

Synthesis and use of (*E*)-1-ethoxy-3-fluoroalkyl-3-hydroxy-4-(4-methylphenylsulfinyl)but-1-enes

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Condensation of the lithium salt of (*R*)-methyl *p*-tolyl sulfoxide **1** with fluorinated α,β -unsaturated ketones **2** leads to (*3R/S,R_S*)-(*E*)-1-ethoxy-3-fluoroalkyl-3-hydroxy-4-(4-methylphenylsulfinyl)but-1-enes **3**, whose absolute stereochemistry was determined by X-ray diffraction and NMR analyses. Reductive removal of the sulfinyl chiral auxiliary allows the preparation of both enantiomers of fluorinated tertiary alcohols of type **8** and **9**.

The arylsulfinyl group is a versatile and flexible functionality that enjoys increasing popularity both as a temporary control element for chirality and as an activating group in organic synthesis.¹ This group, besides creating a chiral environment, stabilizes adjacent carbanions, which are useful in carbon-carbon bond-forming reactions, and can be removed reductively to give a hydrocarbon, or oxidatively through a Pummerer rearrangement² to give an oxygen-bearing functionality like a primary alcohol, an aldehyde or a carboxylic acid.

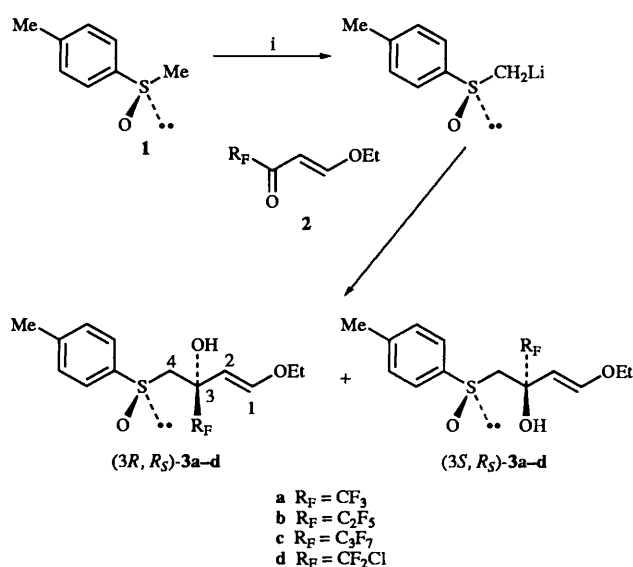
We are currently engaged in the search for new chiral fluorinated synthons, for use in asymmetric synthesis of selectively fluorinated molecules of biological significance:³ chiral aryl alkyl sulfoxides have been chosen as starting materials in order to introduce the sulfinyl sulfur as a chiral auxiliary.⁴

For the construction of a C-5 chiral synthon, useful for the introduction of a fluorinated terpene unit into complex molecules, we thought it would be of interest to study the coupling of the lithium salt of methyl *p*-tolyl sulfoxide **1** with (*E*)-4-ethoxy-1-polyfluoroalkylbut-3-en-2-ones **2** (Scheme 1). Nucleophiles generally add to α,β -unsaturated ketones in a 1,2- and 1,4-way; in the present case, as fluoro-substitution strongly activates carbonyl groups, a large prevalence for the 1,2-addition of the α -sulfinyl carbanion of **1** derived from methyl *p*-tolyl sulfoxide onto α,β -unsaturated ketones **2** would be expected.

Results and discussion

Fluorinated, α,β -unsaturated ketones **2** were prepared in high yields by acylation of ethyl vinyl ether with an appropriate fluorocarboxylic anhydride in the presence of pyridine.⁵ Subsequent treatment of ketones **2** with the lithium salt of (*R*)-methyl *p*-tolyl sulfoxide **1** in THF at -60°C gave a mixture of the two diastereoisomeric alcohols **3a-d** in good yields, which could easily be separated by flash column chromatography. The reaction showed to be poorly stereo- but totally regioselective, affording only tertiary alcohols, through a 1,2-addition of the α -sulfinyl carbanions onto the carbonyl double bond (Scheme 1).

The non-fluorinated analogue of **2**, (*E*)-4-methoxybut-3-en-2-one **4** and the lithium salt of (*R*)-methyl *p*-tolyl sulfoxide **1** gave a more complicated mixture of products (Scheme 2). ¹H and ¹³C NMR analysis of the obtained products showed that



Scheme 1 Reagents and conditions: i, LDA-THF, -78°C

both 1,2- and 1,4-addition had occurred (see Experimental Section). So, interestingly, the presence of the fluorinated moiety R_F induces the peculiar observed regioselectivity through a strong activation of the carbonyl group.

Diastereoisomeric alcohols **3a-d** were obtained in ratios ranging from *ca.* 1:1 to 1:2, in most cases as colourless, crystalline solids. Their structures rely upon analytical and spectroscopic data, mainly ¹⁹F and ¹H NMR, where the presence of two coupled vinyl hydrogens is a clear evidence of their nature as 1,2-addition products.

