Homochiral Fluoro-organic Compounds. Part 12.[1] α-Hydroxy β-Fluoro Aldehydes and Esters, Fluoro Epoxides and Glycols from Fluorinated Sulphinyl Chirons

Pierfrancesco Bravo, Elena Piovosi, and Giuseppe Resnati
CNR-Centro di Studio per le Sostanze Organiche Naturali, Dipartimento di Chimica, Politecnico, Piazza Leonardo da Vinci 32, I-20133, Milano, Italy

α-Fluoro α′-sulphinyl ketones carrying an α′-alkyl or α′-aryl substituent have been reduced with high 1,2- or 1,3-induced diastereoselectivity to give the corresponding α-fluoro α′-sulphinyl secondary alcohols. The chiral sulphinyl auxiliary agent was removed first by selective reduction to a thio group, then by methylation to a sulphonium ion and finally through S_N2 removal by the adjacent secondary alcohol. It is therefore possible to obtain, in an optically pure form, α-fluoro epoxides which are chiral at both the carbon atoms of the oxirane ring, or at the α-fluorinated carbon and at the adjacent oxirane carbon. Furthermore, homochiral α-fluorinated vicinal glycols, β-fluoro α-hydroxy aldehydes, and β-fluoro α-hydroxy esters, which may contain the fluorohydrin moiety with *syn* or *anti* relative stereochemistry, have been obtained in an optically pure form from the corresponding α-fluoro α′-sulphinyl secondary alcohols by use of the varied reactivity of the sulphinyl group.

Until recently the synthesis of selectively fluorinated chiral and non-racemic compounds had been realized exclusively by fluorinating a complex intermediate in an advanced stage of the synthetic sequence.[2] Examples of this strategy include the stereospecific replacement of an hydroxy group with a fluorine atom in a sugar molecule,[2,3] the regiospecific α-fluorination of a carbonyl group,[4] and the stereocontrolled opening of an epoxide ring to give a fluorohydrin.[2,5] The alternative method, which is to build up the framework of chiral carbon atoms and functional groups around a fluorinated key-building block, has been investigated only in recent years. This is mainly because simple fluorinated synthons have been described only recently, and few diastereoselective transformations on low fluorinated substrates have been reported until now.[6]

Of the trifluoromethyl substituted compounds, 3-trifluoromethylbutyrolactone has been transformed into amino acids and vitamin D_3 analogues[7] and 3-hydroxy-4,4,4-trifluorobutyrate has been transformed into γ- and δ-lactones,[8] epoxides,[9] 1,3-amino alcohols, and 1,3-diols.[10] This last trifluorobutyrate was obtained through baker's yeast reduction[11] of the corresponding ketone. Similar enzymatic approaches,[12] or the enzymatic resolution of racemic mixtures[13] were used to prepare several other interesting trifluoromethyl substituted compounds. Very few examples exist of the total synthesis of geminally difluorinated compounds;[14] the preparation of these products is exemplified by the preparation of difluoromethylene sugars through the condensation of methyl iododifluoroacetate[15] or bromodifluoroalkynes[16] on glyceraldehyde acetonide. The enzymatic resolution of racemic mixtures[17] allowed the preparation of both the enantiomers of ethyl 2-fluoro-2-methyl hydrogen malonate[18] which was transformed into several monofluorinated β-keto[19] and β-hydroxy[20] esters or other more complex compounds containing an amine residue.[20b]

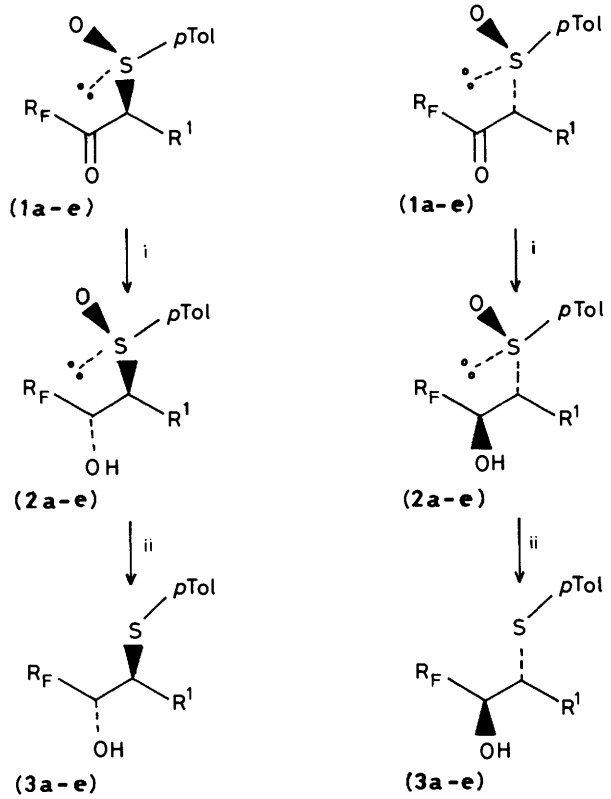
We are, at present, studying the chemistry of some optically pure α-fluoro α′-sulphinyl ketones to be used as chiral fluorinated synthons.[21] In order to extend the diversity of products available from the α-fluoro α′-sulphinyl moiety, we have studied the reduction of the carbonyl group of some of these substrates substituted at the sulphinylated stereocentre. Here we report how this reduction can be realized with good diastereoselection, under control of the chirality of the carbon stereocentre, when di-isobutylaluminium hydride (DIBAH) is used in the presence of a chelating metal. The removal of the auxiliary sulphinyl group from the alcohols so obtained allowed the preparation of some fluorinated and sulphur-free epoxides in optically pure form. By using different conditions for the removal of the auxiliary agent, some enantiomerically and diastereoisomerically pure α-hydroxy β-fluoro alcohols, aldehydes, and esters have also been synthesized.

Results and Discussion

The starting homochiral α-fluoro α′-sulphinyl ketones (**1a—e**) were prepared, in good yields, by alkylation of the monosodium derivative of α-fluoro-α′-sulphinylacetone with alkyl halides or through condensation of the lithium derivative of the appropriate (+)-(*R*)-alkyl *p*-tolyl sulphoxide on the esters of some easily available fluorocarboxylic acids[22] as already described.

Reduction of α-Fluoro-α′-sulphinyl-α′-alkyl Ketones.—Reduction of the carbonyl group of β-keto sulphoxides unsubstituted at the α-carbon has been extensively studied and it has been found that the chirality at sulphur can give rise to high diastereocontrol.[23] In contrast, very few cases of α-substituted compounds have been reported.[24]

A solution of (1*R*,R_S)-3-fluoro-1-phenyl-1-(*p*-tolylsulphinyl)-propan-2-one (**1b**) in tetrahydrofuran (THF) when treated with DIBAH (1.0M in hexane) at −78 °C, gave the corresponding (1*R*,2*S*,R_S)-3-fluoro-1-phenyl-1-(*p*-tolylsulphinyl)propan-2-ol (**2b**) in nearly quantitative yield (Scheme 1). In contrast, under the same reaction conditions, the (1*S*,R_S)-diastereoisomer (**1b**) gave in quantitative yield a mixture (*ca.* 1:1) of the (1*S*,2*S*,R_S)- and (1*S*,2*R*,R_S)-alcohols (**2b**). Much higher diastereoselection was obtained by adding zinc(II) chloride to a solution of the substrates in THF before treatment with DIBAH. In fact, when both (1*S*,R_S)-(**1b**) and (1*R*,R_S)-(**1b**) were reduced under the latter reaction conditions, the alcohols (1*S*,2*R*,R_S)-(**2b**) and (1*R*,2*S*,R_S)-(**2b**) were obtained with a diastereoselectivity >96%. Similarly, (3*S*)-1-fluoro-3(*R*)-(*p*-tolylsulphinyl)butan-2-one (**1c**) gave nearly exclusively the (2*R*,3*S*)-1-fluoro-3(*R*)-(*p*-tolylsulphinyl)butan-2-ol (**2c**) (d.e. ≥97%). The two α′-alkenyl substituted α-fluoro α′-sulphinyl ketones (3*R*,R_S)- and the



