection[7].

In the present paper we report the results of a study on the methylene transfer reaction from diazomethane to the carbonyl of β-keto-γ-fluorosubstituted sulphoxides which proceeds with chemo- and diastereoselection from very high to moderate, presumably due to the unique ability of the sulphinyl group to participate in diazomethane coordination and, simultaneously, in facial selectivity control of the approaching reagent. The regioselective ring opening of epoxides and the chemical elaboration of the chiral auxiliary

sulphinyl group which allow the straightforward access to a large number of optically pure fluorinated intermediates are also examined.

Results and Discussion

Fluorosubstituted β-keto/*gem*-diol sulphoxides **3** and **4** have been obtained through acylation of the lithium derivative of (+)-(R)-methyl-4-methylphenyl sulphoxide (**1**) with methyl or ethyl esters of fluoro[8]-, difluoro[9], trifluoro[9]-, chlorodifluoro[9] acetic acids (**2a - d**) and ethyl esters of perfluoropropionic and perfluorooctanoic[10] acids (**2e - f**), isolated in the keto form (**3a**), in the hydrate *gem*-diol form (**4d**), or as a **3** to **4** mixture (**b,c,e,f**) depending on total number of fluorine atoms in γ position and on length of the fluorinated chain (see Table1).



Scheme 1

Reagents and Conditions: i) LDA, THF, -70°C ii) ethyl ether (methanol / benzene / ethanol), r.t.

Compounds **3**, **4**, or their mixtures were selectively dissolved in different solvent: ethyl ether, methanol, benzene, ethanol and an excess of ethereal solution of diazomethane was added. The solutions were kept at room temperature until the substrate was totally used up, the reaction mixtures were purified by flash chromatography to give the compounds shown in Scheme 1 in chemical isolated yields reported in Table 1.

It is known that diazomethane reacts with carbonyl compounds under very mild conditions to yield a variety of products, ranging from cycloadducts, epoxides, methyl ethers of enol-carbonyls, and products arising from chain elongation due to methylene insertion reactions[11] The mechanism of the addition to the carbon-oxygen double bond implies an initial adduct which can be a cyclic adduct in some special cases, or, more often, a zwitterionic intermediate arising from a carbon-carbon bond between the nucleophilic carbon of diazomethane and the electrophilic carbonyl carbon. The adduct can lose nitrogen and furnish the methylene oxide, but in most cases it has much greater propensity to react in other ways. In general, successful epoxidation of carbonyl compounds improves with the electron-poor character of the carbon-oxygen double bond, and the reaction rate increases in polar solvents as alcohols.

Table 1. Chemo- and diastereoselectivity of diazomethane reaction on keto/hydrate fluorinated derivatives 3/4

Substrates			Reaction Products			
Entry	R_F	3 : 4 Ratio	Solvent	Global Yield (%)	5 : 6 Ratio	5S : 5R Ratio
1	CH_2F	> 97 : 3	$(C_2H_5)_2O$	90	4.6 : 1.0	94:6
2			CH_3OH	92	> 97 : 3	80 : 20
3			C_6H_6	67	5.3 : 1.0	87 : 13
4	CF_2H	1.0 : 3.0	$(C_2H_5)_2O$	78	4.6 : 1.0	83 : 17
5			CH_3OH	97	18.4 : 1.0	79 : 21
6	CF_2Cl	1.0 : 2.0	$(C_2H_5)_2O$	84	1.0 : 2.1	> 97 : 3
7			CH_3OH	85	7.5 : 1.0	
8			C_2H_5OH	80	3.4 : 1.0	
9	CF_3	> 3 : 97	$(C_2H_5)_2O$	89	1.3 : 1.0	> 97 : 3
10			CH_3OH	95	6.3 : 1.0	
11			C_6H_6	88	1.0 : 1.0	
12			C_2H_5OH	92	5.1 : 1.0	
13	CF_2CF_5	1.0 : 1.5	CH_3OH	90	2.5 : 1.0	> 97 : 3
14	$(CF_2)_6CF_3$	3.0 : 1.0	$(C_2H_5)_2O$	20	> 3 : 97	-
15			CH_3OH	20	> 3 : 97	-

Several points emerge from the results on Table 1: first of all, the high (**5** + **6**) product yields obtained in methylene transfer reaction by diazomethane on both keto **3** and *gem*-diol **4** forms of fluoro sulphinyl derivatives should be emphasized. Only when the reactions are run on preparative scale (10-100 mmol) and undried solvents are employed, are small amounts of by-products arising from hydrolytic oxirane ring openings detectable (see experimental).

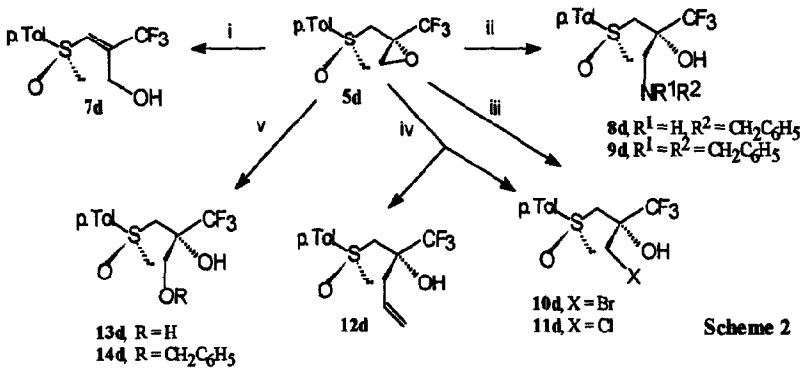
Moreover, reactions of **3/4** give mainly oxiranes **5** in respect to enol ethers **6** (in every tested case except entries 6 and 11). The only great exception is observed with perfluoro heptenyl ketone **3f/4f** (entries 14 and 15) which gives exclusively but in low yields enol ether **6f**: this can be attributable to the extensive degradation of the substrate and to the solvolytic effect of the perfluorinated chain on the carbonyl group which could favor diazomethane attack on the enolic form.

Next, the effect of the solvent mixture on the reaction rate and on the chemo- and diastereoselection is considered. Ethyl ether (entries 1,4,6 and 9) and/or benzene (entries 3 and 11) give rise to mixtures of products **5** and **6** ranging from 5 / 1 to 1 / 2. Methanol (entries 2, 5, 7, 10, and 13) and/or ethanol (entries 8 and 12) were in all cases observed to speed up the reaction and to favor oxirane formation over the enol ether. Diastereoselection in epoxide formation is, in all examined cases and in all tested solvents, good and a slightly higher 5S over 5R ratio in ethyl ether (entries 1 and 4) is obtained[12]. Interesting results are observed in the methylene transfer reaction on perhalogenated compounds **3/4c**, **4d** and **3/4e** leading to diastereoselective formation of the corresponding 5S oxiranes. The peculiar behaviour could be explain through the hypothesis of a precoordination on the partially positive nitrogen of the attacking species performed by the sulphinyl sulphur: diazomethane could be so preferentially oriented towards the *Re* face of the carbonyl. It is notheworthy that hydride-releasing reagents preferentially attack β-keto sulphoxides from the same side[13].

Functional Groups Elaboration

Molecules such as **5** are new useful fluorinated chiral synthons (Scheme 2). In fact, they possess at least three reactive carbon sites to be considered for further elaborations: a) the carbon bearing the chiral auxiliary which possesses hydrogens activated by the sulphinyl group; b) the sulphur itself as a suitable site of reaction; c) the C-2 and C-3 carbons of the epoxide, because the strain of the three membered ring provides two suitable sites of attack for nucleophilic species. Moreover, protic or Lewis acids could be used to coordinate the oxygen atom in the oxirane ring thus modifying the kinetics and the regiochemistry of ring opening by an incoming nucleophile.

However, the first problem which must be faced in the elaboration of synthons **5** is the classical syndrome basicity *versus* nucleophilicity of the considered reactive species[14]. A basic more than nucleophilic one shows a high tendency to abstract one of the hydrogens α in respect with the sulphinyl group. The thus formed carbanion, α to the oxirane ring, easily transfers the negative charge to the oxygen as shown in Figure 1, releasing the ring strain and forming a more stable oxyanion. Following this pathway, primary vinyl alcohols are formed. When compound **5d** was treated with an aqueous solution of potassium hydroxide or with LDA in THF, the corresponding open-chain compounds **7d** were selectively and quantitatively formed.



Scheme 2

Reagents and Conditions: i) KOH, H_2O, or LDA, THF, ii) $C_6H_5CH_2NH_2$ or $(C_6H_5CH_2)_2NH$ iii) LiBr,$CuBr_2$, THF or LiCl, $CuCl_2$, iv) CH_2=CHMgBr, THF, v) $HClO_4$, H_2O, THF, NaH, $C_6H_5CH_2Br$.

In contrast, when **5d** was submitted to reactions with more efficient nucleophilic species, such as amines, bromide or chloride ions, and oxygen nucleophiles, a clean and regioselective ring opening reaction occurred with the incoming species reacting exclusively on the less substituted carbon atom.

The observed trend is quite obvious from steric interaction considerations in the transition state. Furthemore, the same trend should be still favoured when reactions with poor nucleophilic species are run, both under protic or Lewis-acids cathalysis. As shown in Figure 1, upon protonation at the oxirane ring oxygen, transfer of electrons from carbon to oxygen should provide the reaction driving force. Electronic factors should stabilize the formation of the positive charge (δ+) on the quaternary carbon, but the presence of α-

trifluoromethyl group should have a strong destabilizing effect. So, the absolute regioselectivity observed for oxirane ring opening reactions should depend from these combined steric and electronic factors.