In order to establish the stereochemistry of compounds **3**, the crystal structure of one of the two (*E*)-3-(chlorodifluoromethyl)-1-ethoxy-3-hydroxy-4-(*p*-tolylsulfinyl)but-1-enes **3d** was determined by X-ray diffraction.

A view of the molecule, displaying the absolute configuration (3*R*, *R_S*), is shown in Fig. 1,† while selected molecular

† Note that the atomic labels adopted in the crystallographic study correspond to previously described sulfoxides,^{4b} to allow for meaningful comparisons.

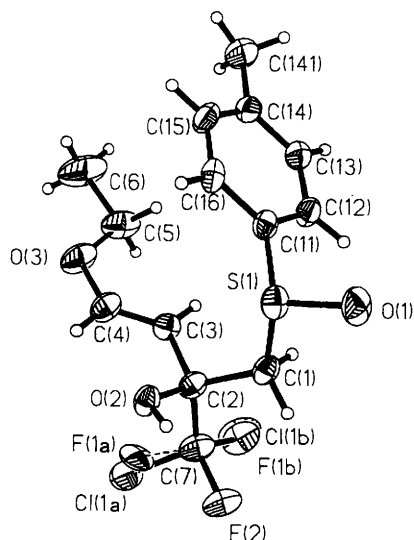
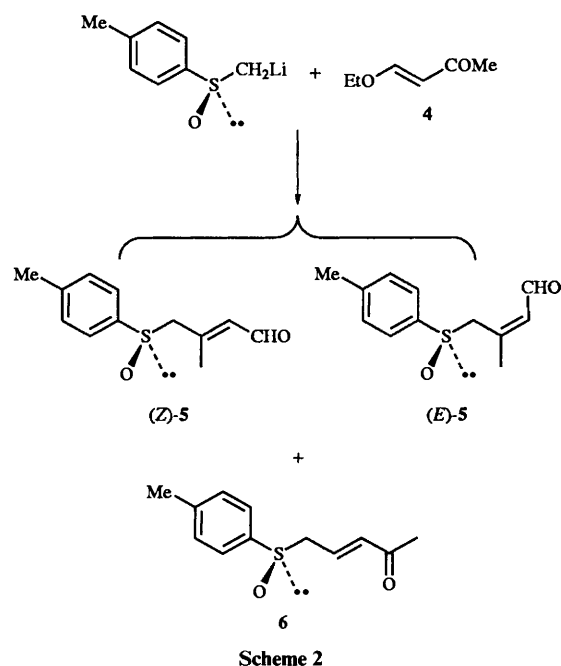


Fig. 1 ORTEP view of compound (3*R*,*R*₅)-3*d*

dimensions are reported in Table 1. Bond lengths and angles fall in the expected range.⁶ Compared with other *p*-tolyl sulfoxide derivatives,^{4b} the compound presents an unusual, folded conformation. This results from the torsion angle C(11)–S(1)–C(1)–C(2), *trans* in the most similar molecules, and in our case near to a *gauche* position (-79.1°). Furthermore, the two planes, defined respectively by the phenyl ring and by the C(2)–C(3)–C(4)–O(3)–C(5)–C(6) chain, form a relatively small angle (25°) and as a result a short non-bonded distance (3.2 \AA) is observed between the two sp^2 carbon atoms C(3) and C(11).

Another distinctive feature of compound (3*R*,*R*₅)-3*d* is the rotational disorder affecting the CF₂Cl group in the crystalline state as shown in Fig. 1. Two positions are shared by Cl and F, labelled in Fig. 1 as Cl(1a), F(1a) and Cl(1b), F(1b). The most satisfactory model was obtained with a hypothesis of a 60:40 statistical distribution of the chlorine atom in the two positions, 1a and 1b, respectively, with constrained values for bond distances C–Cl and C–F, and allowing anisotropic refinement of both atoms in both positions. Bond distances were $1.710(5)$