	R_F	R^1
a	C_3F_7	Ph
b	CH_2F	Ph
c	CH_2F	Me
d	CH_2F	$CH_2CH{=}CMe_2$
e	CH_2F	$CH_2CH_2CH{=}CH_2$

Scheme 1. *Reagents and conditions:* i, $ZnCl_2$, DIBAH (hexane), THF, −78 °C; ii, NaI, $(CF_3CO)_2O$, acetone, −40 °C

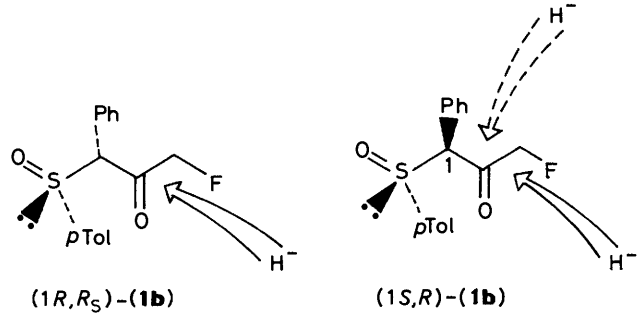


Figure 1. Ground-state conformation of α′sulphinyl ketones (**1b**)

$(3S,R_S)$-(**1d,e**) afforded the corresponding alcohols $(2S,3R,R_S)$- and $(2R,3S,R_S)$-(**2d,e**) in nearly quantitative yield but with lower diastereoselection (d.e. ⩾80%).[25] These stereochemical results can be rationalized in terms of a reaction conformation similar to that already used to explain the reduction and the Michael addition of other similar substrates. In this conformation the C–O and S–O bond dipoles were directed away from each other[26] (Figure 1). In $(1R,R_S)$-(**1b**) both the *p*-tolyl group on the sulphinyl residue and the phenyl ring on the carbon stereocentre encumber the *Si* face of the carbonyl group so that the alcohol $(1R,2S,R_S)$-(**2b**) is formed exclusively through approach of the hydride from the *Re* face. In $(1S,R_S)$-(**1b**) the *p*-tolyl group again

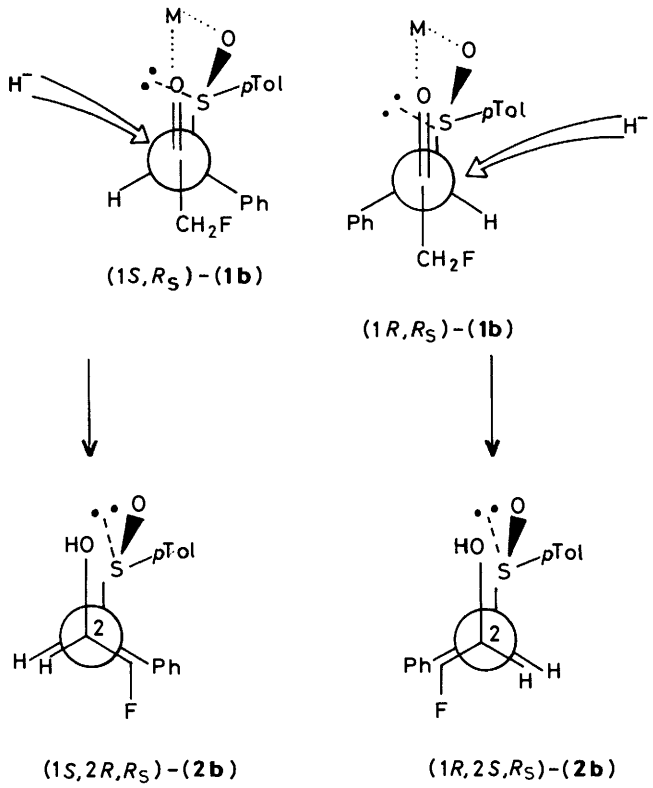


Figure 2. Stereochemical course of the reduction of α-substituted-β-oxo sulphoxides (**1b**) with DIBAH in the presence of a chelating metal

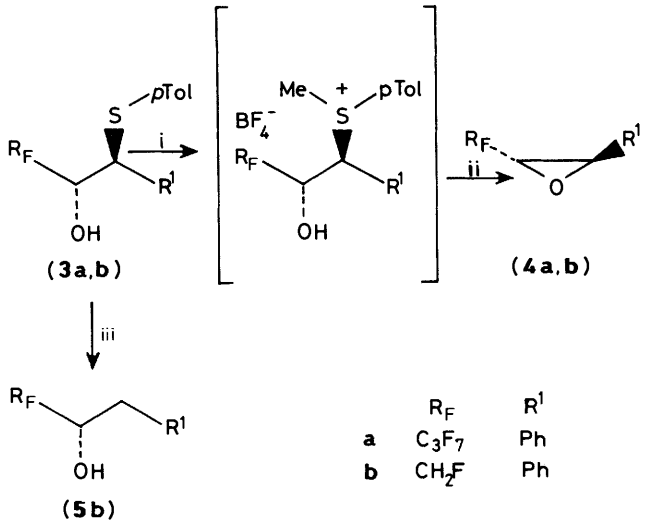
hinders the *Si* face of the carbonyl, but the phenyl ring on C-1 hinders the *Re* face. As a result of these opposing effects the hydride attacks the carbonyl group from both sides and the alcohols $(1S,2R,R_S)$- and $(1S,2S,R_S)$-(**2b**) are formed in comparable amounts.

In the presence of zinc(II) chloride the β-keto sulphoxide entity is expected to chelate the metal[26d,27] and in the resulting conformation the *p*-tolyl group is directed away from the reaction centre. In this conformation, hydride ion approaches the carbonyl face opposite to that hindered by the substituent on the carbon stereocentre (Figure 2). The diastereoselectivity of the reduction by DIBAH now depends only on the stereochemistry of the substituted α-carbon (1,2-asymmetric induction).

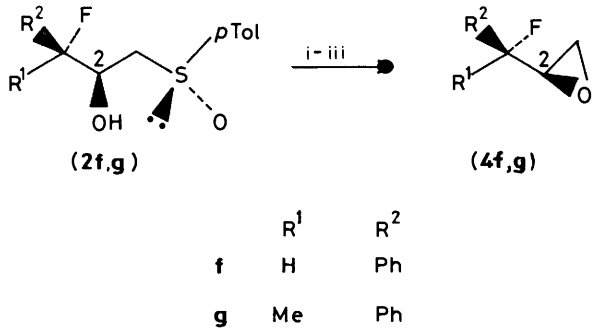
It is interesting to note that on β-keto sulphoxides unsubstituted at the α-position the diastereoselectivity of the DIBAH reduction is controlled by the chirality of the sulphur atom[23,26] (1,3-asymmetric induction) both in the presence and in the absence of a chelating metal. For these substrates the two different reduction conditions afford alcohols having opposite absolute configurations.[21,26d,27a]

Synthesis of Homochiral Fluorinated Epoxides and Alcohols.—The simplest replacement of the auxiliary sulphinyl group in compounds (**2**), that by an hydrogen atom,[21,27b,28] was effected by initial deoxygenation of the sulphinyl sulphur (sodium iodide, trifluoroacetic anhydride)[29] followed by hydrogenolysis (Nickel-Raney) of the α-sulphenyl alcohols (**3**) so obtained.[30] In this manner (2*S*)-1-fluoro-3-phenylpropan-2-ol (**5b**) was obtained in 71% overall yield from (**2b**) and in enantiomerically pure form[31] (Scheme 2).