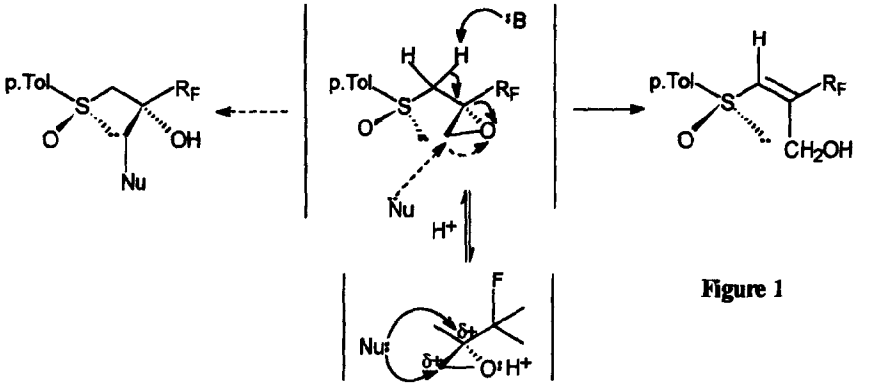
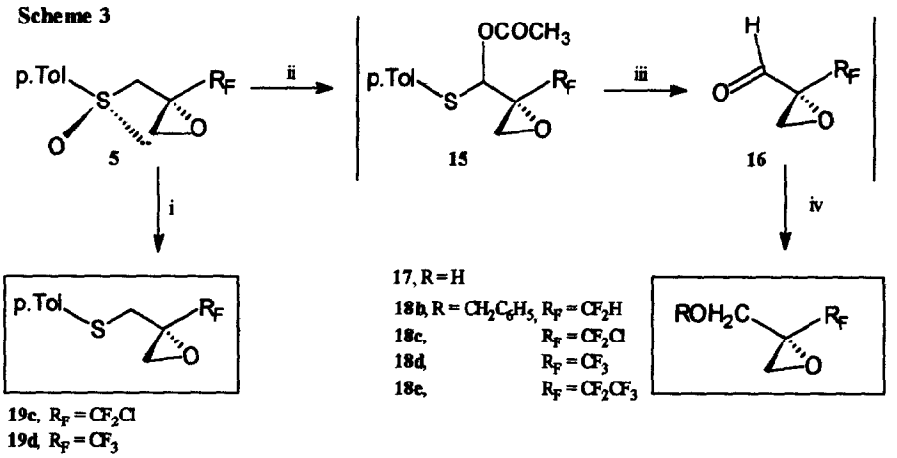


Figure 1

Successful nucleophilic ring opening reactions performed on the trifluoromethyl oxirane derivative **5d**, leading to substituted tertiary alcohols in high chemical yields and with absolute regiospecificity, are reported in Scheme 2. Some examples of the same reactions performed on the chlorodifluoro oxirane **5c** are reported in the experimental section. When using allyl magnesium chloride, the reaction was sluggish and strongly dependent on reaction conditions[15], leading mainly to compounds deriving from oxirane ring opening by halogen counterion.

Having served its purpose for the introduction of the new stereogenic centre at the C-2 carbon during methylene transfer, the sulphinyl chiral auxiliary could now be eliminated. From a synthetic point of view, the most useful and versatile method is by the well known Pummerer rearrangement[16] which allows the replacement of the sulphur atom by an oxygenated functionality. As shown in Scheme 3, starting from the

Scheme 3



17, R = H
18b, R = $CH_2C_6H_5$, $R_F = CF_2H$
18c, $R_F = CF_2Cl$
18d, $R_F = CF_3$
18e, $R_F = CF_2CF_3$

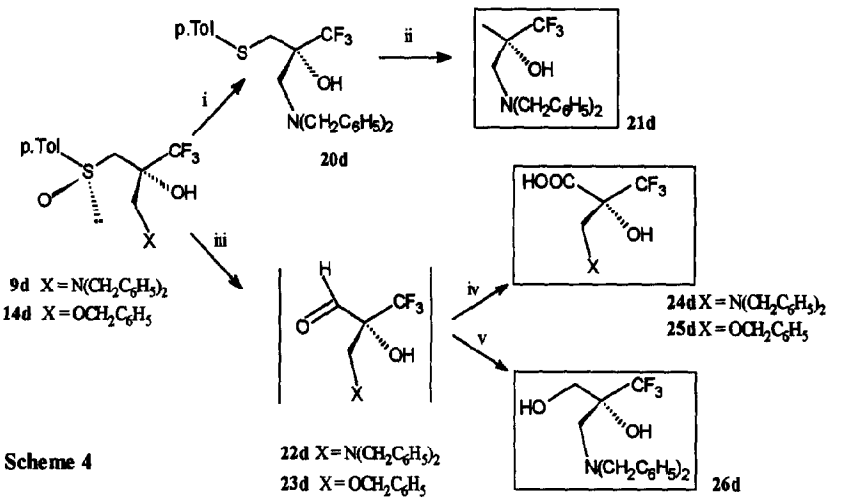
19c, $R_F = CF_2Cl$
19d, $R_F = CF_3$

Reagents and Conditions: i) NaI, $(CF_3CO)_2O$, CH_3COCH_3, - 20°C, ii) $(CF_3CO)_2O$, *syn*-collidine, CH_3CN, - 20°C, iii) $HgCl_2$, K_2CO_3, CH_3CN, r.t., iv) NaH, $C_6H_5CH_2Br$, THF, 0°C.

fluorinated chiral synthons **5**, the desulphurisation of the labile haloacethoxy p-tolylthio intermediates **15** to give aldehydes **16** and their reductive elaboration could be performed without affecting the oxirane ring. As a consequence, α-polyfluoro- and -polyhaloalkyl-α-hydroxybenzyl protected oxiranes **18b-e** could be isolated in rather satisfying yields.

The simplest procedure to eliminate the chiral auxiliary sulphinyl group is its reduction to sulfide derivative through the Oae procedure[17] and through this step, always without affecting the oxirane ring, the thiomethyl oxirane derivatives **19c** and **19d** were obtained from, respectively, **5c** and **5d** in 97.3% and 93.0% yield.

As shown in Scheme 4, the same mild deoxygenation reaction could be performed on the products derived from nucleophilic opening of the oxirane ring: thiomethyl-α-hydroxy-β-amino-trifluoromethyl derivative **20d** was synthesized in 93.5% yield starting from **9d** and subsequently easily desulphenylated to trifluoromethyl amino alcohol **21d** by action of Ni-Raney in 77% isolated yield.



Scheme 4

Reagents and Conditions: i) NaI, $(CF_3CO)_2O$, CH_3COCH_3, - 20°C, ii) Ni-Raney, C_2H_5OH, 80°C, iii) $(CF_3CO)_2O$, *syn*-collidine, CH_3CN, - 20°C, $HgCl_2$, K_2CO_3, r.t., iv) $NaClO_2$, KH_2PO_4, $(CH_3)_3COH$, 2-methyl-2-butene, H_2O, r.t., v) $NaBH_4$, 0°C

Pummerer rearrangement, both under reductive and under oxidative conditions was performed on acyclic derivatives: trifluoromethyl-α-hydroxy-β-amino acid **24d** could be obtained in good yields starting from α,β-hydroxyamino sulphinyl derivative **9d** and submitting the intermediate aldehyde **22d** to mild oxidative process (see experimental).

Following the same method, starting from α,β-dihydroxy benzylprotected compound **14d**, trifluoromethyl-α,β-dihydroxy acid **25d** was obtained. On the other hand, reductive elaboration of the intermediate α-hydroxy-β-amino trifluoromethyl aldehyde **23d** allowed the synthesis of trifluoromethyl-α,β-dihydroxy-γ-amino derivatives **26d**. The same synthetic sequence, performed on **5c** allowed the obtainment of the chlorodifluoro analogue **26c** (see experimental). In all the examined cases, the products were obtained in high optical and chemical yields.

Structural Assignments

All described compounds gave satisfactory elemental analyses or high resolution mass spectral ions and all ^{1}H and ^{19}F NMR spectra were in accordance with the assigned structure (see experimental).

The absolute stereochemistry at the C-2 carbon in trifluoromethyl oxirane **5d** was confirmed by X-ray crystallographic analysis on the (2R,S_S)-**10d** bromo derivative enantiomer, synthesized using (1S)-menthyl (S)-*p*-toluenesulphinate as the source of chirality. An arbitrary view of compound **10d** is shown in Figure 2 with appropiate atomic labelling. Final position parameters and molecular dimension are respectively reported in Tables 2 and 3. Values for bond lenghts and angles fall in the expected range[18]. The conformation of the molecule is characterized by the value of torsion angles C(11)-S-C(1)-C(2) and S-C(1)-C(2)-C(4) which are respectively -174.2(4) and -160.0(4), in agreement with other similar sulphoxide compounds[19]. The main features characterizing the molecular packing is the intermolecular hydrogen bonding between the hydroxyl hydrogen and the sulphoxide oxigen.

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br	4468(1)	1073(1)	1853(1)	71(1)
S	3846(1)	3620(1)	4470(2)	46(1)
F(1)	5767(4)	2678(3)	-12(4)	68(1)
F(2)	6740(4)	3829(3)	924(5)	74(1)
O(2)	6458(4)	3260(3)	3866(5)	54(1)
F(3)	7517(4)	2471(3)	1169(5)	80(1)
O(1)	3531(4)	2710(3)	5207(5)	63(1)
C(12)	1510(6)	3564(4)	3052(7)	50(1)
C(11)	2415(5)	4108(4)	3770(6)	42(1)
C(13)	384(5)	3959(5)	2613(7)	50(1)
C(1)	4503(6)	3357(4)	2610(6)	45(1)
C(2)	5729(5)	2822(4)	2717(6)	42(1)
C(16)	2189(5)	5045(4)	4036(7)	51(2)
C(15)	1072(6)	5423(4)	3540(8)	53(2)
C(14)	161(5)	4905(4)	2830(7)	49(2)
C(4)	6437(6)	2936(4)	1192(7)	52(2)
C(17)	-1075(6)	5333(5)	2332(9)	66(2)
C(3)	5592(6)	1801(4)	3159(7)	50(1)

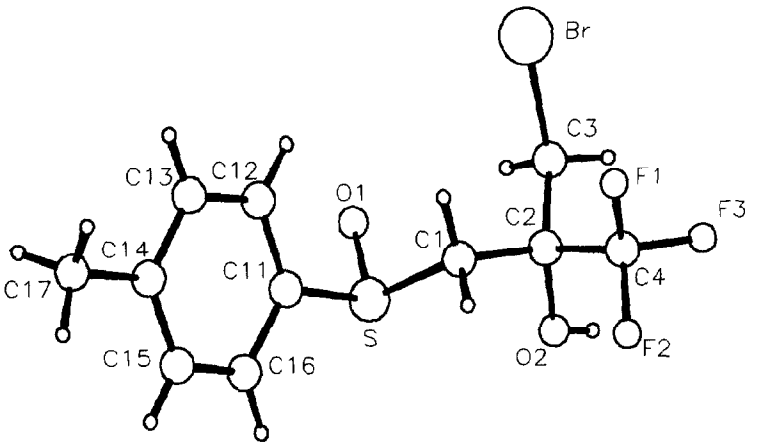


Figure 2

Table 3. Selected bond lengths [Å] and angles [deg]