Table 1 Selected molecular dimensions of (3*R*,*R*₅)-3*d*

| | Bond lengths/ \AA |
|-----------------------|----------------------------|
| S(1)–O(1) | 1.500(3) |
| S(1)–C(11) | 1.784(4) |
| S(1)–C(1) | 1.812(4) |
| C(1)–C(2) | 1.525(6) |
| C(2)–C(3) | 1.514(5) |
| C(2)–C(7) | 1.553(6) |
| O(2)–C(2) | 1.411(5) |
| Cl(1a)–C(7) | 1.699(4) |
| F(1b)–C(7) | 1.357(5) |
| F(1a)–C(7) | 1.351(5) |
| Cl(1b)–C(7) | 1.707(5) |
| F(2)–C(7) | 1.352(5) |
| C(3)–C(4) | 1.311(6) |
| O(3)–C(4) | 1.351(5) |
| O(3)–C(5) | 1.430(7) |
| C(5)–C(6) | 1.526(7) |
| | Bond angles/ $^\circ$ |
| O(1)–S(1)–C(11) | 105.4(2) |
| O(1)–S(1)–C(1) | 102.7(2) |
| C(11)–S(1)–C(1) | 101.5(2) |
| C(2)–C(1)–S(1) | 115.6(3) |
| C(4)–C(3)–C(2) | 121.7(4) |
| C(3)–C(4)–O(3) | 127.6(5) |
| C(4)–O(3)–C(5) | 117.2(4) |
| C(3)–C(2)–C(1) | 111.5(3) |
| O(3)–C(5)–C(6) | 107.1(6) |
| | Torsion angles/ $^\circ$ |
| C(11)–S(1)–C(1)–C(2) | $-79.1(3)$ |
| C(1)–S(1)–C(11)–C(12) | $-58.8(4)$ |
| O(1)–S(1)–C(11)–C(12) | 47.9(4) |
| S(1)–C(1)–C(2)–C(3) | 72.2(4) |
| S(1)–C(1)–C(2)–C(7) | $-168.4(3)$ |
| C(3)–C(2)–C(7)–F(2) | 179.2(4) |
| O(2)–C(2)–C(3)–C(4) | $-16.5(5)$ |
| C(2)–C(3)–C(4)–O(3) | 178.8(4) |
| C(5)–O(3)–C(4)–C(3) | $-1.6(6)$ |
| C(4)–O(3)–C(5)–C(6) | $-172.6(4)$ |

and $1.350(5) \text{ \AA}$ respectively, averaging the values found in compounds containing a C–CF₂Cl group.⁷ On the contrary, the position of F(2) is not affected by disorder. These findings appear to be in accordance with preliminary conformational energy calculations performed with the MM2 forcefield,⁸ which assign higher energy to the conformation with the chlorine atom in the position of F(2), and with packing analysis showing that both the positions 1a and 1b are less sterically crowded in comparison with the F(2) site and can thus be accessed by the chlorine atom.

Analogies with the other sulfoxides are found in the molecular packing, characterized by intermolecular hydrogen bonding between the sulfoxide oxygen O(1) and the hydroxy hydrogen H(2), of a molecule related to the reference one by the symmetry operator $1 - x, 0.5 + y, 2 - z$. This bonding scheme gives rise to helical structures developing in the *b* direction (Fig. 2).

Consequently, the other diastereoisomeric compound 3*d* was given the (3*S*,*R*₅) configuration, while the configuration of the three other pairs of diastereoisomers 3*a*–*c* could be identified by comparison of their ¹H and ¹⁹F NMR spectra with those of the 3*d* pair. Significant differences are observed, *e.g.*, in the chemical shifts of the vinyl protons, which resonate downfield in the alcohol (3*R*)-3*d* with respect to those of (3*S*)-3*d*: the same pattern appears in the NMR spectra of the three other pairs (3*R*)- and (3*S*)-3*a*–*c*, and is of diagnostic evidence. Moreover, in the alcohols (3*R*)- and (3*S*)-3*d*, as well as in the (3*R*)- and (3*S*)-3*a*–*c* pairs, the methylene protons of the ethoxy group give rise to different spin systems: in alcohols of type (3*R*)-3 the two protons resonate at the same frequency (A₂X₃ system), while in

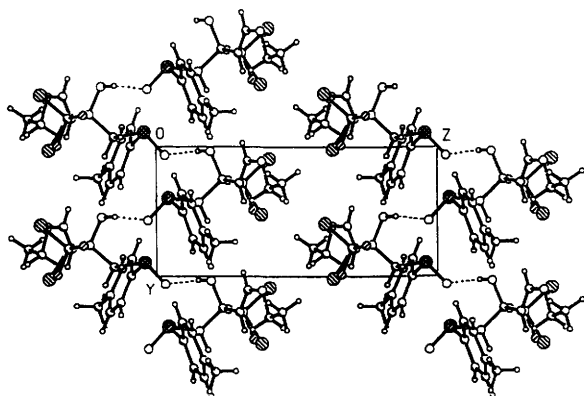
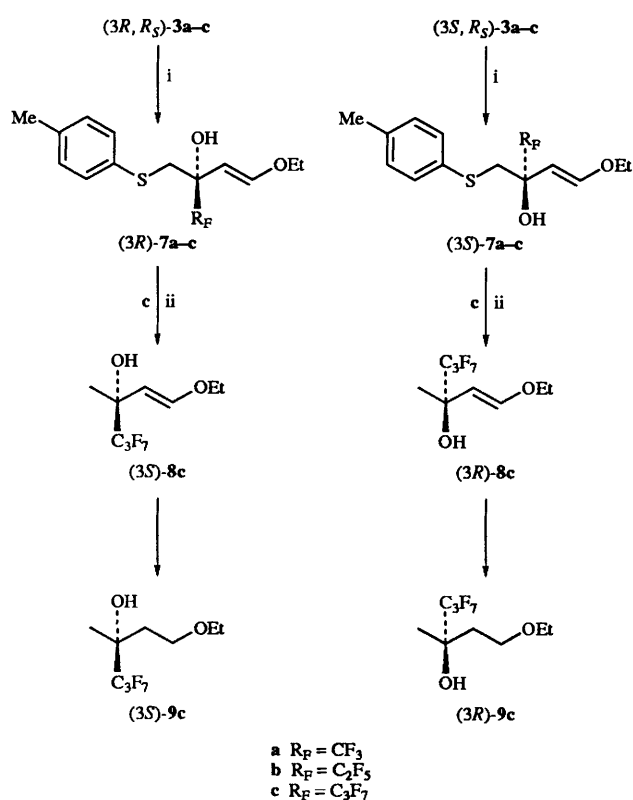