A more interesting transformation of the α-sulphenyl alcohols (**3**) involves the formation of a sulphonium salt, through methylation with trimethyloxonium tetrafluoroborate, and the



Scheme 2. *Reagents and conditions:* i, Me_3OBF_4, THF; ii, NaH, THF; Raney-Nickel (W-2), EtOH, heat



Scheme 3. *Reagents and conditions:* i, NaI, $(CF_3CO)_2O$, acetone, −40 °C; ii, Me_3OBF_4, THF; iii, NaH, THF

successive intramolecular nucleophilic substitution of the sulphonium residue by the action of the α-hydroxy group in a one-pot reaction.[26d,32,33] Thus, (1*S*,2*R*)-3,3,4,4,5,5,5-heptafluoro-1-phenyl-1-(*p*-tolylthio)pentan-2-ol (**3a**) and (1*S*,2*R*)-3-fluoro-1-phenyl-1-(*p*-tolylthio)propan-2-ol (**3b**) afforded the (1*R*,2*S*)-3,3,4,4,5,5,5-heptafluoro-1-phenyl-1,2-epoxypentane (**4a**) and the (1*R*,2*S*)-1-phenyl-3-fluoro-1,2-epoxypropane (**4b**) in 73 and 81% yields respectively. Removal of the auxiliary thio group in this manner preserved the carbon stereocentres present in the sulphinyl alcohols (**2**) in the final epoxides (**4**).[26d,32]

The *trans* relative stereochemistry of the two hydrogen atoms on the oxirane ring of the epoxides (**4a,b**) was assigned from the value of the coupling constant of the protons on the epoxide ring ($^3J_{H,H}$ = 1.9 Hz) and from the clear positive n.O.e. effect on the phenyl ring when the C-2 hydrogen was saturated (see Experimental section).

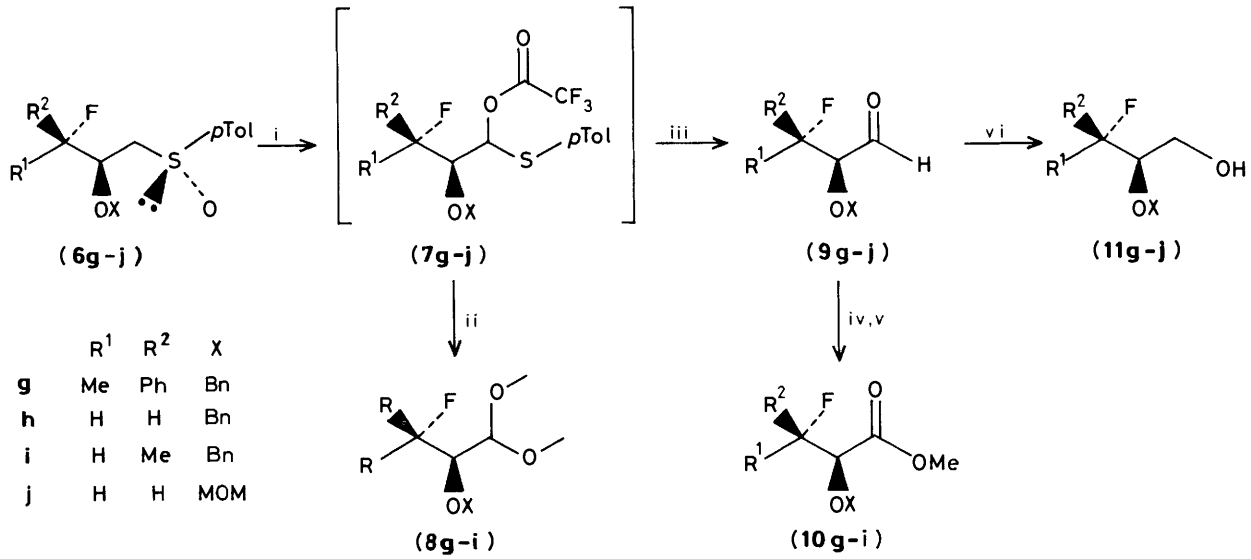
The same procedure was performed with some α-fluoro α′-sulphinyl alcohols with a chiral fluorinated stereocentre. (2*S*,3*R*)-3-Fluoro-3-phenyl-1-(*p*-tolylthio)propan-2-ol (**2f**) afforded (2*R*,3*R*)-3-fluoro-3-phenyl-1,2-epoxypropane (**4f**) in 76% yield and the 3-fluoro-3-phenyl-1-(*p*-tolylthio)butan-2-ols (**2g**), with both (2*S*,3*R*) and (2*S*,3*S*) configurations, gave (2*R*,3*R*)- and (2*R*,3*S*)-3-fluoro-3-phenyl-1,2-epoxybutanes (**4g**) respectively (Scheme 3).

The absolute configuration at the hydroxy carbon of compounds (**3**), and the related products (**2**), (**4**), and (**5**), was assigned through the chemical shift differences of external diastereotopic protons in the ^{1}H n.m.r. spectra of their esters with (*R*)- and (*S*)-2-phenylpropionic acids as already described.[24c,25,34,35] The two diastereoisomeric β-hydroxy sulphoxides (**2**) reported in Scheme 1 [which were the main reduction products of β-oxosulphoxides (**1**) when a chelating metal was used] were shown to have the same relative configuration at the adjacent carbon stereocentres because on deoxygenation of the sulphinyl group, the enantiomeric β-hydroxy sulphides (**3**) were obtained in all cases. The *anti* relative stereochemistry for (**2a,b**) follows from the configuration established for the corresponding epoxide derivatives (**4**) and for (**2d,e**) from the configuration assigned to some corresponding tetrahydropyran derivatives described elsewhere.[25,31] The relative configuration of (**2c**) was assigned on the assumption that a unique stereochemical course was operating in the reduction of the carbonyl precursors (**1**) when the same reaction conditions were employed. Some similarities in optical rotations and ^{1}H n.m.r. data were also considered.

Synthesis of Homochiral α-Hydroxy β-Fluoro Alcohols, Aldehydes, and Esters.—The Pummerer rearrangement is a well known method for the removal of a sulphinyl group[36] and it has already been employed for the synthesis of complex chiral compounds such as sugars and aminoacids.[37] In a preceding paper[21] we showed how this rearrangement can be used to transform α-fluoro α′-sulphinyl ketones into α-fluoro α′-hydroxy ketones and α-oxo β-fluoro aldehydes. A successful application to the transformation of β-alkoxy γ-fluoro sulphoxides (**6**) into the corresponding α-alkoxy β-fluoro alcohols, aldehydes, and esters (**11**), (**8**), and (**10**) has now been achieved.