Br-C(3)	1.953(6)	O(1)-S-C(11)	107.4(3)
S-O(1)	1.494(5)	O(1)-S-C(1)	106.9(3)
S-C(11)	1.782(6)	C(11)-S-C(1)	96.0(3)
S-C(1)	1.805(5)	C(2)-C(1)-S	112.5(4)
F(1)-C(4)	1.321(8)	O(2)-C(2)-C(1)	106.9(5)
F(2)-C(4)	1.342(8)	O(2)-C(2)-C(3)	107.5(5)
O(2)-C(2)	1.414(7)	C(1)-C(2)-C(3)	114.9(5)
F(3)-C(4)	1.328(7)	O(2)-C(2)-C(4)	107.3(4)
C(1)-C(2)	1.516(8)	C(1)-C(2)-C(4)	108.3(5)
C(2)-C(3)	1.522(8)	C(3)-C(2)-C(4)	111.6(5)
C(2)-C(4)	1.536(8)	F(1)-C(4)-F(3)	108.3(5)
		F(1)-C(4)-F(2)	105.0(5)
		F(3)-C(4)-F(2)	105.7(5)
		F(1)-C(4)-C(2)	113.1(5)
		F(3)-C(4)-C(2)	112.6(5)
		F(2)-C(4)-C(2)	111.7(5)
		C(2)-C(3)-Br	115.2(4)

Conclusions

A highly stereoselective method for preparing a variety of differently functionalized fluorosubstituted tertiary alcohols from easily available fluorinated acetic acid or perfluorinated carboxylic acid esters and optically active methyl p-tolyl sulphoxide has been developed. It has been demonstrated that the methylene addition on the carbonyl of β-keto-γ-fluoro- or -perfluoroalkyl substituted sulphoxides or on the corresponding hydrate forms proceeds with high sito specificity and with high facial selectivity to give methylene oxides, all isolated in optically pure form. Promising synthetic potential of oxirane ring opening by nucleophiles as well as efficiency of oxidative or reductive chiral auxiliary removal have been shown.

Experimental Section

General Details. ^1H and ^{19}F NMR spectra were recorded on a Brucker CXP 300 or a Brucker AC 250L spectrometer; chemical shifts are in p.p.m. (δ); tetramethylsilane was used as internal standard (δ_H) for ^1H nucleus, while C_6F_6 was used as internal standard (δ_F = -162.90) for ^{19}F nucleus. $[\alpha]_D$ Values were obtained on a Jasco DIP-181 polarimeter. Mass spectra were performed on Hitachi Perkin-Elmer RMU-6D (Magnetic Analyzer). Melting points are uncorrected and were obtained on a capillary apparatus. TLC were run on silica gel $60F_{254}$ Merck plates; column chromatographies were performed with silica gel 60 (60-200 μm, Merck). Tetrahydrofuran (THF) was freshly distilled from lithium aluminium hydride; diisipropylamine was distilled from calcium hydride and stored over molecular sieves (4Å); in all other cases, commercially available reagent-grade solvents were employed without purification.

Synthesis of (R$_S$)-3,3-difluoro-1-[(4-methylphenyl)sulphinyl]-4,4,4-trifluoro-butan-2-one/ol (3/4b). To a solution of LDA (1.2 mmol) in THF (5.0 ml) stirred under nitrogen atmosphere at - 60°C was added dropwise a solution of methyl p-tolyl sulphoxide (1) (1.0 mmol) in THF (2.0 ml) and the yellow solution of the anion was cooled at - 78°C. Neat ethyl pentafluoropropionate (**2b**) (1.5 mmol) was added at the same temperature and the reaction was quenched by addying a saturated solution of ammonium chloride. The organic layers were extracted with ethyl acetate and dried over anhydrous sodium sulphate. After flash chromatographic purification (n-hexane / ethyl acetate 6 : 4), (R$_S$)-**3/4b** was obtained in 85% yield and in a 1.0 : 1.5 keto / hydrate form; $[\alpha]_D^{20}$ + 150.0 (c 1.2, $CHCl_3$); m.p. 80-82°C (isopropylether); ^1H ($CDCl_3$) δ: 1.65 (brm,2H,OH hydrate form,) 2.48 (s,3H, $ArCH_3$), 3.10 (dd,2H,CH_2S, hydrate form), 4.06 (d, 1H, CH_aS keto form, $^2J_{H-H}$ = 15.0 Hz), 4.26 (d,1H,CH_bS keto form), 7.20-7.60 (m,4H,ArH); ^{19}F: hydrate form: - 129.7 (d,1F,CF_aF, $^2J_{F-F}$ = 300.0 Hz), - 127.6 (d,1F,CF_bF) - 84.2 (s,3F,CF_3); keto form: - 122.8 (d,1F,CF_aF, $^2J_{F-F}$ = 120.0 Hz), - 122.2 (d,1F,CF_bF), - 80.0 (s,3F,CF_3).

Oxirane Ring Formation General Procedure. ***Ethyl ether.*** To a solution of ketone, ketone/hydrate mixture, or hydrate (1.0 mmol) in ethyl ether (5 ml), a solution of diazomethane (*c.a.* 0.5 M) in the same solvent was added portionwise at 0°C up to persistance of the yellow colour of the slurry. Excess CH_2N_2 was removed by bubbling a nitrogen stream and solvent was evaporated under reduced pressure. Isolation of pure products was accomplished by flash chromatography and fractional crystallization. Global chemical yields, diastereoisomeric excess, and **5/6** ratio are given in Table 1.From **3b/4b** mixture, in 4 hours and after purification (n-hexane / ethyl acetate 6 : 4), the following products were isolated: (2S,R$_S$) / (2R,R$_S$)-2-(difluoromethyl)-2-{[(4-methylphenyl)sulphinyl]methyl} oxiranes (**5b**) mixture (78% yield) (R_F 0.35) and (R$_S$)-(Z)-3,3-difluoro-2-methoxy-1-[(4-methylphenyl)sulphinyl]-propene[20] (**6b**) in 17% yield: R_F 0.30; $[\alpha]_D^{20}$ - 191.3 (c 0.4, $CHCl_3$); m.p. 66-68°C; b.p. 232°C; ^1H ($CDCl_3$) δ: 2.41 (s,3H,$ArCH_3$), 4.16 (s,3H,OCH_3), 5.90 (s,1H,CH=C), 5.97 (t,1H,CHF_2,$^2J_{H-F}$ = 55.0 Hz), 7.30-7.60 (m,4H,ArH); ^{19}F: - 122.2 (dd,1H,CHF_a,$^2J_{F-F}$ = 300.0,$^2J_{F-H}$ = 55.0 Hz), - 120.3 (dd,1H,CHF_b). The (2S/2R)-**5b** mixture was submitted to fractional chrystallization by isopropylether to give optically pure (2S)-**5b**: $[\alpha]_D^{20}$ + 232.3 (c 1.1, $CHCl_3$); m.p. 88-89°C (isopropylether); $C_{11}H_{12}F_2O_2S$ calcd: C 53.66, H 4.88; found C 53.60, H 4.90; ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 3.02 (d,1H,CH_aS,$^2J_{H-H}$ = 14.5 Hz), 3.02 (d,1H,CH_aO,$^2J_{H-H}$ = 4.0 Hz), 3.29 (ddd,1H,CH_bO,$^2J_{H-H}$ = 4.0,$^4J_{H-F}$ = 4.0,$^4J_{H-F}$ = 2.0 Hz), 3.46 (d,1H,CH_bS), 5.59 (t,1H,CHF_2,$^2J_{H-F}$ = 54.0 Hz); ^{19}F: - 127.5 (ddd,1F,CHF_a,$^2J_{F-F}$ =