Fig. 2 Packing diagram of compound (3*R*,*R*_S)-3d



Scheme 3 Reagents and conditions: i, NaI, $(CF_3CO)_2O$, acetone, $-20^\circ C$; ii, H_2 , Raney Ni, ethanol, reflux

alcohols of type (3*S*)-3 their chemical shifts are differentiated (ABX₃ system).

The sulfinyl chiral auxiliary can be removed in a reductive way: treatment of the sulfoxides (3*R*)- and (3*S*)-3a-c with sodium iodide and trifluoroacetic anhydride gave the corresponding sulfides (3*R*)- and (3*S*)-7a-c, respectively, as viscous oils in good yields (Scheme 3 and Table 2). Further reduction of the sulfides with hydrogen in the presence of Raney Ni afforded the corresponding fluorinated, sulfur-free tertiary alcohols (3*S*)- and (3*R*)-8, respectively, along with varying amounts of alcohols (3*S*)- and (3*R*)-9, where the double bond has been hydrogenated, depending on the reaction conditions.

In conclusion, the synthesis describes an entry to (*E*)-1-ethoxy-3-fluoroalkyl-3-hydroxy-4-(4-methylphenylsulfanyl)-but-1-enes: these compounds, beside their intrinsic interest, are also useful synthetic intermediates for the preparation of both enantiomers of sulfur-free fluorinated tertiary alcohols.

Experimental

Mps were taken using a Büchi apparatus and are uncorrected. IR spectra were obtained on a Perkin Elmer 177 spectrophotometer. ¹H, ¹³C and ¹⁹F NMR spectra were taken using a Bruker AC 250 spectrometer in CDCl₃ with tetramethylsilane or hexafluorobenzene as internal standard. Mass spectra were recorded with a VG-70EQ apparatus. Optical rotations were obtained on a Jasco DIP-181 polarimeter; $[\alpha]_D$ values are given in $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. Compounds 2a-c were prepared according to previously reported procedures.⁹

(*E*)-1-Chloro-1,1-difluoro-4-ethoxybut-3-en-2-one 2d

A solution of ethyl vinyl ether (1.0 g, 13.9 mmol) and pyridine (0.55 g, 6.9 mmol) in CH₂Cl₂ (12.5 cm³) was cooled to 0 °C, then chlorodifluoroacetic anhydride (4.86 g, 20 mmol) was added. The solution was stirred overnight at room temperature, then was washed with 5% aqueous NaOH, with 1 mol dm⁻³ HCl and with water. After drying (Na₂SO₄) the solvent was removed under reduced pressure to give the ketone 2d as an oil (1.49 g, 58%) (Found: C, 38.9; H, 3.7. C₆H₇ClF₂O₂ requires C, 39.1; H, 3.8%); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 1710 (CO); δ_{H} 1.41 (3 H, t, *J* 7, CH₃), 4.12 (2 H, q, *J* 7, CH₂), 5.87 (1 H, d, *J* 11, =CHC), 7.91 (1 H, d, *J* 11, =CHO); δ_{F} -68.55 (2 F, s); *m/z* 184 (M⁺).

Condensation reaction on fluorinated electrophiles 2

General procedure. A solution of (*R*)-methyl *p*-tolyl sulfoxide 1 (5.8 mmol) in anhydrous THF (10 cm³) was added at $-78^\circ C$ over a period of 10 min under nitrogen to a solution of LDA, prepared from diisopropylamine (6.0 mmol) and 2.5 mol dm⁻³ butyllithium (2.4 cm³) in THF (10 cm³). The mixture was stirred for 15 min, then compound 2 (6.0 mmol) was added at $-60^\circ C$ and the whole was allowed to warm to room temperature when it was quenched with a saturated aqueous ammonium chloride (20 cm³) and extracted with ethyl acetate (3 × 15 cm³). The extracts were dried (Na₂SO₄) and the solvent was removed under reduced pressure to give a residue, which was flash chromatographed on silica gel with hexane-ethyl acetate (4:1) to give in order of elution the alcohols (3*R*,*R*_S)-3 and (3*S*,*R*_S)-3 (Tables 2 and 3).

X-Ray crystal structure determination of 3d

Crystals of one of the diastereoisomeric alcohols 3d, which were suitable for X-ray analysis, were obtained by crystallization from diisopropyl ether.