Treatment of (2*S*,R_S)-2-benzyloxy-3-fluoro-1-(*p*-tolylsulphinyl)propane (**6h**) with sodium acetate in refluxing acetic anhydride gave the corresponding (2*S*)-1-acetoxy-2-benzyloxy-3-fluoro-1-(*p*-tolylthio)propane in moderate yields. In contrast, when trifluoroacetic anhydride and 2,4,6-trimethylpyridine were used,[38] much milder reaction conditions sufficed, and the trifluoroacetoxythio intermediate (**7h**) formed in nearly quantitative yields (Scheme 4). These reaction conditions were also compatible with acid-labile hydroxy-protecting groups and the methoxymethyl protected substrate (**6j**) underwent smoothly the desired rearrangement to the intermediate (**7j**). The trifluoroacetoxythio compound (**7h**), obtained as described above, was not isolated but subjected to solvolysis *in situ* to give compounds containing either a free formyl group or its acetal. Treatment of (*S*)-(**7h**) with mercury(II) chloride in methanol solution at room temperature gave the dimethyl acetal of (*R*)-2-benzyloxy-3-fluoropropanal (**8h**), whereas use of aqueous mercury salt yielded the benzyl protected 3-fluorolactic aldehyde (*R*)-(**9h**). Reduction of the formyl group (with sodium borohydride) afforded the (*R*)-3-fluoropropane-1,2-diol (**11h**) in 78% overall yield. Oxidation of the fluorolactic aldehyde (**9h**) (with sodium chlorite),[39] followed by methylation (diazomethane) of the acid formed gave the (*R*)-methyl O-benzyl-3-fluorolactate (**10h**) in 79% yield. The ^{1}H n.m.r. spectra of (**11h**) and (**10h**) in the presence of tris[3-(heptafluoropropylhydroxymethylene)camphorato]europium(III) [Eu(hfc)$_3$] showed that no loss of optical purity at the hydroxylated carbon stereocentre had occurred during the synthetic sequence from (**6h**).

Starting from the diastereoisomerically and enantiomerically pure 2-benzyloxy 3-fluorosulphoxides (**6g,i**), employment of the reaction conditions described above allowed us to isolate the dimethyl acetals of (2*R*,3*S*)-2-benzyloxy-3-fluoro-3-phenylbutanal (**8g**) and (2*R*,3*S*)-2-benzyloxy-3-fluorobutanal (**8i**) [following methanolysis of the primary products (**7g,i**) from the Pummerer rearrangement]. Alternatively, the same intermediates (**7g,i,j**) were hydrolysed with water and the aldehydes (**9**) formed either oxidized or reduced. The α-alkoxy β-fluoroalcohols (**11g,i,j**) or the α-benzyloxy β-fluoro esters (**10g,i**)



	R^1	R^2	X
g	Me	Ph	Bn
h	H	H	Bn
i	H	Me	Bn
j	H	H	MOM

Scheme 4. *Reagents and conditions:* i, $(CF_3CO)_2O$, 2,4,6-trimethylpyridine, MeCN; ii, $HgCl_2$, MeOH; iii, $HgCl_2$, H_2O; iv, $NaClO_2$, Bu^{t}OH, 2-methylbut-1-ene, KH_2PO_4; v, CH_2N_2, Et_2O; vi, $NaBH_4$, MeCN, Pr^{i}OH

were prepared as enantiomerically and diastereoisomerically pure compounds.

The absolute configurations of the final sulphur-free compounds (**8**), (**10**), and (**11**) follows from those of the sulphinylated precursors (**6**). The absolute configuration at the hydroxylated stereocentre of these products was assigned through the chemical shift differences in the ^{1}H n.m.r. spectra of esters with (*S*)- and (*R*)-2-phenylpropionic acid.[24c,25,34,35] The absolute configuration at the fluorinated stereocentre derived from spectroscopic determinations of the relative stereochemistry of the fluorohydrin moiety as already described.[34]

Conclusions

The reduction of the fluorinated α-alkyl or α-aryl substituted β-oxo sulphoxides (**1**) to the corresponding secondary alcohols (**2**) has been studied, and reasonable to high diastereoselection has been achieved. The chirality and the degree of diastereoselection may be determined either by the chirality of the carbon atom (1,2-induction) or of the sulphur atom (1,3-induction), depending on the reaction conditions chosen (addition of DIBAH to a chelated or to a free β-oxo sulphoxide). The presence of the optically pure sulphinyl auxiliary group allowed us to obtain single diastereoisomers of the secondary alcohols in optically pure form in all the cases examined. Transformation of the sulphinyl group into a sulphonium group followed by S_N2 displacement by the adjacent secondary alcohol gave the corresponding homochiral α-fluoro epoxides (**4**) in high yields. Reduction of the sulphoxide to a sulphide and replacement by hydrogen gave the corresponding fluorohydrins (**5**) while the Pummerer rearrangement followed by reductive, hydrolytic, or oxidative work-up, gave the corresponding homochiral α-alkoxy β-fluoro alcohols (**11**), β-fluoro α-benzyloxy aldehydes (**8**), and esters (**10**), respectively. All of the functionalized fluorinated compounds (**4**), (**5**), (**8**), (**10**), and (**11**) have been obtained in optically pure form. The enantiomers of the final sulphur-free fluorinated compounds can be constructed easily because both enantiomers of the fluoro sulphinyl chirons used can be prepared starting from the commercially available (−)- and (+)-menthol.[22]

Experimental

I.r. spectra were recorded on a Perkin-Elmer 177 Infracord spectrophotometer; ^{1}H and ^{13}C n.m.r. spectra were recorded with a Bruker CPX-300, Bruker AC 250, or a Varian EM 390 spectrometer using tetramethylsilane as internal standard and $CDCl_3$ as solvent. ^{19}F N.m.r. spectra were recorded in $CDCl_3$ on a Bruker WP 80 SY instrument (75.39 MHz); δ_F values are p.p.m. upfield from $CFCl_3$ and C_6F_6 was used as internal standard ($\delta_F = -162.9$). $[\alpha]_D$ Values were obtained on a Jasco DIP-181 polarimeter. Mass spectra were registered on an Hitachi–Perkin-Elmer RMU 6D or on a VGMM ZAB 2F instrument. M.p.s are uncorrected and were obtained on a capillary apparatus. T.l.c. was performed on silica gel 60 F_{254} Merck and column chromatography was performed with silica gel (63—200 μm, Merck). Reactions with lithium derivatives and with DIBAH were carried out under an argon atmosphere free from oxygen and water; THF was freshly distilled from lithium aluminium hydride; di-isopropylamine was distilled from calcium hydride and stored over molecular sieves (4 Å); DMF was stored over 4 Å and 13 Å molecular sieves. A 2.6M solution of butyl-lithium in hexane (Aldrich) and a 1.0M solution of DIBAH in hexane (Fluka) were employed. In other cases, commercially available reagent-grade solvents were employed without purification.

Reduction of (1R,R_S)-3-*Fluoro*-1-*phenyl*-1-(p-*tolylsulphinyl*)-*propan*-2-*one* (**1b**) *with* DIBAH.—A solution of DIBAH in hexane (1M; 10.75 ml) was dropped with stirring at −78 °C into a solution of (1*R*,R_S)-3-fluoro-1-phenyl-1-(*p*-tolylsulphinyl)-propan-2-one (**1b**) (2.20 g, 7.5 mmol) in THF (22.5 ml). After 20 min at the same temperature an excess of saturated aqueous sodium hydrogen carbonate was added, the mixture was vigorously stirred for 15 min, then the pH was adjusted to *ca.* 4 with hydrochloric acid (1M). The aqueous layer was extracted with methylene dichloride (3 × 150 ml), the collected organic phases were dried over anhydrous sodium sulphate and the solvent was removed under reduced pressure. Flash chromatography afforded pure (1*R*,2*S*,R_S)-3-fluoro-1-phenyl-1-(*p*-tolylsulphinyl)propan-2-ol (**2b**) (2.0 g; 91%). The presence of the (1*R*,2*R*,R_S)-diastereoisomer (**2b**) could not be detected using ^{19}F n.m.r. spectroscopy.

(1*R*,2*S*,R_S)-(**2b**), R_F(diethyl ether–chloroform, 1:2), 0.33; m.p. 152—153 °C (ethyl acetate); $[\alpha]_D^{20}$ −184° (*c* 0.44 in $CHCl_3$) (Found: C, 65.6; H, 6.05; S, 10.9. $C_{16}H_{17}FO_2S$ requires C, 65.73; H, 5.86; S, 10.97%); δ_H(300 MHz) 3.77 (1 H, d, CHS, $J_{H,H}$ 2.7 Hz), and 4.0—4.5 (3 H, m, CH_2FCHO); δ_F(75 MHz) −227.7.