294.0,$^4J_{F-H}$ = 4.0 Hz), - 125.2 (dd,1F,CHF_b). (2R)-**5b** Was not isolated in optically pure form : ^1H ($CDCl_3$) δ : 2.44 (s,3H,$ArCH_3$), 2.89 (dd,1H,CH_aS,$^2J_{H-H}$ = 15.0,$^4J_{H-F}$ = 1.5 Hz), 3.09 (dd,1H,CH_aO,$^2J_{H-H}$ = 4.5,$^4J_{H-F}$ = 1.0 Hz), 3.13 (m,1H,CH_bO), 3.32 (d,1H,CH_bS), 5.86 (t,1H,CHF_2,$^2J_{F-H}$ = 55.0 Hz), 7.30-7.60 (m,4H,ArH); ^{19}F: - 127.3 (dd,1F,CHF_a,$^2J_{F-F}$ = 294.0,$^2J_{F-H}$ = 54.0 Hz), - 125.4 (dd,1F,CHF_b). When reaction was carried on starting from larger quantities of **3b/4b** (10-100 mmol in 500 ml of solvent), an about 12% of unresolved 10 : 7 (2S,R_S)/(2R,R_S)-3,3-difluoro-2-{[(4-methylphenyl)sulphinyl]methyl}-propan-1,2-diol (**13b**) (R_F0.20) was isolated. (2S)-**13b** ^1H and ^{19}F NMR spectra are identical to those of the compound obtained from acidic opening of (2S)-**5b** (see above). (2R)-**13b**: ^1H ($CDCl_3$) δ: 2.43 (s,3H,$ArCH_3$), 2.96 (dd,1H,CH_aS,$^2J_{H-H}$ = 14.0Hz), 3.09 (dd,1H,CH_bS,$^4J_{H-H}$ = 1.4 Hz), 3.91 (ddd,1H,CH_aO,$^2J_{H-H}$ = 12.6,$^3J_{H-O-H}$ = 7.0,$^4J_{H-H}$ = 1.4 Hz), 4.07 (m,1H,CH_bO,$^4J_{H-F}$ = 7.0,$^4J_{H-H}$ = 1.4 Hz), 4.10 (t,1H,$CH_2O\underline{H}$,$^3J_{H-O-H}$ = 7.0 Hz), 4.85 (brs,1H,OH), 5.88 (t,1H,CHF,$^2J_{H-F}$ = 55.3 Hz), 7.30-7.60 (m,4H,ArH); ^{19}F: - 134.3 (ddd,1F,CHF_a,$^2J_{F-F}$ = 287.0,$^2J_{F-H}$ = 56.0,$^4J_{F-H}$ = 7.0 Hz), - 133.0 (dd,1F,CHF_b). From **3c/4c** mixture, in 5 hours and after purification (n-hexane / ethyl acetate 6 : 4), (2S,R_S)-2-(chlorodifluoromethyl)-2-{[(4-methylphenyl)sulphinyl]methyl} oxirane (**5c**) (27% yield) was isolated: R_F 0.35; $[\alpha]_D^{20}$ + 163.2 (c 1.1, $CHCl_3$); $C_{11}H_{11}ClF_2O_2S$ calcd: C 47.06, H 3.92; found: C 47.10, H 3.90; ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 3.19 (dd,1H,CH_aS,$^2J_{H-H}$ = 14.5,$^4J_{H-H}$ = 0.75 Hz), 3.29 (dd,1H,CH_aO,$^2J_{H-H}$ = 4.0,$^4J_{H-H}$ = 0.75 Hz), 3.52 (dt,1H,CH_bO,$^4J_{H-F}$ = 2.0 Hz), 3.56 (d,1H,CH_bS), 7.30-7.60 (m,4H,ArH); ^{19}F: - 65.5. (R_S)-(Z)-3-chloro-3,3-difluoro-2-methoxy-1-[(4-methylphenyl)sulphinyl]-propene[20] (**6c**) (57% yield): R_F 0.30; $[\alpha]_D^{20}$ - 161.6 (c 1.1, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 4.23 (s,3H,OCH_3), 6.17 (s,1H,CH=C), 7.20-7.60 (m,4H,ArH); ^{19}F: - 58.5 (d,1F,$^2J_{F-F}$ = 165.0 Hz), - 59.4 (d,1F). When the reaction was performed in bulky quantities, small amounts of three byproducts were detectable: (Z)-3-chloro-3,3-difluoro-2-methoxy-1-[(4-methylphenyl)sulphenyl] propene (**27c**) in 0.7% isolated yields: R_F 0.60; ^1H ($CDCl_3$) δ: 2.35 (s,3H,$ArCH_3$), 3.92 (s,3H,OCH_3), 6.43 (s,1H,CH=C), 7.10-7.35 (m,4H,ArH); ^{19}F: - 55.8. (2S)-2-(chlorodifluoromethyl)-2-{[(4-methylphenyl)sulphenyl]methyl} oxirane (**19c**) in 3% isolated yield (R_F 0.50); (2S,R_S)-3-chloro-3,3-difluoro-{2-[(4-methylphenyl)sulphinyl] methyl}-propan-1,2-diol (**13c**) whose ^1H and ^{19}F NMR spectra were identical to those of the same derivative obtained through acidic opening of (2S)-**5c** (see above) was isolated in 4.7% yields (R_F 0.20). From **4d**, in 3 hours and after purification (chloroform / ethyl acetate 95 : 5), (2S,R_S)-2-{[(4-methylphenyl)sulphinyl]methyl}-2-(trifluoromethyl) oxirane (**5d**) was obtained in 51% yield:R_F 0.30; $[\alpha]_D^{20}$ + 165.8 (c 1.1, $CHCl_3$); $C_{11}H_{11}F_3O_2S$ calcd: C 50.00, H 4.17; found: C 50.08, H 4.12; ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 3.10 (dd,1H,CH_aS,$^2J_{H-H}$ = 14.5,$^4J_{H-H}$ = 0.6 Hz), 3.21 (dd,1H,CH_aO,$^2J_{H-H}$ = 4.3 Hz), 3.40 (dq,1H,CH_bO,$^4J_{H-H}$ = 2.0 Hz), 3.49 (d,1H,CH_bS), 7.34-7.50 (m,4H,ArH); ^{19}F: - 78.0 among with (R_S)-(Z)-2-methoxy-1-[(4-methylphenyl)sulphenyl]-3,3,3-trifluoro propene[20] (**6d**) (39% yield): R_F 0.35; $[\alpha]_D^{20}$ - 247.5 (c 1.2, $CHCl_3$); m.p. 53-54°C (ethyl ether); ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 4.18 (s,3H,OCH_3), 6.20 (s,1H,CH=C), 7.32-7.48 (m,4H,ArH); ^{19}F: - 71.2 (dq,$^4J_{F-H}$ = 0.7 Hz). When reaction was carried on in larger quantities, small amounts of the following byproducts were detected: (Z)-2-methoxy-1-[(4-methylphenyl)sulphenyl]-3,3,3-trifluoro propene (**27d**) in 5% yield: R_F 0.75; ^1H ($CDCl_3$) δ: 2.35 (s,3H,$ArCH_3$), 3.87 (s,3H,OCH_3), 6.42 (d,1H,CH=C,$^4J_{H-F}$ = 0.7 Hz), 7.12-7.35 (m,4H,ArH); ^{19}F: - 69.7. (2S)-2-{[(4-methylphenyl)sulphenyl]methy} -2-(trifluoromethyl) oxirane (**19d**) in 5% yield (R_F 0.72); From **3f**, in 10 hours and after purification (chloroform / ethyl acetate 99 : 1) (R_S)-(Z)-2-methoxy-1-[(4-methylphenyl)sulphinyl]-perfluorononene[20] (**6f**) was obtained in 20% yield: R_F 0.35; $[\alpha]_D^{20}$ - 110.0 (c 1 0, CHCl3); ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 4.26

(s,3H,OCH_3), 6.19 (s,1H,CH=C), 7.30-7.60 (m,4H,ArH); ^{19}F: - 127.2 (s,1CF_2), - 124.0 (s,1CF_2), - 123.3 (s,4CF_2), - 116.4 ($C\underline{F}_2CF_3$), - 82.0 (CF_3).

Methanol. from **3b/4b** mixture, after 2 hours, **5b** was isolated in 92% yield while **6b** was detected only in traces < 5% at ^{19}F NMR), but carrying on the reaction in bulky, also a 18% yield of an about 1 : 1 mixture of (2R)/(2S)-**13b** was detected. From **3c/4c** mixture, in 3 hours, **5c** was isolated in 75% yield and enolether **6c** in 10% yield. From **4d**, in 2 hours, **5d** was obtained in 82% yield, among with a 13% yield of (Z)-**6d**, but when the reaction was performed in big quantities, 3.2% yield of (2S,R_S)-2-[(4-methylphenyl)sulphinyl]methyl-3,3,3-trifluoro-propan-1,2-diol (**13d**) (R_F 0.20) (^1H and ^{19}F NMR spectra superimposable to those of the same derivative obtained by acidic opening of (2S)-**5d**) and 1.2% yield of (2R,R_S)-(**13d**): R_F 0.22; $[\alpha]_D^{20}$ + 12.2 (c 1.0, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 3.09 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.20 (d,1H,CH_bS), 4.01 (d,1H,CH_aO,$^2J_{H-H}$ = 12.5 Hz), 4.17 (d,1H,CH_bO), 4.87 (brs,1H,OH), 5.7 (brs,1H,OH), 7.33-7.60 (m,4H,ArH); ^{19}F: - 81.6. From **4e**, in 2 hours and after purification (chloroform / ethylether 98 : 2), (2S,R_S)-2-{[(4-methylphenyl)sulphinyl]methyl}2-pentafluoroethyl oxirane (**5e**) in 64% yield: R_F 0.30; $[\alpha]_D^{20}$ + 160.2 (c 0.8, $CHCl_3$); m.p. 45-46°C (isopropylether); $C_{12}H_{11}F_5O_2S$ calcd: C 45.86, H 3.50; found: C 45.31, H 3.60; ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 3.12 (d,1H,CH_aS,$^2J_{H-H}$ = 15.0 Hz), 3.21 (d,1H,CH_aO,$^2J_{H-H}$ = 5.0 Hz), 3.42 (d,1H,CH_bS), 3.55 (dt,1H,CH_bO,$^4J_{H-F}$ = 2.5 Hz), 7.35-7.60 (m,4H,ArH); ^{19}F: - 126.5 (d,1F,CF_aF,$^2J_{F-F}$ = 270.0 Hz), - 125.5 (d,1H,CF_bF), - 82.3 (s,3F,CF_3) and 26% isolated yields of (R_S)-(Z)-3,3-difluoro-1-[(4-methylphenyl)sulphinyl]-2-methoxy-4,4,4-trifluoro-butene[20] (**6e**): R_F 0.35; $[\alpha]_D^{20}$ - 213.0 (c 1.9, $CHCl_3$); m.p. 53.5-54.0°C (isopropylether); $C_{12}H_{11}F_5O_2S$ calcd: C 45.86, H 3.50; found: C 45.36, H 3.58; ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 4.25 (s,3H,OCH_3), 6.20 (s,1H,CH=C), 7.35-7.60 (m,4H,ArH); ^{19}F: - 119.8 (s,2F,CF_2), - 04.0 (s,3F,CF_3). Performing reaction in bulky, a 1 : 1 mixture of (2R,R_S) / (2S,R_S)-3,3-difluoro-2-{[(4-methylphenyl)sulphinyl]methyl}-4,4,4-trifluoro-butan-1,2-diol (**13e**) (10.5% yield) was detected. By fractional crystalization performed in isopropylether, (2R)-**13e** was isolated in optically pure form: R_F 0.10; $[\alpha]_D^{20}$ + 98.4 (c 1.1, $CHCl_3$); m.p. 118-119°C (isopropylether); ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 3.15 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.16 (d,1H,CH_bS), 3.34 dd,1H,OH,$^3J_{H-O-H}$ = 7.2,$^3J_{H-O-H}$ = 6.6 Hz), 4.07 (dd,1H,CH_aO,$^2J_{H-H}$ = 12.6,$^3J_{H-O-H}$ = 7.2 Hz), 4.23 (dd,1H,CH_bO,$^3J_{H-O-H}$ = 6.6 Hz), 4.90 (brs,1H,OH), 7.30-7.60 (m,4H,ArH); ^{19}F: - 125.0 (d,1F,CF_aF,$^2J_{F-F}$ = 285.0 Hz), - 123.6 (d,1F,CF_bF), - 79.9 (s,3F,CF_3); (2S)-**13e** was characterized only by NMR spectra: ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 3.03 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.22 (d,1H,CH_bS), 3.90 (d,2H,$C\underline{H}_2OH$,$^2J_{H-H}$ = 7.5 Hz), 4.82 (brs,1H,OH), 7.30-7.60 (m,4H,ArH); ^{19}F: - 125.4 (d,1F,CF_aF,$^2J_{F-F}$ = 275.0 Hz), - 123.8 (d,1F,CF_bF), - 79.8 (s,3F,CF_3). From **3f**, in four hours and after purification (n-hexane / ethyl acetate 85 : 15), **6f** was obtained in 60% yield.