Crystal data. C₁₄H₁₇O₃F₂ClS, *M* = 338.79. Monoclinic, *a* = 10.2420(4), *b* = 6.0630(5), *c* = 13.4940(6) Å, β = 101.842(3)°, *V* = 820.11(8) Å³, space group *P*2₁, *Z* = 2, *D*_x = 1.372 Mg m⁻³, μ = 3.509 mm⁻¹, *F*(000) = 352. Colourless prismatic crystal, dimensions: 0.4 × 0.15 × 0.05 mm.

Data collection. Siemens P4 diffractometer, θ-2θ scan technique, graphite monochromated Cu-Kα radiation; 2630 reflections measured (3.35 < θ < 57.43, +h, +k, +l and -h, -k, -l), 2245 unique. Three standard reflections measured every 250 reflections showed no significant decay. Data were corrected for Lorentz and polarization effects, while no absorption correction was applied.

Structure analysis and refinement. The crystal structure was solved with direct methods (SHELXTL),¹⁰ and refined with full-matrix least squares on *F*² values (SHELXL-93).¹¹ Non-hydrogen atoms were refined with anisotropic temperature factors. Hydrogen atoms were included at calculated positions and refined in the riding mode. Final value of the residual *R* and *wR*2 [for 1996 reflections with *I* > 2σ(*I*)] were respectively 0.0440 and 0.1111. The highest and lowest peaks in final difference-Fourier map were 0.215 and -0.18 h e Å⁻³, while the refined value of Flack's *x* parameter¹² was 0.04(3), establishing the absolute configuration as (3*R*,*R*_S).

Table 2 Physical and analytical data for the fluoro substituted alcohols **3** and **7**

| Compound (formula) | Yield ^a (%) | Mp/°C | [α] _D ²⁰ (c, CHCl ₃) | Found (%) (required) | |
|---|---------------------------|----------------------|--|-------------------------|--------------|
| | | | | C | H |
| (3 <i>R</i> , <i>R</i> _S)- 3a (C ₁₄ H ₁₇ F ₃ O ₃ S) | 38 | 61–63 ^b | +224 (0.8) | 52.0 (52.2) | 5.3 (5.3) |
| (3 <i>S</i> , <i>R</i> _S)- 3a (C ₁₄ H ₁₇ F ₃ O ₃ S) | 35 | 106–108 ^c | +222 (1.0) | 52.1 (52.2) | 5.5 (5.3) |
| (3 <i>R</i> , <i>R</i> _S)- 3b (C ₁₅ H ₁₇ F ₅ O ₃ S) | 26 | 70–71 ^b | +201 (0.8) | 48.5 (48.4) | 4.4 (4.6) |
| (3 <i>S</i> , <i>R</i> _S)- 3b (C ₁₅ H ₁₇ F ₅ O ₃ S) | 49 | 88–89 ^d | +192 (1.0) | 48.4 (48.4) | 4.7 (4.6) |
| (3 <i>R</i> , <i>R</i> _S)- 3c (C ₁₆ H ₁₇ F ₇ O ₃ S) | 28 | oil | +163 (0.9) | 45.7 (45.5) | 4.0 (4.1) |
| (3 <i>S</i> , <i>R</i> _S)- 3c (C ₁₆ H ₁₇ F ₇ O ₃ S) | 58 | 113–114 ^b | +168 (1.3) | 45.5 (45.5) | 4.3 (4.1) |
| (3 <i>R</i> , <i>R</i> _S)- 3d (C ₁₄ H ₁₇ ClF ₂ O ₃ S) | 36 | 80–81 ^e | +226 (1.0) | 49.5 (49.6) | 4.9 (5.1) |
| (3 <i>S</i> , <i>R</i> _S)- 3d (C ₁₄ H ₁₇ ClF ₂ O ₃ S) | 38 | 112–113 ^e | +199 (1.1) | 49.8 (49.6) | 5.0 (5.1) |
| (3 <i>R</i>)- 7a (C ₁₄ H ₁₇ F ₃ O ₂ S) | 40 | oil | +13 (0.9) | 54.7 (54.9) | 5.8 (5.6) |
| (3 <i>R</i>)- 7b (C ₁₅ H ₁₇ F ₅ O ₂ S) | 84 | oil | +18 (1.0) | 50.7 (50.6) | 4.6 (4.8) |
| (3 <i>R</i>)- 7c (C ₁₆ H ₁₇ F ₇ O ₂ S) | 68 | oil | +17 (1.1) | 47.1 (47.3) | 4.3 (4.2) |
| (3 <i>S</i>)- 7a (C ₁₄ H ₁₇ F ₃ O ₂ S) | 94 | oil | –13 (0.4) | 55.1 (54.9) | 5.5 (5.6) |
| (3 <i>S</i>)- 7b (C ₁₅ H ₁₇ F ₅ O ₂ S) | 54 | oil | –16 (1.0) | 50.4 (50.6) | 4.9 (4.8) |
| (3 <i>S</i>)- 7c (C ₁₆ H ₁₇ F ₇ O ₂ S) | 43 | oil | –18 (0.5) | 47.5 (47.3) | 4.0 (4.2) |

^a After flash column chromatography. ^b From pentane–hexane (2:1). ^c From hexane. ^d From pentane–diisopropyl ether (15:1). ^e From diisopropyl ether.