Reduction of (1*S*,R_S)-(**1b**) under the same reaction conditions afforded in 93% yield a 1:1 mixture of (1*S*,2*R*,R_S)-(**2b**) and (1*S*,2*S*,R_S)-(**2b**).

(1*S*,2*R*,R_S)-(**2b**): R_F(diethyl ether–chloroform, 1:2), 0.38; m.p. 166—168 °C (ethyl acetate); $[\alpha]_D^{20}$ +358° (*c* 0.30 in $CHCl_3$) (Found: C, 65.85; H, 5.8; S, 10.8. $C_{16}H_{17}FO_2S$ requires C, 65.73; H, 5.86; S, 10.97%); δ_H(300 MHz) 3.71 (1 H, d, CHS, $^3J_{H,H}$ 6.5 Hz), and 4.4—4.8 (3 H, m, CH_2FCHO); δ_F(75 MHz) −232.9.

(1*S*,2*S*,R_S)-(**2b**), R_F(diethyl ether–chloroform, 1:2), 0.28; m.p. 170—171 °C (ethyl acetate); $[\alpha]_D^{20}$ +341° (*c* 0.50 in $CHCl_3$) (Found: C, 65.95; H, 6.05; S, 10.85. $C_{16}H_{17}FO_2S$ requires C, 65.73; H, 5.86; S, 10.97%); δ_H(300 MHz) 3.80 (1 H, d, CHS, $^3J_{H,H}$ 9.5 Hz), 4.1—4.5 (2 H, m, CH_2F), and 4.78 (1 H, m, CHO); δ_F(75 MHz) −234.3.

Reduction of α-Fluoro α′-Sulphinyl α′-Substituted Ketones (**1b—e**) *with* DIBAH *and* $ZnCl_2$.—A suspension of the α-fluoro α′-sulphinyl α′-substituted ketone (**1**) (7.0 mmol) and $ZnCl_2$ (0.95 g, 7.0 mmol) in THF was stirred at room temperature for 20 min, after which the mixture was cooled at −78 °C and DIBAH (1.0M solution in hexane; 9.1 ml, 9.1 mmol) was added dropwise with stirring. After 20 min at room temperature, the reaction mixture was quenched and worked-up as described above. In the reduction of (1*R*,R_S)-(**1b**), the alcohol (1*R*,2*S*,R_S)-(**2b**) was formed in 92% yield, none of the diastereoisomer (1*R*,2*R*,R_S)-(**2b**) being detected in the crude reaction mixture (h.p.l.c. and ^{19}F n.m.r. analyses); in the reduction of (1*S*,R_S)-(**1b**), the alcohols (1*S*,2*R*,R_S)-(**2b**) and (1*S*,2*S*,R_S)-(**2b**) were formed in 90% yield and in a ratio of 96:4. Under similar reaction conditions, the reduction of (3*S*,R_S)-1-fluoro-3-(*p*-tolylsulphinyl)butan-2-one (**1c**) afforded exclusively (2*R*,3*S*,R_S)-1-fluoro-3-(*p*-tolylsulphinyl)butan-2-ol (**2c**) in 94% yield (d.e. ≥97%): R_F(hexane–ethyl acetate), 0.35; m.p. 57—59 °C (ethyl acetate–hexane); $[\alpha]_D^{20}$ +202° (*c* 0.48 in $CHCl_3$) (Found: C, 57.6; H, 6.4; S, 13.75. $C_{11}H_{15}FO_2S$ requires C, 57.37; H, 6.56; S, 13.92%); δ_H(250 MHz) 1.08 (3 H, d, CH_3), 2.80 (1 H, m, CHS), and 4.3—4.7 (3 H, m, CH_2FCHO). Reduction with DIBAH–$ZnCl_2$ of a 65:35 mixture of the two epimers at the carbon site of (R_S)-1-fluoro-6-methyl-3-(*p*-tolylsulphinyl)hept-5-en-2-one (**1d**) afforded in 94% yield the diastereoisomeric (R_S)-1-fluoro-6-methyl-3-(*p*-tolylsulphinyl)hept-5-en-2-ols (**2d**) with (2*R*,3*S*), (2*S*,3*R*), (2*S*,3*S*), and (2*R*,3*R*) in a 62:30:3:5 ratio. Flash chromatography (hexane–ethyl acetate, 6:4) furnished the pure diastereoisomers.

(2*R*,3*S*,R_S)-(**2d**): m.p. 55—57 °C (diethyl ether–pentane) (Found: C, 63.3; H, 7.4; S, 11.1. $C_{15}H_{21}FO_2S$ requires C, 63.35; H, 7.44; S, 11.27%); $[\alpha]_D^{20}$ +115° (*c* 0.84 in $CHCl_3$); δ_H(300 MHz) 4.85 (1 H, m, =CH), 4.64 and 4.48 (2 H, m, CH_2F), 1.57 and 1.48 (6 H, brs, 2 × Me), 2.44 and 2.25 (2 H, m, CH_2CS), 2.76 (1 H, m, CHS), and 4.48 (1 H, m, CHO); δ_C(63 MHz; $CDCl_3$) 141.50, 137.80, 129.88, 124.50, and 21.39 (tolyl), 134.75 (=C), 120.28 (=CH), 84.52 (C–F, $J_{C,F}$ 169.2 Hz), 69.71 (C–O, $J_{C,F}$ 21.3 Hz), 66.00 (C–S, $J_{C,F}$ 5.6 Hz), 25.67 and 17.67 (2 × Me), and 19.62 (CH_2).

(2*S*,3*R*,R_S)-(**2d**): $[\alpha]_D^{20}$ +149° (*c* 1.40 in $CHCl_3$) (Found: C, 63.5; H, 7.3. $C_{15}H_{21}FO_2S$ requires C, 63.35; H, 7.44%); δ_H(300 MHz) 1.70 and 1.76 (6 H, brs, 2 × Me), 2.51 (1 H, m, CHS), 2.63 and 2.80 (2 H, m, CH_2CS), 4.15 and 4.25 (2 H, m, CH_2F), 4.35 (1 H, m, CHO), and 5.23 (1 H, m, =CH).

(2*S*,3*S*,R_S)-(**2d**): $[\alpha]_D^{20}$ +101° (*c* 1.25 in $CHCl_3$) (Found: C, 63.25; H, 7.35; S, 11.3. $C_{15}H_{21}FO_2S$ requires C, 63.35; H, 7.44; S, 11.27%); δ_H(300 MHz) 1.49 and 1.64 (6 H, brs, 2 × Me), 2.01 and 2.38 (2 H, m, CH_2CS), 2.95 (1 H, m, CHS), 4.18 (1 H, m, CHO), 4.53 and 4.63 (2 H, m, CH_2F), and 4.96 (1 H, m, =CH).

Reduction with DIBAH–$ZnCl_2$ of a 65:35 mixture of the two epimers at the carbon stereocentre of (R_S)-1-fluoro-3-(*p*-tolylsulphinyl)hept-6-en-2-one (**1e**) afforded the (R_S)-1-fluoro-3-(*p*-tolylsulphinyl)hept-6-en-2-ols (**2e**) with (2*R*,3*S*), (2*S*,3*R*), (2*S*,3*S*), and (2*R*,3*R*) absolute configurations in a 55:38:4:3 ratio.