Benzene. from **3d/4d** mixture, **5d** was obtained in 44% yield, among with **6d** in the same (44%) isolated yield.

Ethanol. from **3c/4c** mixture, **5c** was obtained in 62% yield and **6c** was isolated in 18% yield and from **3d/4d** mixture, **5d** was obtained in 77% yield, among with **6d** isolated in 15% yield.

Synthesis of (R_S)-2-(chlorodifluoromethyl)-3-[(4-methylphenyl)sulphinyl]-prop-2-en-1-ol (7c). To a solution of oxirane (2S,R_S)-**5c** (400 mg, 1.43 mmol) in anhydrous THF (5.0 ml) stirred at room temperature was added dropwise a solution of potassium hydroxide (96.5 mg, 1.72 mmol) in water (2.0 ml). After 5 hours, THF was evaporated and organic layers were extracted with ethyl acetate (3x5.0 ml). After the usual work-up, the residue was purified by flash chromatography (chloroform/ethyl acetate 8 : 2) to give **7c** as the only product in 98.0% yield: R_F 0.34; $[\alpha]_D^{20}$ + 13.4 (c 1.6, CHCl3); ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 4.52

(d,1H,CH_aO,$^2J_{H-H}$ = 12.5 Hz), 4.65 (d,1H,CH_bO), 6.61 (brs,1H,CH=C), 7.30-7.60 (m,4H,ArH); ^{19}F: - 57.3 (d,1F,$^2J_{F-F}$ = 16.0 Hz), - 56.7 (d,1F). (E)/(Z) steric relation was not assigned.

Synthesis of (R_S)-2-(trifluoromethyl)-3-[(4-methylphenyl)sulphinyl]-prop-2-en-1-ol (7d). To a solution of LDA (5.6 mmol) in anhydrous THF (10.0 ml) stirred under nitrogen at - 70°C, was added dropwise a solution of oxirane (2S,R_S)-**5d** (123 mg, 4.7 mmol) in 5.0 ml of the same solvent. After 5 min. a saturated aqueous solution of ammonium chloride was added and, after the usual work-up, the residue was purified by flash chromatography (n-hexane/ethyl acetate 5 : 5) to give: (Z)-**7d** in 42% yield; R_F 0.49; $[\alpha]_D^{20}$ + 123.4 (c 1.3, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.43 (s,3H,$ArCH_3$), 4.28 (q,1H,OH,$^3J_{Ha-O-H}$ = 6.0,$^3J_{HbO-H}$ = 7.5 Hz), 4.49 (dd,1H,CH_aO,$^2J_{H-H}$ = 14.0 Hz), 4.60 (d,1H,CH_bO), 6.71 (q,1H,CH=C,$^4J_{H-F}$ = 1.0 Hz), 7.30-7.68 (m,4H,ArH); ^{19}F: - 69.0; and (E)-**7d** in 40% yield: R_F 0.30; $[\alpha]_D^{20}$ - 44.8 (c 1.7, CHCl3); ^1H ($CDCl_3$) δ: 2.40 (s,3H,$ArCH_3$), 4.14-4.20 (brm,1H,OH), 4.20-4.46 (brm,2H,$C\underline{H}_2OH$), 6.80 (t,1H,CH=C,$^4J_{H-H}$ = 2.0 Hz), 7.30-7.60 (m,4H,ArH); ^{19}F: - 60.8.

Synthesis of (2S,R_S)-1-(benzylamino)-2-{[(4-methylphenyl)sulphinyl]methyl}-3,3,3-trifluoro-propan-2-ol (8d). To a solution of **5d** (180 mg, 0.68 mmol) in anhydrous THF (2 ml) neat benzylamine (87.5 mg, 0.82 mmol) was added. Reaction mixture was kept 10 hours at room temperature and, after removal of the solvent under reduced pressure, purified by flash chromatography (n-hexane/ethyl acetate 8 : 2) to give (2S)-**9d** in 87.0% yield: R_F 0.35; $[\alpha]_D^{20}$ + 133.0 (c 1.1, $CHCl_3$); m.p. 75-76°C (isopropylether); $C_{18}H_{20}F_3NO_2S$ calcd: C 58.22, H 5.39, N 3.77; found: C 58.10, H 5.42, N 3.70; ^1H ($CDCl_3$) δ: 2.43(s,3H,$ArCH_3$), 2.97(d,1H,CH_aN,$^2J_{H-H}$ = 13.25 Hz), 3.01(d,1H,CH_aS,$^2J_{H-H}$ = 13.5 Hz), 3.02(d,1H,CH_bN), 3.35(dq,1H,CH_bS,$^4J_{H-F}$ = 1.0 Hz), 3.90(s,2H,$ArCH_2$), 7.20-7.60(m,9H,ArH); ^{19}F: - 82.3.

Synthesis of (2S,R_S)-1-chloro-3-(dibenzylamino)-1,1-difluoro--2-{[(4-methylphenyl)sulphinyl]methyl}-propan-2-ol (9c). To a solution of **5c** (300 mg, 1.07 mmol) in anhydrous THF (4 ml) neat dibenzylamine (253 mg, 1.28 mmol) was added at room temperature. Solution was stirred at the same temperature for 18 hours, solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography (n-hexane/ethyl acetate 5 : 5) to give (2S)-**9c** in 89.0% yield: RF 0.45; $[\alpha]_D^{20}$ + 96.7 (c 1.0, $CHCl_3$); $C_{25}H_{26}ClF_2NO_2S$ calcd: C 62.83, H 5.44, N 2.93; found: C 62.28, H 5.50, N 2.95; ^1H ($CDCl_3$) δ: 2.43 (d,1H,CH_aN,$^2J_{H-H}$ = 14.30 Hz), 2.49(s,3H,$ArCH_3$), 3.10(d,1H,CH_aS,$^2J_{H-H}$ = 15.0 Hz), 3.20 (dq,1H,CH_bS), 3.28(d,1H,CH_bN), 3.57 (d,2H,CH_aAr,$^2J_{H-H}$ = 13.5 Hz), 3.99 (d,2H,CH_bAr), 6.24 (brs,1H,OH), 7.20-7.55 (m,14H,ArH); ^{19}F. - 65.5.

Synthesis of (2S,R_S)-1-(dibenzylamino)-2-{[(4-methylphenyl)sulphinyl]methyl}-3,3,3-trifluoro-propan-2-ol (9d). To a solution of **5d** (1.23g, 4.66 mmol) in anhydrous THF (15 ml) neat dibenzylamine (1.10g, 5.6 mmol) was added After 18 hours, the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (n-hexane/ethyl acetate 8 : 2) to give (2S)-**9d** in 93.0% yield: R_F 0.42; $[\alpha]_D^{20}$ + 114.8 (c 1.2, $CHCl_3$); m.p. 96-97°C (isopropylether); $C_{25}H_{26}F_3NO_2S$ calcd: C 65.07, H 5.64, N 3.04; found: C 65.10, H 5.60, N 2.95 ^1H ($CDCl_3$) δ: 2.29(d,1H,CH_aS,$^2J_{H-H}$ = 14.25 Hz), 2.47 (s,3H,$ArCH_3$), 2.99 (d,1H,CH_aN,$^2J_{H-H}$ = 14.75 Hz), 3.09 (d,1H,CH_bN), 3.18 (dq,1H,CH_bS, $^4J_{H-F}$ = 1.0 Hz),

3.59(d,2H,CH_aAr,$^2J_{H-H}$ = 13.5 Hz), 3.96(d,2H,CH_bAr), 5.98(brs,1H,OH), 7.20-7.52(m,14H,ArH); ^{19}F: - 80.5.

Synthesis of (2S,R_S)-1-bromo-2-{[(4-methylphenyl)sulphinyl]methyl}-3,3,3-trifluoro-propan-2-ol (10d). Cupric bromide (1.33 g, 6.06 mmol) and lithium bromide (1.03 g, 12.12 mmol) were dissolved in anhydrous THF (10 ml) at 0°C to afford a dark green solution which was immediately warmed to room temperature. Oxirane **5d** (1.0 g, 3.79 mmol) in anhydrous THF (2 ml) was added dropwise and the mixture was stirred for five days. The reaction was quenched by addying 5 ml of buffered phosphate solution (pH 7.0) and the organic layers were extracted with chloroform (3x10 ml), the combined organic layers were dried over anhydrous sodium sulphate, the solvent was evaporated under reduced pressure and the residue was submitted to flash chromatographic purification (n-hexane/ethyl acetate 75 : 25) to give (2S)-**10d** in 74.0%yield: R_F 0.35; $[\alpha]_D^{20}$ + 195.3 (c 1.2, $CHCl_3$); m.p. 146-147°C (isopropylether); $C_{11}H_{12}BrF_3O_2S$ calcd: C 38.26, H 3.48; found: C 38.12, H 3.51; ^1H ($CDCl_3$) δ: 2.45 (s,3H,$ArCH_3$), 2.98 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.30 (dq,1H,CH_bS, $^4J_{H-F}$ = 1.5 Hz), 3.58(d,1H,CH_aBr,$^2J_{H-H}$ = 11.5 Hz), 3.63 (d,1H,CH_bBr), 5.94 (s,1H,OH), 7.37-7.64 (m,4H,ArH); ^{19}F: - 80.5.

X-Ray analysis of (2R,S_S)-10d. Colorless crystals of enantiomer (2R,S_S)-**10d** {$[\alpha]_D^{20}$ - 194.5 (c 1.1, $CHCl_3$)} suitable for X-ray analysis were obtained by crystallization from isopropylether. Diffraction data were collected on a Philips PW1100 diffractometer, with monochromated Cu-Kα radiation (λ=1.5418). The selected crystal had dimension of 0.4 x 0.3 x 0.7 mm. Cell constants were obtained by least squares refinement on 2θ values of 24 reflections with 2θ>40. Crystal data are: $C_{11}H_{12}O_2F_3SBr$, f.w. 345.18, orthorhombic, space group $P2_12_12_1$, a=10.632(2) Å, b=14.351(6) Å, c=8.714(2) Å, V=1329.6(7) $Å^3$, Z=4, D_c=1.724 Mg/m^3, μ=5.977 mm^{-1} , F(000)=688. Intensity data were collected using the θ-2θ scan technique 2 octants (±h, +k, +l) in the range 3<θ <55°, corresponding to 1658 independent reflections. 3 Standard reflections were measured every 100 reflections and showed no significant decay. The data were corrected for Lorenz and polarization effects, but no absorption correction was applied. The structure was solved using the SIR92[21]program and refined by full-matrix least squares on F^2 values with SHELXL-93[22]. Non-hydrogen atoms were refined with anisotropic temperature factors. The hydroxyl hydrogen was located by difference-Fourier map, and refined, while the other hydrogens were included at calculated positions and refined in the riding mode, with group temperature factors. The final value of the residual R and wR2 were, respectively, 0.0441 and 0.1159 for 1629 reflections with I>2σ(I). The highest and lowest residual peaks in final difference-Fourier map were respectively 0.53 and - 0.61 $eÅ^{-3}$. Determination of the absolute configuration was based on the refinement of Flack's *x* parameter[23]. The resulting value of 0.03(4) unambiguously determines the absolute configuration as S(S), C2(R).