Condensation reaction on non-fluorinated electrophile **4**

The same procedure, applied to *trans*-4-methoxybut-3-en-2-one **4** gave a mixture of products which was purified by flash chromatography eluting with hexane–ethyl acetate (7:3). The less polar product (*R*_f 0.35, 42% yield) resulted in an unresolvable 1.2:1.0 mixture of (*E*)- and (*Z*)-3-methyl-4-(4-methylphenylsulfinyl)but-2-en-1-al **5**, whilst the more polar one (*R*_f 0.30, 40% yield) was the product of 1,4-attack, (*E*)-1-(4-methylphenylsulfinyl)pent-2-en-4-one **6**.

(*E*)-**5**: δ_{H} 2.22 (3 H, d, ⁴*J*_{H-H} 1.5, CH₃CH=), 2.43 (3 H, s, CH₃), 3.60 (2 H, s, CH₂S), 5.73 (1 H, dq, ³*J*_{H-H} 5.0, ⁴*J*_{H-H} 1.5, CHCHO), 7.3–7.6 (4 H, m, Ph) and 9.95 (1 H, d, ³*J*_{H-H} 5.0, CHO); δ_{C} 19.0 (CH₃Ph), 21.5 (CH₃C=), 68.0 (CH₂S), 130.0 (4 C, Ph), 132.0 (C=CH), 139.0 (CH₃C), 143.0 (CS), 149.0 (CH=CCH₃) and 189.5 (CHO). (*Z*)-**5**: δ_{H} 1.91 (3 H, d, ⁴*J*_{H-H} 1.1, CH₃CH=), 2.43 (3 H, s, CH₃), 3.91 (1 H, d, *J* 12.5, CHHSO), 4.04 (1 H, d, *J* 12.5, CHHSO), 6.11 (1 H, dq, ³*J* 7.0, ⁴*J* 1.1, CHCHO), 7.3–7.5 (4 H, m, Ph) and 9.45 (1 H, d, ³*J* 7.0, CHO); δ_{C} 19.0 (CH₃), 26.5 (CH₃C=), 61.0 (CH₂S), 124.0 (4 C, Ph), 132.5 (C=CH), 139.5 (CH₃C), 143.0 (CS), 149.0 (CH=CCH₃) and 190.0 (CHO).

(*E*)-**6**: δ_{H} 2.22 (3 H, s, CH₃CO), 2.39 (3 H, s, CH₃), 3.54 (1 H, ddd, ²*J* 13.2, ³*J* 8.8, ⁴*J* 1.8, CHHSO), 3.74 (1 H, ddd, ²*J* 13.2, ³*J* 8.8, ⁴*J* 1.8, CHHSO), 6.07 (1 H, dt, ³*J* 16.2, ⁴*J* 1.8, CH=CHCO), 6.55 (1 H, dt, ³*J* 16.2, ⁴*J* 1.8, CH=CHCO) and 7.3–7.6 (4 H, m, Ph).

Reduction of sulfinyl alcohols **3**

General procedure. A solution of trifluoroacetic anhydride (31.0 mmol) in acetone (15 cm³) was added to a solution of the alcohol **3** (6.2 mmol) and sodium iodide (2.8 g, 18.6 mmol) in acetone (80 cm³) at –20 °C over a period of 20 min, then the reaction mixture was treated with an excess of saturated

aqueous sodium sulfite and sodium hydrogen carbonate. Acetone was removed under reduced pressure and the residue was extracted with diethyl ether (3 × 20 cm³). The extracts were dried (Na₂SO₄) and the solvent was evaporated under reduced pressure. The residue was flash chromatographed on silica gel eluting with hexane–ethyl acetate (9:1) to give the sulfides **7** (Tables 2 and 3).

Hydrogenation of sulfides **7c**

To a solution of sulfides **7c** (0.27 mmol) in absolute ethanol (2.0 cm³) was added Raney Ni (300 mg) and the slurry was heated at 80 °C and stirred for 20 h under hydrogen at atmospheric pressure. Then Raney Ni was filtered off and washed with ethanol (2 cm³). Without evaporating the solvent, the ethanolic solution was directly introduced onto a flash chromatography column and washed with pentane (40 cm³). Elution with pentane–diethyl ether (10:1) gave the fluorinated alcohols (3*S*)-**8c**, **9c** and (3*R*)-**8c**, **9c**, respectively.