(2*R*,3*S*,R_S)-(**2e**): R_F(hexane–ethyl acetate, 70:35), 0.30; m.p. 37—38 °C (from diethyl ether); $[\alpha]_D^{20}$ +111° (*c* 1.0 in $CHCl_3$) (Found: C, 62.4; H, 7.12; S, 11.65. $C_{14}H_{19}FO_2S$ requires C, 62.19; H, 7.08; S, 11.86%); δ_H(300 MHz) 1.6—1.9 (4 H, m, 2 × CH_2), 2.75 (1 H, m, CHS), 4.47 (1 H, m, CHO), 4.50 and 4.64 (2 H, m, CH_2F), 4.82 and 4.89 (2 H, each brd, *J* 16.7 and 10.0 Hz, $=CH_2$), and 5.48 (1 H, m, =CH).

(2*S*,3*R*,R_S)-(**2e**): R_F(hexane–ethyl acetate, 70:35), 0.36; m.p. 88—89 °C (from ethyl acetate–hexane); $[\alpha]_D^{20}$ +236° (*c* 1.05 in $CHCl_3$) (Found: C, 62.3; H, 7.25; S, 11.7. $C_{14}H_{19}FO_2S$ requires C, 62.19; H, 7.08; S, 11.86%); δ_H(300 MHz) 1.9—2.5 (4 H, m, 2 × CH_2), 2.50 (1 H, m, CHS), 4.1—4.5 (3 H, m, CH_2F, CHO), 5.10 and 5.12 (2 H, m, $=CH_2$), and 5.78 (1 H, m, =CH).

(2*S*,3*S*,R_S)-(**2e**): R_F(hexane–ethyl acetate, 70:35), 0.18; $[\alpha]_D^{20}$ +148° (*c* 1.0 in $CHCl_3$) (Found: C, 62.1; H, 7.2; S, 11.7. $C_{14}H_{19}FO_2S$ requires C, 62.19; H, 7.08; S, 11.86%); δ_H(300 MHz) 1.51 (2 H, m, CH_2), 1.88 and 2.04 (2 H, m, $C=CH_2$), 2.92 (1 H, m, CHS), 4.15 (1 H, m, CHO), 4.55 and 4.66 (2 H, each ddd, *J* 47.0, 10.0, 4.4, and 47.5, 10.0, 4.6 Hz, CH_2F), 4.90 (2 H, m, $=CH_2$), and 5.50 (1 H, m, =CH).

Deoxygenation of the Sulphinyl Residues of the α-Fluoro α′-Sulphinyl Alcohols (**2**).—Trifluoroacetic anhydride (2.47 ml, 17.50 mmol) in acetone (3.5 ml) was dropped into a stirred suspension of the α′-sulphinyl alcohol (**2**) (3.50 mmol) and sodium iodide (1.57 g, 10.5 mmol) in acetone (25 ml) at −40 °C under an argon atmosphere. The reaction mixture was stirred for 20 min after which an excess of saturated aqueous sodium sulphite and sodium hydrogen carbonate were added. Acetone was removed under reduced pressure, the aqueous layer was extracted with diethyl ether (3 × 100 ml), and the combined organic phases were dried (Na_2SO_4). The residue was dissolved in THF (30 ml) and sodium hydroxide (1M; 9.5 ml) was added with stirring. After 30 min at room temperature dilute hydrochloric acid was added until pH 3 was reached; the organic products were then extracted with ether (3 × 100 ml). The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure to give the α-fluoro α′-thio alcohols (**3**). Yields, physical, and selected spectral data have been already reported.[24c,25,34]

Synthesis of the Epoxides (**4**).—Trimethyloxonium tetrafluoroborate (0.78 g, 5.25 mmol) was added at −20 °C to a stirred solution of the α-fluoro α′-thio alcohol (**3**) (3.50 mmol) in THF (7.0 ml) under an argon atmosphere. The mixture was stirred at room temperature for 90 min after which a suspension of oil-free sodium hydride (55% mineral oil dispersion; 229 mg, 5.25 mmol) in the same solvent was added dropwise at −40 °C. The temperature was raised to 20 °C and after 10 min the mixture was poured into an excess of saturated aqueous ammonium chloride. The organic products were extracted with ether (3 × 50 ml) and the combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude products which were chromatographed (hexane–diethyl ether) to give the desired epoxide (**4**) as a single diastereoisomer in enantiomerically pure form.

Starting from (1*S*,2*R*)-(**3a**) (1*R*,2*S*)-3,3,4,4,5,5,5-heptafluoro-1-phenyl-1,2-epoxypentane (**4a**) was obtained in 73% yield as a yellowish oil, R_F(pentane), 0.36; $[\alpha]_D^{20}$ +20.9° (*c* 1.0 in $CHCl_3$) (Found: C, 45.95; H, 2.35. $C_{11}H_7F_7O$ requires C, 45.84; H, 2.45%); δ_H(250 MHz) 3.50 (1 H, m, $CHCF_2$, $^3J_{1\text{-}H,2\text{-}H}$ 1.9 Hz; $^3J_{H,F}$ 9.0, 10.0 Hz; $^4J_{H,F}$ 4.5, 4.5 Hz) and 4.18 (1 H, m, C*H*Ph); δ_F(75 MHz) −81.9 (3 F, t, CF_3), −125.6, −129.2 (2 F each, m each, CF_2CF_2). N.O.e. experiments: in a degassed acetone

Table. Yields, physical and selected spectral data of compounds (**4**), (**8**), (**10**), and (11); R^1R^2FC–CHYOX

Compound	R^1	R^2	X	Y	Yields (%)[a]	$[\alpha]_D^{20}$ (*c* in $CHCl_3$/ mol dm^{-3})	^{19}F N.m.r.[b] δ_F	^{19}F N.m.r.[b] $^3J_{2\text{-H.F}}$	^1H N.m.r.[c] R^1 ($^3J_{R.F}$)	^1H N.m.r.[c] R^2 ($^3J_{R.F}$)	^1H N.m.r.[c] 2-H	^1H N.m.r.[c] X	^1H N.m.r.[c] Y
(2*R**,3*R**)-(**4f**)	*H*	Ph	CH_2		72	*d*	−189.7		5.59	7.35	3.57		2.85 (14.0, 7.0) 3.01 (5.5)
(2*R*,3*R*)-(**4g**)	Me	Ph	CH_2		78	+33.4 (1.5)	−154.3	11.2	1.63 (22.5)	7.4	3.30		2.70 (4.2) 2.82 (2.8)
(2*R*,3*S*)-(**4g**)	Ph	Me	CH_2		81	+54.6 (0.93)	−160.6	14.8	7.4	1.77 (22.5)	3.22		2.77 (10.4, 4.0) 2.87 (2.6)
(2*R*,3*S*)-(**8g**)	Ph	Me	$PhCH_2$	$CH(OMe)_2$	87	−25.5 (0.87)	−154.2	14.0	7.2—7.4	1.74 (23.5)	3.64	4.40, 4.75	4.30 ($^4J_{H.F}$ = 1.0), 3.22, 3.47
(*R*)-(**8h**)	H	H	$PhCH_2$	$CH(OMe)_2$	81	−24.1 (0.98)	−207.9	22.0	4.6		3.67	4.73, 7.4	4.38 ($^4J_{H.F}$ = 0.8), 3.43, 3.45
(2*R*,3*S*)-(**8i**)	Me	H	$PhCH_2$	$CH(OMe)_2$	80	−11.3 (1.1)	−155.9	14.0	1.38 (25.2)	4.86 (46.0)	3.77	4.75, 7.35	4.25 ($^4J_{H.F}$ = 0.8), 3.40, 3.43
(2*R*,3*S*)-(**10g**)	Ph	Me	$PhCH_2$	CO_2Me	77	−45.3 (1.1)	−154.5	10.5	7.2—7.4	1.80 (23.5)	4.12	4.29, 4.62	3.73
(*R*)-(**10h**)	H	H	$PhCH_2$	CO_2Me	73	−94.5 (1.0)	−118.8	23.0	4.69 (47.0)		4.23	4.60, 4.85	3.80
(2*R*,3*S*)-(**10i**)	Me	H	$PhCH_2$	CO_2Me	79	−80.9 (1.1)	−153.2	12.0	1.40 (24.5)	4.92 (46.0)	4.13	4.55, 4.75	3.78
(2*R*,3*R*)-(**11g**)[e]	Me	Ph	$PhCH_2$	CH_2OH	81	+10.9 (1.0)	−146.3	14.0	1.81 (24.0)	7.43	3.79	4.69, 4.83	3.47
(2*R*,3*S*)-(**11g**)[f]	Ph	Me	$PhCH_2$	CH_2OH	83	−14.9 (1.0)	−155.3	*g*	7.4	1.76 (24.0)	3.70	4.53	3.70
(*R*)-(**11h**)	H	H	$PhCH_2$	CH_2OH	71	−15.3 (1.0)	−231.1	*g*	4.53 (47.0)		3.70	4.64, 4.74, 7.4	3.70
(2*R*,3*S*)-(**11i**)	Me	H	$PhCH_2$	CH_2OH	78	−13.3 (0.95)	−180.8		1.41 (25.0)	4.74 (47.0)	3.7	4.64, 4.73, 7.4	3.6
(**11j**)	H	H	CH_2OMe	CH_2OH	73	*d*	−198.0	16.5	4.52 (47.0)		3.95	3.48, 4.80	3.71