Synthesis of (2S,R_S)-1,3-dichloro-3,3-difluoro-2-{[(4-methylphenyl)sulphinyl]methyl}-propan-2-ol (11c). Cupric chloride (743 mg, 5.70 mmol) and lithium chloride (462 mg, 11.40 mmol) were dissolved in anhydrous THF (10 ml) at 0°C. Immediately after suspention had reached room temperature, a solution of **5c** (1.0 g, 3.56 mmol) in the same solvent (2 ml) was added dropwise. The reaction mixture was stirred at room temperature for 40 hours. After the usual work-up and upon flash chromatographic purification in n-hexane/ethyl acetate 6 : 4, (2S)-**11c** was obtained in 98.0% yield: R_F 0.35; $[\alpha]_D^{20}$ + 241.0 (c 1.2, $CHCl_3$); m.p. 148-149°C (isopropylether); $C_{11}H_{12}Cl_2F_2O_2S$ calcd: C 41.64, H 3.78; found: C 41.78, H 3.65; ^1H ($CDCl_3$) δ: 2.45

(s,3H,$ArCH_3$), 3.07 (d,1H,CH_aS,$^2J_{H-H}$ = 15.0 Hz), 3.34 (d,1H,CH_bS), 3.85 (s,2H,CH_2Cl), 6.01 (s,1H,OH), 7.30-7 60 (m,4H,ArH); ^{19}F· - 62.9

Synthesis of (2S,R$_S$)-1-chloro-2-{[(4-methylphenyl)sulphinyl]methyl}-3,3,3-trifluoro-propan-2-ol (11d). Starting from **5d** (1.0 g, 3.79 mmol) and following the same procedure described above, (2S)-**11d** was obtained in 95.0% yield: R_F 0.40 (n-hexane/ethyl acetate 6 : 4); $[\alpha]_D^{20}$ + 209.5 (c 1.1, $CHCl_3$); m.p. 128-129°C (isopropylether); ^1H ($CDCl_3$) δ: 2.45 (s,3H,$ArCH_3$), 3.00 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.24 (dq,1H,CH_bS,$^4J_{H-F}$ = 1.5 Hz), 3.72 (dq,1H,CH_aCl,$^2J_{H-H}$ = 12.5, $^4J_{H-F}$ = 0.5 Hz), 3.78(d,1H,CH_bCl), 5.93 (s,1H,OH), 7.30-7.60 (m,4H,ArH); ^{19}F: - 78.5.

Synthesis of (4S,R$_S$)-4-hydroxy-5-[(4-methylphenyl)sulphinyl]-4-(trifluoromethyl)-pent-1-ene (12d). A solution of epoxide **5d** (722 mg, 2.73 mmol) in 2 ml anhydrous THF was added dropwise at -40°C into a solution of vinylmagnesium chloride (356 mg, 4.1 mmol) dissolved in 4 ml of the same solvent under nitrogen atmosphere. After 30 min., an excess of aqueous ammonium chloride solution was added and the organic phases were extracted with ethyl acetate (3x30 ml). The collected organic layers were dried with anhydrous sodium sulphate and evaporated under reduced pressure. The oily residue was purified by flash chromatography in n-hexane/ethyl acetate 3 : 1 to give two main products: (2S)-**12d** in 4.0% yield: R_F 0.33; $[\alpha]_D^{20}$ + 117.2 (c 0.7, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.45 (s,3H,$ArCH_3$), 2.40 (dd,1H,CH_aC=C,$^2J_{H-H}$ = 15.0,$^3J_{H-H}$ = 6.5 Hz), 2.66 (dd,1H,CH_bC=C), 2.78 (d,1H,CH_aS,$^2J_{H-H}$ = 15.0 Hz), 3.02 (dt,1H,CH_bS,$^4J_{H-F}$ = 0.4 Hz), 5.09-5.24 (m,2H,CH_2=C), 5.48 (s,1H,OH), 5.70-5.93 (m,1H,CH=C), 7.30-7.60 (m,4H,ArH); ^{19}F: - 72.6; and (2S)-**11d** in 54.8% yield whose ^1H and ^{19}F NMR spectra were superimposable to those described above.

Synthesis of (2S,R$_S$)-2-polihaloalkyl-3-[(4-methylphenyl)sulphinyl]-propan-1,2-diols (13b-e). General Procedure. A solution of oxirane (1.0 mmol), water (1.0 ml), perchloric acid (97% acqueous solution) (0.1 ml) in THF (2.0 ml) was kept at room temperature for 3 days. THF was removed under reduced pressure and the residue was extracted with chloroform (3x1.0 ml). After usual work-up, purification by flash chromatography gave: from (2S)-**5b** (chloroform/ethyl acetate 6 : 4; R_F 0.40), (2S)-**13b** in 90% yield: ^1H ($CDCl_3$) δ: 2.43 (s,3H,$ArCH_3$), 2.97 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.19 (dd,1H,CH_bS,$^4J_{H-F}$ = 1.2 Hz), 3.38 (dd,1H,CH_2OH,$^3J_{H-O-H}$ = 7.7,$^3J_{H-O-H}$ = 7.0 Hz), 3.73 (ddd,1H,CH_aO,$^2J_{H-H}$ = 12.6,$^3J_{H-O-H}$ = 7.7,$^4J_{H-F}$ = 2.1 Hz), 3.87 (ddt,1H,CH_bO,$^3J_{H-O-H}$ = 7.0,$^4J_{H-F}$ = 1.5 Hz), 4.72 (brs,1H,OH), 5.83 (dd,1H,CHF,$^2J_{H-F}$ = 54.6, $^2J_{H-F}$ = 56.0 Hz), 7.30-7.60 (m,4H,ArH); ^{19}F: - 136.8 (dd,1F,CHF_a,$^2J_{F-F}$ = 210.0,$^2J_{F-H}$ = 56.0 Hz), - 132.0 (dd,1F,CHF_b,$^2J_{F-H}$ = 54.6 Hz); from (2S)-**5c** (chloroform/ethyl acetate 5 : 5; R_F 0.37), (2S)-**13c** in 91.3% yield: $[\alpha]_D^{20}$ + 92.2 (c 0.5, $CHCl_3$); m.p. 97-98°C (isopropylether); $C_{11}H_{13}ClF_2O_3S$ calcd: C 44.22, H 4.36; found: C 44.12, H 4.32; ^1H ($CDCl_3$) δ: 2.44 (s,3H,$ArCH_3$), 3.08 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.29 (d,1H, CH_bS), 3.92 (dd,1H,CH_aO,$^2J_{H-H}$ = 12.5,$^3J_{H-O-H}$ = 8.0 Hz), 3.98 (dd,1H,CH_bO,$^3J_{H-O-H}$ = 7.0 Hz), 4.52 (dd,1H,OH,$^3J_{H-O-H}$ = 8.0,$^3J_{H-O-H}$ = 7.0 Hz), 5.18 (s,1H,OH), 7.30-7.60 (m,4H,ArH); ^{19}F: - 66.4; from (2S)-**5d** (chloroform/ethyl acetate 5 : 5; R_F 0.42), (2S)-**13d** in 87.3% yield: $[\alpha]_D^{20}$ + 180.4 (c 0.8, $CHCl_3$); m.p. 116-117°C (isopropylether); $C_{11}H_{13}F_3O_3S$ calcd: C 46.81, H 4.61; found: C 46.16, H 4.71; ^1H ($CDCl_3$) δ: 2.41 (s,3H,$ArCH_3$), 2.98 (d,1H,CH_aS,$^2J_{H-H}$ = 13.75 Hz), 3.24 (d,1H,CH_bS), 3 88 (d,2H,CH_2OH,$^3J_{H-O-H}$ = 7.5 Hz), 4.30 (t,1H,OH,$^3J_{H-O-H}$ = 7.5 Hz), 5.10 (brs,1H,OH), 7.30-7.60 (m,4H,ArH); ^{19}F: - 81.2.

Synthesis of (2S,R_S)-1-(benzyloxy)-2-{[(4-methylphenyl)sulphinyl]methyl}-3,3,3-trifluoro-propan-2-ol (14d). To a suspention of sodium hydride (50% mineral oil, 100 mg, 2.24 mmol) in THF (3.0 ml) a solution of (2S)-**13d** (420 mg, 1.49 mmol) and benzylbromide (0.5 ml, 4.47 mmol) in DMF (3.0 ml) was added dropwise. Reaction mixture was stirred 10 min at room temperature, then poured into an ice/water bath and extracted with ethyl ether (3x6 ml). After usual work-up, purification by flash chromatography (chloroform/ethyl acetate 8 : 1) gave (2S)-**14d** in 75.8% isolated yield: R_F 0.42; $[\alpha]_D^{20}$ + 31.2 (c 1.3, $CHCl_3$); m.p. 110-112°C (isopropylether); M^+ 372 (372); ^1H ($CDCl_3$) δ: 2.42 (s,3H,$ArCH_3$), 3.01 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.10 (dq,1H,CH_bS,$^4J_{H-F}$ = 1.0 Hz), 3.65 (dq,1H,CH_aO,$^2J_{H-H}$ = 10.5,$^4J_{H-F}$ = 1.0 Hz), 3.88(dd,1H,CH_bO), 4.59 (s,2H,$C\underline{H}_2OH$), 5.21 (s,1H,OH), 7.20-7.58 (m,4H,ArH); ^{19}F: - 79.3.