α,β -Unsaturated alcohol (3*S*)-8c**:** 11% yield, oil; [α]_D²⁰ –1.1 (c 0.3 in EtOH); δ_{H} 1.29 (3 H, t, *J* 7, CH₂CH₃), 1.52 (3 H, br s, CH₃), 2.05 (1 H, br s, OH), 3.78 (2 H, q, *J* 7, CH₂), 4.91 (1 H, d, *J* 13, =CHC) and 6.68 (1 H, d, *J* 13, =CHO); δ_{F} –82.1 (br s, CF₃), –121.8 (1 F, d, *J* 280, CF₂), –123.6 (1 F, d, *J* 280, CF₂), –123.8 (1 F, d, *J* 280, CF₂) and –125.5 (1 F, d, *J* 280, CF₂); *m/z* 284 (M⁺).

Enantiomer (3*R*)-8c**:** 16% yield, oil; [α]_D²⁰ +1.2 (c 0.6 in EtOH).

Saturated alcohol (3*S*)-9c**:** 35% yield, oil; [α]_D²⁰ +2.6 (c 0.5 in EtOH); δ_{H} 1.20 (3 H, t, *J* 7, CH₂CH₃), 1.44 (3 H, br s, CH₃), 1.8–1.9 (1 H, m, CHH), 2.2–2.3 (1 H, m, CHH), 3.52 (2 H, q, *J* 7, CH₂CH₃), 3.7–3.8 (2 H, m, CH₂O) and 4.66 (br s, 1 H, br s, OH); δ_{F} –82.1 (br s, CF₃), –123.8 (1 F, d, *J* 280, CF₂), –121.8 (1 F, d, *J* 280, CF₂), –123.6 (1 F, d, *J* 280, CF₂) and –123.8 (1 F, d, *J* 280, CF₂); *m/z* 286 (M⁺).