[a] Correct microanalyses (C ±0.21, H ±0.19, S ±0.14) or exact mass spectra were obtained. [b] ^{19}F N.m.r. (75 MHz; solvent $CDCl_3$; standard C_6F_6; δ_F values in p.p.m.; *J*/Hz). [c] ^1H N.m.r. (250 MHz; solvent $CDCl_3$; standard TMS; δ_H values in p.p.m.; *J*/Hz). [d] The reaction was performed on a racemic sample of the precursor (**2f**). [e] M.p. (hexane–Et_2O) 59—61 °C. [f] M.p. (pentane–Et_2O) 37—38 °C. [g] The value could not be obtained since a second order spectrum was obtained.

solution irradiation of $CHCF_2$ caused a 1% enhancement of the Ph signal; irradiation of the Ph signal caused a 4.9% enhancement of the $CHCF_2$ signal. Starting from (1*S**,2*R**)-(**3b**) (1*R**,2*S**)-1-phenyl-3-fluoro-1,2-epoxypropane (**4b**) was isolated in 81% yields as an oil, R_F(hexane–di-isopropyl ether, 9:1), 0.30 (Found: C, 71.15; H, 5.85. C_9H_9FO requires C, 71.04; H, 5.96%); δ_H(300 MHz) 3.32 (1 H, m, $CHCH_2F$, $^3J_{H.F}$ 13 Hz; $^3J_{1\text{-H,2-H}}$ 2.0 Hz), 3.86 (1 H, dd, $CHPh$), 4.50 (1 H, ddd, $^3J_{H.F}$ 47.5 Hz; $^2J_{H,H}$ 10.6 Hz; $J_{H.H}$ 5.2 Hz), and 4.74 (1 H, ddd, $^3J_{H,H}$ 2.7 Hz); δ_F(75 MHz) −200.5. N.O.e. experiments: in a degassed chloroform solution irradiation of the phenyl ring caused a 1.6—3.2% enhancement of the $CHCH_2F$ signal; irradiation of the $CHCH_2F$ signal caused a 0.6% enhancement of the Ph signal. Yields, physical and selected spectral data of the epoxides (2*R**,3*R**)-(**4f**), (2*R*,3*R*)-(**4g**), and (2*R*,3*S*)-(**4g**) are reported in the Table.

Dethiolation with Raney-Nickel of (1S,2R)-3-*Fluoro*-1-*phenylthiopropan*-2-*ol* (**3b**).—The thio substrate (**3b**) (1.8 mmol) was refluxed in ethanol (8 ml) for 15 min in the presence of Raney-Nickel (W-2, 0.6 g) and under an hydrogen atmosphere. The nickel was filtered off, washed with ether (×2) and the combined organic phases were evaporated. Flash chromatography of the residue (hexane–ethyl ether, 7:3) afforded pure (*S*)-1-fluoro-3-phenylpropan-2-ol (**5b**) in 77% yield as a white oil, $[\alpha]_D^{20}$ +28.2° (*c* 0.6 in $CHCl_3$) (Found: C, 70.25; H, 7.05. $C_9H_{11}FO$ requires C, 70.11; H, 7.19%); δ_H(300 MHz) 2.83 (2 H, m, CH_2Ph), 4.10 (1 H, m, CHO), 4.31 (1 H, m, CHF), and 4.47 (1 H, m, CHF); δ_F(75 MHz) −231.1.

Benzylation of α-*Fluoro* α′-*Sulphinyl Alcohols* (**2g—j**).—Benzyl bromide (0.95 ml, 8.0 mmol) in anhydrous dimethylformamide (DMF) (3.0 ml) was dropped at 0 °C to a stirred solution of the α-fluoro α′-sulphinyl alcohol (**2**) (4.0 mmol) and oil-free sodium hydride (6.0 mmol) in THF–DMF (1:1; 4.0 ml). After 1 h at room temperature, saturated aqueous ammonium chloride (10 ml) was added to the mixture which was then diluted with water (200 ml) and extracted with diethyl ether (3 × 50 ml). The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. The crude benzyl ether (**6**) from the starting α-fluoro α′-sulphinyl alcohol was 95% pure (^1H n.m.r.) and was used without further purification. An analytical sample was obtained through flash-chromatography (hexane–ethyl acetate).

(2*S*,3*S*,R_S)-2-Benzyloxy-3-fluoro-3-phenyl-1-(*p*-tolylsulphinyl)butane (**6g**): 93% yield; m.p. 136—137 °C (diethyl ether–pentane); $[\alpha]_D^{20}$ +180° (*c* 0.8 in $CHCl_3$) (Found: C, 72.8; H, 6.25; S, 8.0. $C_{24}H_{25}FO_2S$ requires C, 72.69; H, 6.35; S, 8.09%); δ_H(90 MHz) 1.73 (3 H, d, Me, $^3J_{H.F}$ 23 Hz), 2.92 (2 H, d, CH_2S), 4.3 (1 H, m, CHO), and 4.46 and 4.82 (2 H, AB system, CH_2Ph); δ_F(75 MHz) −154.8 ($^3J_{H\text{-}2,F}$ 14.2 Hz).

(2*S*,3*R*,R_S)-2-Benzyloxy-3-fluoro-3-phenyl-1-(*p*-tolylsulphinyl)butane (**6g**): 97% yield; m.p. 100—101 °C (diethyl ether–pentane); $[\alpha]_D^{20}$ +158° (*c* 1.3 in $CHCl_3$) (Found: C, 72.55; N, 6.55; S, 7.95. $C_{24}H_{25}FO_2S$ requires C, 72.69; H, 6.35; S, 8.09%); δ_H(90 MHz) 1.78 (3 H, d, Me, $^3J_{H.F}$ 22 Hz), 2.78 (2 H, m, CH_2S), 4.35 (1 H, m, CHO), and 4.57 and 4.83 (2 H, AB system, CH_2Ph); δ_F(75 MHz) −152.2 ($^3J_{H\text{-}2,F}$ 13.7 Hz).

(*S*)-2-Benzyloxy-3-fluoro-1-(R)-(*p*-tolylsulphinyl)propane

(**6h**): 91% yield; $[\alpha]_D^{20}$ +176° (*c* 1.6 in $CHCl_3$) (Found: C, 66.8; H, 6.4; S, 10.3. $C_{17}H_{19}FO_2S$ requires C, 66.64; H, 6.25; S, 10.46%); δ_H(90 MHz) 2.40 (3 H, s, CH_3), 2.95 (2 H, m, CH_2S), 4.2—4.9 (3 H, m, CH_2F, and CHO), and 4.77 (2 H, s, CH_2Ph).