Synthesis of (2S)-2-(benzyloxymethyl)-2-(polihalomethyl) oxiranes (18b-e). General Procedure. To a stirred solution of (2S,R_S)-**5b-e** oxiranes (1.0 mmol) and *syn*-collidine (1.2 mmol) in acetonitrile (4.0 ml) stirred under nitrogen at - 20°C, was added dropwise a solution of trifluoroacetic anhydride (1.2 mmol) in the same solvent (2.0 ml). Reaction mixture was warmed up to room temperature and, after 20 min at the same temperature, a suspension of mercuric chloride (1.5 mmol) in acetonitrile (2.0 ml) was added portionwise. White mercuric sulfide precipitated and the reaction was left under stirring for 30 min. Then, HgS was removed by filtration and the clear collected yellow solution was cooled at 0°C. A suspension of sodium boro hydride (1.1 mmol) in acetonitrile (2.0 ml) was added portionwise. Metallic mercury precipitated and was removed by filtration, solvent was removed under reduced pressure and the residue was purified by flash chromatography. The so obtained alcohols **17b-e** were not isolated, but the clear acetonitrile solutions obtained after removal of Hg(0) were added with benzylbromide (10.0 mmol) and dropped into a cooled (0°C) suspension of NaH (1.5 mmol) in anhydrous THF (6.0 ml). After complete evaluation of gas, the reaction mixture was poured into an ice/water bath, extracted with ethyl ether (3x10.0 ml) and worked-up as usual. Flash chromatography purifications allowed the obtainment of: (2S)-2-(benzyloxymethyl)-2-(difluoromethyl) oxirane **18b** in 70% yield, R_F 0.25 (n-pentane / ethyl ether 96 : 4), $[\alpha]_D^{20}$ + 3.2 (c 1.6, $CHCl_3$); $C_{11}H_{12}F_2O_2$ calcd: C 61.68, H 5.61; found: C 61.50, H 5.70; ^1H ($CDCl_3$) δ: 2.91 (dt,1H,CH_aO epox,$^2J_{H-H}$ = 4.95,$^4J_{H-F}$ = 2.5 Hz), 3.07 (d,1H,CH_bO epox), 3.73 (dd,1H,CH_aO,$^2J_{H-H}$ = 11.5,$^4J_{H-F}$ = 1.5 Hz), 3.85 (dd,1H,CH_bO,$^4J_{H-F}$ = 1.5 Hz), 4.58 (s,2H,$ArCH_2$), 5.87 (t,1H,CHF,$^2J_{H-F}$ = 55.0 Hz), 7.20-7.40 (m,4H,ArH); ^{19}F: - 131.25 (dd,1F,CF_aF,$^2J_{F-F}$ = 394.0,$^2J_{H-F}$ = 55.0 Hz), - 129.30 (ddd,1F,CF_bF,$^2J_{F-H}$ = 55.0,$^4J_{F-H}$ = 2.5 Hz); (2S)-2-(benzyloxymethyl)-2-(chlorodifluoromethyl) oxirane **18c** in 50% yield, R_F 0.20 (n-pentane / ethyl ether 95 : 5), $[\alpha]_D^{20}$ + 0.2 (c 0.5, $CHCl_3$); $C_{11}H_{11}ClF_2O_2$ calcd: C 53.12, H 4.42; found: C 53.20, H 4.41; ^1H ($CDCl_3$) δ: 3.71 (s,2H,CH_2O epox), 3.79 (dt,1H,CH_aO,$^2J_{H-H}$ = 10.0,$^4J_{H-F}$ = 1.0 Hz), 3.85 (dt,1H,CH_bO,$^4J_{H-F}$ = 1.0 Hz), 4.62 (s,2H,$ArCH_2$), 7.27-7.40 (m,4H,ArH); ^{19}F: - 63.3; (2S)-2-(benzyloxymethyl)-2-(trifluoromethyl) oxirane **18d** in 55% yield, R_F 0.35 (n-pentane/ethyl ether 98 : 2), $[\alpha]_D^{20}$ + 5.1 (c 1.6, $CHCl_3$), $[\alpha]_{365}^{20}$ + 20.6 (c 1.6, $CHCl_3$); $C_{11}H_{11}F_3O_2$ calcd: C 56.89, H 4.74; found: C 56.72, H 4.51; ^1H ($CDCl_3$) δ: 3.04 (dq,1H,CH_aO epox,$^2J_{H-H}$ = 5.25,$^4J_{H-F}$ = 1.5 Hz), 3.10 (d,1H,CH_bO epox), 3.84 (d,1H,CH_aO,$^2J_{H-H}$ = 12.0 Hz), 3.90 (d,1H,CH_bO), 4.58 (s,2H,$ArCH_2$), 7.20-7.40 (m,4H,ArH), ^{19}F: -76.8; (2S)-2-(benzyloxymethyl)-2-(pentafluoroethyl) oxirane **18e** in 40% yield, R_F 0.30 (n-pentane), $[\alpha]_D^{20}$ + 4.02 (c 0.7, $CHCl_3$), ^1H ($CDCl_3$) δ: 3.10 (brs,2H,CH_2O epox), 3.80 (d,1H,CH_aO,$^2J_{H-H}$ = 12.5), 3.94 (d,1H,CH_bO), 4.56 (s,2H,$ArCH_2$), 7.28-7.45 (m,4H,ArH); ^{19}F: - 124.9 (s,CF_2), - 83.2 (s,CF_3).

Synthesis of (2S)-2-(chlorodifluoromethyl)-2-{[(4-methylphenyl)sulphenyl]methyl} oxirane (19c). A solution of trifluoroacetic anhydride (0.74 ml, 5.35 mmol) in acetone (0.5 ml) was added dropwise to a stirred solution of oxirane **5d** (300 mg, 1.07 mmol) and sodium iodide (478 mg, 3.21 mmol) in acetone (3.0 ml) stirred under nitrogen at - 40°C. After 10 min, saturated solutions of sodium sulfite and sodium hydrogen carbonate were added dropwise up to pH 7. Acetone was removed under reduced pressure and the residue was extracted with ethyl ether (3x3 ml). After the usual work-up, the residue was purified by flash chromatography (n-hexane/ethyl ether 9 : 1) to give (2S)-**19c** in 92.8% yield: $[\alpha]_D^{20}$ - 16.4 (c 0.6, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.32 (s,3H,$ArCH_3$), 3.11 (d,1H,CH_aO,$^2J_{H-H}$ = 5.0 Hz), 3.17 (dt,1H,CH_bO,$^4J_{H-F}$ = 1.8 Hz), 3.44 (d,1H,CH_aS,$^2J_{H-H}$ = 15.5 Hz), 3.60 (d,1H,CH_bS), 7.05-7.30 (m,4H,ArH); ^{19}F: - 63.7 (d,1F,CF_a,$^2J_{F-F}$ = 170.0 Hz), - 63.0 (d, 1F,CF_b).

Synthesis of (2S)-2-{[(4-methylphenyl)sulphenyl]methyl}-2-(trifluoromethyl) oxirane (19d). Following the same procedure described above, starting from oxirane **5d**, (2S)-**19d** was obtained in 97.3% yield: $[\alpha]_D^{20}$ - 5.3 (c 1.4, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.31 (s,3H,$ArCH_3$), 3.04 (s,2H,CH_2O), 3.33 (d,1H,CH_aS,$^2J_{H-H}$ = 15.5 Hz), 3.49 (d,1H,CH_bS), 7.18-7.30 (m,4H,ArH); ^{19}F: - 76.7.

Synthesis of (2S)-1-(dibenzylamino)-2{-[(4-methylphenyl)sulphenyl]methyl}-3,3,3-trifluoro-propan-2-ol (20d). Following the same procedure described above, starting from (2S,R_S)-**9d**, the sulphenyl derivative (2S)-**20d** was obtained in 93.5% yield: R_F 0.35 (n-hexane/ethyl acetate 95 : 5); $[\alpha]_D^{20}$ - 26.5 (c 1.0, $CHCl_3$); ^1H ($CDCl_3$) δ: 2.34 (s,3H,$ArCH_3$), 3.03 (s,2H,CH_2N), 3.06 (d,1H,CH_aS,$^2J_{H-H}$ = 14.0 Hz), 3.18 (d,1H,CH_bS), 3.63 (d,2H,CH_aAr,$^2J_{H-H}$ = 13.5 Hz), 3.87 (d,2H,CH_bAr), 5.06 (brs,1H,OH), 7.15-7.35 (m,14H,ArH); ^{19}F: - 81.0.

Synthesis of (2S)-1-(dibenzylamino)-2-methyl-3,3,3-trifluoro-propan-2-ol (21d). To a stirred solution of (2S)-**20d** (497 mg, 1.12 mmol) in ethanol (5.0 ml) was added Ni Raney (3x500 mg) and the suspension was refluxed for 2 hours. Ni Raney was removed by filtration, ethanol was evaporated under reduced pressure and the residue was purified by flash chromatography (n-hexane/ethyl ether 95 : 5) to give (2S)-**21d** in 77.0% yield: R_F 0.15; $[\alpha]_D^{20}$ + 32.4 (c 1.0, $CHCl_3$); $C_{18}H_{20}NF_3O$ calcd: C 66.87, H 6.19, N 4.33; found: C 66.80, H 6.21, N 4.25; ^1H ($CDCl_3$) δ: 1.12 (q,3H,CH_3,$^4J_{H-F}$ = 1.0 Hz), 2.64 (dd,1H,CH_aN,$^2J_{H-H}$ = 14.75,$^4J_{H-F}$ = 1.0 Hz), 3.04 (d,1H,CH_bN), 3.60 (d,2H,CH_aAr,$^2J_{H-H}$ = 13.5 Hz), 3.83 (d,2H,CH_bAr), 4.32 (brs,1H,OH), 7.20-7.40 (m,10H,ArH); ^{19}F: - 82.9.

Synthesis of (2R)-3-(dibenzylamino)-2-hydroxy-2-(trifluoromethyl)-propanoic acid (24d). From (2S,R_S)-**9d** (267 mg, 0.6 mmol) after removal of HgS by filtration, the clear yellow solution was cooled to 0°C, added with *tert.*butanol (4.0 ml) and 2-methyl-but-2-ene (3.5 ml) and kept under stirring at the same temperature. A solution of $NaClO_2$ (350 mg, 3.8 mmol) and KH_2PO_4 (520 mg, 3.8 mmol) in water (4.0 ml) was added dropwise at the same temperature. An exothermic effect was observed. pH Was adjusted to 2 by addying some diluted hydrogen chloride and organic layers were extracted by ethyl acetate (3x10.0 ml). After the usual work-up, the residue was purified by flash chromatography (chloroform/ethyl acetate/acetic acid 5 : 5 : 0.1) to give (2R)-**24d** in 68.4% yield: R_F 0.25 ; $[\alpha]_D^{20}$ + 2.4 (c 0.6, CH_3OH); M^+ 353 (353); $C_{18}H_{18}F_3NO_3$ calcd: C 61.19, H 5.10, N 3.97; found: C 61.12, H 5.02, N 3.90; ^1H (CH_3OH) δ: 3.08 (d,1H,CH_aN,$^2J_{H-H}$ = 14.0 Hz),

3.30 (d,1H,CH_bN), 3.73 (d,2H,CH_aAr,$^2J_{H-H}$ = 11.0 Hz), 3.88 (d,2H,CH_bAr), 4.98 (brs,2H,COOH,OH); ^{19}F: - 74.4.