Table 3 Spectral data for the fluoro-substituted alcohols **3** and **7**

| Compound | $\delta_{\text{H}}(\text{CDCl}_3)^a$ | $\delta_{\text{F}}(\text{CDCl}_3)^a$ | m/z (M^+) |
|--|---|---|---------------------------|
| (3 <i>R</i> , <i>R</i> _S)- 3a | 1.35(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.45(3H,s,CH ₃),2.83(1H,d, <i>J</i> 13,CHHSO),3.17(1H,d, <i>J</i> 13,CHHSO),3.92(2H,q, <i>J</i> 7,CH ₂),5.01(1H,d, <i>J</i> 12.5,=CHC),5.45(1H,br s,OH),7.03(1H,d, <i>J</i> 12.5,=CHO) and 7.4–7.6(4H,m,Ph) | –84.45(s,CF ₃) | 322 |
| (3 <i>S</i> , <i>R</i> _S)- 3a | 1.26(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.43(3H,s,CH ₃),2.96(1H,d, <i>J</i> 14,CHHSO),3.08(1H,d, <i>J</i> 14,CHHSO),3.66 and 3.72(2H,ABX ₃ , <i>J</i> _{AB} 10.5, <i>J</i> _{AX} = <i>J</i> _{BX} 7,CH ₂),4.67(1H,d, <i>J</i> 12.5,=CHC),5.7(1H,br s,OH),6.81,d, <i>J</i> 12.5,=CHO) and 7.3–7.6(4H,m,Ph) | –81.05(s,CF ₃) | 322 |
| (3 <i>R</i> , <i>R</i> _S)- 3b | 1.35(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.44(3H,s,CH ₃),2.83(1H,d, <i>J</i> 13,CHHSO),3.23(1H,d, <i>J</i> 13,CHHSO),3.93(2H,q, <i>J</i> 7,CH ₂),5.0(1H,d, <i>J</i> 12.5,=CHC),5.52(1H,br s,OH),6.96(1H,d, <i>J</i> 12.5,=CHO) and 7.4–7.6(4H,m,Ph) | –78.65(s,CF ₃), –124.6(1F,d, <i>J</i> 280,CF ₂) and –126.2(1F,d, <i>J</i> 280,CF ₂) | 372 |
| (3 <i>S</i> , <i>R</i> _S)- 3b | 1.25(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.43(3H,s,CH ₃),2.87(1H,d, <i>J</i> 14,CHHSO),3.16(1H,d, <i>J</i> 14,CHHSO),3.65 and 3.69(2H,ABX ₃ , <i>J</i> _{AB} 9.0, <i>J</i> _{AX} = <i>J</i> _{BX} 7,CH ₂),4.63(1H,d, <i>J</i> 12.5,=CHC),5.9(1H,br s,OH),6.78(1H,d, <i>J</i> 12.5,=CHO) and 7.3–7.6(4H,m,Ph) | –79.14(s,CF ₃), –122.1(1F,d, <i>J</i> 280,CF ₂) and –123.9(1F,d, <i>J</i> 280,CF ₂) | 372 |
| (3 <i>R</i> , <i>R</i> _S)- 3c | 1.35(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.44(3H,s,CH ₃),2.84(1H,d, <i>J</i> 14,CHHSO),3.23(1H,d, <i>J</i> 14,CHHSO),3.92(2H,q, <i>J</i> 14,CH ₂),5.02(1H,d, <i>J</i> 12.5,=CHC),5.55(1H,br s,OH),6.96(1H,d, <i>J</i> 12.5) and 7.4–7.6(4H,m,Ph) | –82.05(br s,CF ₃), –122.1(br s,CF ₂), –123.05(1F,d, <i>J</i> 280,CF ₂) and –125.05(1F,d, <i>J</i> 280,CF ₂) | 422 |
| (3 <i>S</i> , <i>R</i> _S)- 3c | 1.26(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.44(3H,s,CH ₃),2.91(1H,d, <i>J</i> 14,CHHSO),3.17(1H,d, <i>J</i> 14,CHHSO),3.66 and 3.70(2H,ABX ₃ , <i>J</i> _{AB} 10.5, <i>J</i> _{AX} = <i>J</i> _{BX} 7,CH ₂),4.66(1H,d, <i>J</i> 2.5,=CHC),5.96(1H,br s,OH),6.78(1H,d, <i>J</i> 12.5,=CHO) and 7.4–7.6(4H,m,Ph) | –81.9(br s,CF ₃), –119.1(br s,CF ₂), –122.8(1F,d, <i>J</i> 280,CF ₂) and –125.65(1F,d, <i>J</i> 280,CF ₂) | 422 |
| (3 <i>R</i> , <i>R</i> _S)- 3d | 1.35(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.43(3H,s,CH ₃),2.88(1H,d, <i>J</i> 13,CHHSO),3.20(1H,d, <i>J</i> 13,CHHSO),3.92(2H,q, <i>J</i> 7,CH ₂),5.03(1H,d, <i>J</i> 12,=CHC),5.5(1H,br s,OH),7.01(1H,d, <i>J</i> 12,=CHO) and 7.3–7.6(4H,m,Ph) | –68.2(1F,d, <i>J</i> 160,CF ₂) and –69.2(1F,d, <i>J</i> 160,CF ₂) | 338 |
| (3 <i>S</i> , <i>R</i> _S)- 3d | 1.26(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.43(3H,s,CH ₃),3.01(1H,d, <i>J</i> 13,CHHSO),3.22(1H,d, <i>J</i> 13,CHHSO),3.66 and 3.72(2H,ABX ₃ , <i>J</i> _{AB} 10.5, <i>J</i> _{AX} = <i>J</i> _{BX} 7,CH ₂),4.72(1H,d, <i>J</i> 13,=CHC),5.6(1H,br s,OH),6.81(1H,d, <i>J</i> 13,=CHO) and 7.3–7.6(4H,m,Ph) | –65.5(1F,d, <i>J</i> 160,CF ₂) and –66.5(1F,d, <i>J</i> 160,CF ₂) | 338 |
| (3 <i>R</i>)/(3 <i>S</i>)- 7a | 1.25(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.32(3H,s,CH ₃),3.0(1H,br s,OH),3.28(1H,d, <i>J</i> 14,CHHS),3.33(1H,d, <i>J</i> 14,CHHS),3.5–3.7(2H,m,CH ₂),4.56(1H,d, <i>J</i> 13,=CHC),6.72(1H,d, <i>J</i> 13,=CHO) and 7.1–7.7(4H,m,Ph) | –82.3(s,CF ₃) | 306 |
| (3 <i>R</i>)/(3 <i>S</i>)- 7b | 1.25(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.32(3H,s,CH ₃),3.15(1H,br s,OH),3.32(1H,d, <i>J</i> 14,CHHS),3.39(1H,d, <i>J</i> 14,CHHS),3.4–3.7(2H,m,CH ₂),4.49(1H,d, <i>J</i> 13,=CHC),6.67(1H,d, <i>J</i> 13,=CHO) and 7.1–7.3(4H,m,Ph) | –79.1(s,CF ₃), –123.7(1F,d, <i>J</i> 280,CF ₂) and –125.8(1F,d, <i>J</i> 280,CF ₂) | 356 |
| (3 <i>R</i>)/(3 <i>S</i>)- 7c | 1.25(3H,t, <i>J</i> 7,CH ₂ CH ₃),2.30(3H,s,CH ₃),3.2(1H,br s,OH),3.33(1H,d, <i>J</i> 14,CHHS),3.41(1H,d, <i>J</i> 14,CHHS),3.4–3.7(2H,m,CH ₂),4.51(1H,d, <i>J</i> 13,=CHC),6.68(1H,d, <i>J</i> 13,=CHO) and 7.05–7.35(4H,m,Ph) | –82.1(br s,CF ₃), –120.4(1F,d, <i>J</i> 280,CF ₂), –122.2(1F,d, <i>J</i> 280,CF ₂), –122.8(1F, <i>J</i> 280,CF ₂) and –125.2(1F,d, <i>J</i> 280,CF ₂) | 406 |

^a *J* Values in Hz.

Enantiomer (3*R*)-9c****: 41% yield, oil; $[\alpha]_{\text{D}}^{20}$ –2.9 (*c* 0.2 in EtOH).

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