(2*S*,3*S*,R_S)-2-Benzyloxy-3-fluoro-1-(*p*-tolylsulphinyl)butane (**6i**): 94% yield; m.p. 49—51 °C (hexane–ethyl acetate); $[\alpha]_D^{20}$ +174° (*c* 1.1 in $CHCl_3$); δ_H(90 MHz) 1.32 (3 H, dd, CH_3CF, $^3J_{H,F}$ 22 Hz), 2.9 (2 H, m, CH_2S), 4.23 (1 H, m, CHO), 4.77 (2 H, m, CHF), and 4.86 (2 H, s, CH_2Ph).

The Methoxymethyl Ether (**6j**) *from* 3-*Fluoro*-1-(p-*tolylsulphinyl*)*propan*-2-*ol*.—3-Fluoro-1-(*p*-tolylsulphinyl)propan-2-ol (5.0 g, 23.2 mmol) was magnetically stirred in chloroform–dimethoxymethane (1:1, 60 ml) in the presence of phosphoric anhydride (50.0 g) at 0 °C for 1 h. The organic phase was then poured into saturated aqueous sodium hydrogen carbonate (300 ml) and phosphoric anhydride was washed with chloroform (3 × 100 ml). The combined organic phases were washed with water (50 ml), dried (Na_2SO_4) and evaporated under reduced pressure. The oily residue which remained was the desired methoxymethyl ether (**6j**), formed in nearly pure form and in quantitative yield. An analytical sample was obtained using flash chromatography (hexane–ethyl acetate, 1:5) (Found: C, 55.5; H, 6.55; S, 12.25. $C_{12}H_{17}FO_3S$ requires C, 55.36; H, 6.58; S, 12.32%); δ_H(90 MHz) 2.95 (2 H, m, CH_2S), 3.51 (3 H, s, MeO), 4.1—4.7 (3 H, m, CH_2F and CHO), and 4.87 (2 H, s, OCH_2O).

Pummerer Rearrangement of the α-*Alkoxy* β-*Fluoro Sulphoxides* (**6g—j**) *to the Corresponding Aldehydes* (**9**).—*Acetic anhydride–sodium acetate method.* A solution of (2*S*)-(**6h**) (4.6 mmol) and sodium acetate (1.3 g, 15.85 mmol) were refluxed in acetic anhydride (20 ml) for 100 min under argon. Excess of acetic anhydride was removed under reduced pressure and the residue was dissolved in water (50 ml) and the solution extracted with ethyl acetate (3 × 80 ml). The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure and the residue was flash chromatographed (hexane–ethyl acetate, 9:1) to give (2*S*)-1-acetyloxy-2-benzyloxy-3-fluoro-1-*p*-tolylthio)propane (450 mg, 33%; 8:2 mixture of epimers at the sulphur-substituted carbon): δ_H(250 MHz) 2.03 and 2.04 (3 H, s each, MeCO), 3.93 (1 H, m, CHO), 4.67 (2 H, m, CH_2F), 4.72 (2 H, br s, CH_2Ph), and 6.25 and 6.28 (1 H, each d, OC*H*S).

Trifluoroacetic anhydride–2,4,6-*trimethylpyridine method.* A solution of trifluoroacetic anhydride (1.13 ml, 8.0 mmol) in acetonitrile (16 ml) was added dropwise, at 0 °C and under argon, to a stirred solution of the γ-fluoro sulphoxide (**6**) (2.0 mmol) and 2,4,6-trimethylpyridine (1.06 ml, 8.0 mmol) in the same solvent (40 ml). After 30 min at room temperature the starting compound had disappeared and the formation of a higher R_F product [probably the α-trifluoroacetyloxy β-alkoxy γ-fluoro thio derivative (**7**)] could be observed. A solution of mercury(II) chloride (0.76 g, 2.8 mmol) in water (15 ml) was added and the resulting mixture was stirred at room temperature for 2 h. The white precipitate formed was filtered off and washed with ethyl acetate (2 × 50 ml) and the filtrate was dried (Na_2SO_4) and evaporated under reduced pressure. The residue consisted of the crude hygroscopic α-alkoxy β-fluoro aldehyde (**9**). The simplest compound, *i.e.* 2-benzyloxy-3-fluoropropanal (**9h**), was examined using ^1H n.m.r. spectroscopy (250 MHz) and the signal for the aldehyde proton was clearly observed (δ 9.71, dd, *J* 3.0 Hz, 1.0 Hz). In all cases the crude aldehyde was used without further purification in the oxidation to the esters (**10**) and in the reduction to the alcohols (**11**).

Synthesis of the α-*Benzyloxy* β-*Fluoro Dimethyl Acetals* (**8g—i**).—To a solution of the crude α-trifluoroacetoxy β-alkoxy γ-fluoro thio derivative (**7**) (2.5 mmol; obtained as described above) was added a solution of mercury(II) chloride (0.95 g, 3.5 mmol) in methanol (5 ml). After being stirred for 2 h at room temperature the precipitate was filtered off and washed with ethyl acetate (3 × 20 ml) and the combined organic phases were evaporated under reduced pressure. The residue obtained was flash chromatographed (pentane–diethyl ether mixtures) to give the dimethyl acetals of the α-benzyloxy β-fluoro aldehydes (**8g—i**) in diastereoisomerically and enantiomerically pure form. Yields and physical and selected spectral data of the obtained compounds are reported in the Table.

Synthesis of the α-*Benzyloxy* β-*Fluorocarboxylic Esters* (**10g—i**).—To a solution of the crude α-benzyloxy β-fluoro aldehyde (**9**) [obtained as described above starting from β-benzyloxy γ-fluorosulphoxide (**6**) (4.5 mmol)] dissolved in t-butyl alcohol (50 ml) and 2-methylbut-1-ene (11 ml) was added slowly at room temperature a solution of sodium chlorite (1.42 g, 15.7 mmol) and potassium dihydrogen phosphate (1.93 g, 14.2 mmol) in water (17 ml). The mixture was stirred for 1 h after which it was evaporated under reduced pressure and the aqueous layer was extracted with diethyl ether. The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dissolved in ether (15 ml) and an ethereal solution of diazomethane was added dropwise at 0 °C until the light-yellow colour remained. A drop of acetic acid was added, solvent was removed under reduced pressure, and the residue was flash chromatographed (toluene–ethyl acetate mixtures) to give the pure α-benzyloxy β-fluoro carboxylic esters (**10**). Yields and physical and selected spectral data are reported in the Table.

Synthesis of the α-*Alkoxy* β-*Fluoro Alcohols* (**11g—j**).—To a solution of the crude α-alkoxy β-fluoro aldehyde (**9**) [obtained as described above starting from the β-alkoxy γ-fluoro sulphoxide (**6**) (2.5 mmol)] in acetonitrile–isopropyl alcohol (1:1, 6.0 ml), was added sodium borohydride in one portion (189 mg, 5.0 mmol) at 0 °C. The mixture was stirred at room temperature for 2.0 h after which hydrochloric acid (1M) was added dropwise at −20 °C until pH 2 was reached. Water was added (30 ml) to the mixture which was then evaporated under reduced pressure. The residue was extracted with ethyl acetate and the combined organic phases were dried (Na_2SO_4). The pure α-alkoxy β-fluoro alcohols (**11g—j**) were isolated through flash chromatography (hexane–diethyl ether or hexane–ethyl acetate mixtures). Yields and physical and selected spectral data are reported in the Table.

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