Synthesis of (2R)-3-(benzyloxy)-2-hydroxy-2-(trifluoromethyl)-propanoic acid (25d). Starting from (2S,R_S)-**14d** and following the same procedure described above, the α,β-dihydroxy acid (2R)-**25d** was obtained in 72.5% yield: RF 0.35 (chloroform/ethyl acetate/acetic acid 8 : 2 : 0.1); $[\alpha]_D^{20}$+ 14.2 (c 0.3, CH_3OH / CH_3COCH_3 1 : 1); m.p. 270-272°C (dec.); M^+ 264 (264); $C_{11}H_{11}F_3O_4$ calcd: C 50.00, H 4.17; found: C 49.80, H 4.16; ^1H (CH_3OH) δ: 3.83 (d,1H,CH_aO,$^2J_{H-H}$ = 9.8 Hz), 3.95 (d,1H,CH_bO), 4.57 (d,1H,CH_aAr,$^2J_{H-H}$ = 11.9 Hz), 4.61 (d,2H,CH_bAr), 4.97 (brs,2H,COOH,OH); ^{19}F: - 74.7.

Synthesis of (2R)-2-(chlorodifluoromethyl)-3-(dibenzylamino)-2-hydroxy-propan-1-ol (26c). Following the same experimental procedure described for the synthesis of **17b-e**, after purification of the crude by flash chromatography (n-hexane/ethyl ether 7 : 3), (2R)-**26c** was obtained in 78.6% yield: R_F 0.35; $[\alpha]_D^{20}$ + 47.0 (c 1.1, $CHCl_3$); $C_{18}H_{20}ClF_2NO_2$ calcd: C 60.76, H 5.62, N 3.94; found: C 60.70, H 5.60, N 3.92; ^1H ($CDCl_3$) δ: 1.40-1.80 (brs,1H,OH), 3.02 (d,1H,CH_aN,$^2J_{H-H}$ = 16.0 Hz), 3.21 (d,1H,CH_bN), 3.45 (d,1H,CH_aO,$^2J_{H-H}$ = 14.0 Hz), 3.50 (d,2H,CH_aAr,$^2J_{H-H}$ = 13.0 Hz), 3.52 (d,1H,CH_bO), 3.53 (s,1H,OH), 3.91 (d,2H,CH_bAr), 7.10-7.50 (m,10H,ArH); ^{19}F: - 65.0 (d,1F,$^2J_{F-F}$ = 14.0 Hz), - 64.5 (d,1F).

Synthesis of (2R)-1-(dibenzylamino)-2-hydroxy-2-(trifluoromethyl)-propan-3-ol (26d). Starting from (2S,R_S)-**9d** and following the same procedure described above, (2R)-**26d** was obtained in 72.3% yield: R_F 0.35 (n-hexane/ethyl ether 6 : 4); $[\alpha]_D^{20}$ + 15.9 (c 0.5, $CHCl_3$); $C_{18}H_{20}F_3NO_2$ calcd: C 63.72, H 5.90, N 4.13; found: C 63.70, H 5.86, N 4.20; ^1H ($CDCl_3$) δ: 1.50-1.80 (brs,1H,OH), 2.96 (d,1H,CH_aN,$^2J_{H-H}$ = 14.5 Hz), 3.06 (d,1H,CH_bN), 3.27 (d,1H,CH_aO,$^2J_{H-H}$ = 11.5 Hz), 3.58 (d,1H,CH_bO), 3.54 (d,2H,CH_aAr,$^2J_{H-H}$ = 13.0 Hz), 3.80 (s,1H,OH), 3.98 (d,2H,CH_bAr), 7.25-7.40 (m,10H,ArH); ^{19}F: - 81.0.

Acknowledgment. *National Research Council (C.N.R.) - Progetto Chimica Fine and National Committee for Technologies are gratefully acknowledged for the financial support and for the visiting fellowship to dr. Vadim Soloshonok of Ukrainian Academy of Sciences. Dr. Giovanni Fronza and Dr. Roberta Silvia Rolla are gratefully acknowledged for ^1H and ^{19}F NMR assistance.*

References and Notes

1. Crossley, R.; *Tetrahedron* **1992**, *48*, 8155-8178.
2. a) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha Ltd.: Tokyo, 1981. b) Welch, J.T.; Esvarakrisnan, S. *Fluorine in Bioorganic Chemistry*; John Whiley and Sons, Inc.: New York, 1991.
3. Neidleman,S.L.; Geigert, J. *Biohalogenation: Principles, Basic Roles and Applications;* Horwood, Eds.; John Wiley and Sons, Inc., New York, 1986.
4. Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1320-1367.
5. a) Bravo, P.; Piovosi, E.; Resnati, G. *Synthesis* **1986**, 579-582; b) Bravo, P.; Resnati, G. *Tetrahedron Asymmetry* **1990**, 661-692.

6. a) Bravo, P.; Piovosi, E.; Resnati, G. *J. Chem. Res. (S)* **1989**, 134-135; *(M)* **1989**, 1115-1147; b) Posner, G.H. Asymmetric Synthesis Using α-Sulphinyl Carbanions and β-Unsaturated Sulphoxides.. In *The Chemistry of Sulphone and Sulphoxides;* Patai, S.; Rappoport, A.; Stirling, C. Eds.; John Wiley and Sons, Inc.: New York, 1988; pp.823-849.
7. a) Fujisawa, T.; Fujimura, A.; Ukaji, Y. *Chem. Lett.* **1988**, 1541-1544. b) Carreno, M.C.; Gareia Ruano, J.R.; Maestro, M.C.; Gonzales, M.P.; Bueno, A.B.; Fischer, J. *Tetrahedron*, **1993**, *49*, 11009-110018.
8. For a preliminary report on monofluoro derivatives: Arnone, A.; Bravo, P.; Cavicchio, G.; Frigerio, M.; Marchetti, V.; Viani, F.; Zappalà, C. *Tetrahedron Lett.* **1992**, *33*, 5609-5612.
9. Bravo, P.; Piovosi, E.; Resnati, G. *Synthesis Commun.* **1986**, *7*, 579-582.
10. Bravo, P.; Piovosi, E.; Resnati, G. *Gazz. Chim. Ital.* **1988**, *118*, 115-122.
11. For some reviews on the subject: a) Cowell, G.W.; and Ledwith, A. *Q. Rev., Chem. Soc.* **1970**, *24*, 119-145; b) Wulfman, D.S.; Linstrumelle, G.; Cooper, C.F. Synthetic Application of Diazoalkanes, Diazocyclopentadienes, and Diazoazacyclopentadienes. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S. Eds.; John Wiley and Sons, Inc.: New York, 1978; pp. 821-976; c) Gutsche, C.D. *Org. React. (N. Y.)* **1954**, *8*, 364-429; d) Pizey, J.S. *Synthetic Reagents*; Horwood, E.; Chichester, T. Eds. **1974**, *2*, 65-142.
12. Stereochemistry at C-2 on compounds **5b**, **5c** and **5e** was attributed through NMR correlations and optical rotatory power value comparisons on their biologically interesting compounds (see: Bravo, P.; Frigerio, M.; Soloshonok, V.; Viani, F. *Tetrahedron Lett.* **1993**, *48*, 7771-7772.) supported by X-ray analyses (results to be published).
13. a) Bravo, P.; Resnati, G. *Tetrahedron Lett.* **1987**, *28*, 4865-4866. b) Bravo, P.; Resnati, G. in *Perspectives in the Organic Chemistry of Sulphur* Zwanenburg, B.; Klunder, A.J.M., Eds.; Elsevier, Amsterdam, 1987; pp.89-90.
14. a) Stirling, C.J.M. *Chem. Rev.* **1978**, *78*, 517-567; b) Stirling, C.J.M. *Acc. Chem. Res.* **1979**, *12*, 198-203.
15. a) Palmer, R.J.; Stirling, C.J.M. *J. Am. Chem. Soc.* **1980**, *102*, 7888-7892; b) Tanikawa, R.; Hosoya, K.; and Kaji, A. *J. Chem. Soc., Chem. Commun.* **1986**, 836-837.
16. Horner, L.; Kaiser,P. *Justus Liebigs Ann. Chem.* **1959**, *626*, 19-25.
17. Drabowicz, J.; Oae, S. *Synthesis* **1977**, *6*, 404-405.
18. Allen, F.M.; Kennard, O.; Watson, D.G.; Btammer, L.; Orpen, A.G.; Taylor, R. *J. Chem. Soc. Perkin Trans. II*, **1987**, S1-S19.
19. a) Bravo, P.; Cavicchio, G.; Fabrizi, G.; Frigerio, M.; Fronza; Lamba, D.; Soloshonok, V.; Viani, F. *J. Can. Chem.* **1994** , in press; b) De la Champ, U.; Hope, H. *Acta Cryst.* **1970**, *B26*, 846-853; c) Hua, D.H.; Badejo, I.; McCann, P.J.; Takusagawa, F. *Acta Cryst.*, **1984**, *C43*, 1112-1116; d) Robinson, D.H.; Shan Chen, J.; Saha, S. *Acta Cryst.*, **1991**, 594-596; e) Hamdouchi, C. *Tetrahedron Lett.*, **1992**, *33*, 1701-1704; f) Fabrizi, G.; Fedeli, W.; Lamba, D. *Acta Cryst.*, **1992**, *C48*, 1131-1133.
20. The (Z) isomery was established by omo- and eteronuclear NOE experiments.
21. Altomare, A.; Burla, M.C.; Camalli, M.; Cascarano, G.; Giacovazzo, G.; Guagliardi, A.; Polidori, G. *J. Appl. Cryst.* **1994**, in preparation.
22. Sheldrick, G.M. *J. Appl. Cryst.* **1994**, in preparation.
23. Flack, H.D. *Acta Cryst.* **1983**, *A 39*, 876-880.

(*Received* 23 *March* 1994)