Homochiral Fluoroorganic Compounds. Part 17.[1] 2-(*p*-Tolylsulphinylmethyl)-3-fluorotetrahydro-pyrans and -furans through Intramolecular Oxymercuriation

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The four unsaturated α-fluoro alcohols, 3-fluoro-1-[(*p*-tolyl)sulphinyl]hept-5-en-2-ols and 3-fluoro-6-methyl-1-[(*p*-tolyl)sulphinyl]hept-5-en-2-ols **3** having the (2*S*,3*S*,R_S) or (2*S*,3*R*,R_S) absolute configuration, gave the corresponding 6-methyl- or 6,6-dimethyl-substituted 5-chloromercurio-3-fluoro-2-[(*p*-tolyl)sulphinyl]tetrahydropyrans **5** and **6** and the 5-[1'-(chloromercurio)ethyl]-3-fluoro-2-[(*p*-tolyl)sulphinyl]tetrahydrofurans **4** by *'endo'* or *'exo'* cyclooxymercuriation promoted by mercury(II) trifluoroacetate. All the synthesized compounds have been isolated in optically pure form and their structure, absolute configuration, and preferred conformation have been established by ^1H, ^{13}C and ^{19}F NMR studies. Elaboration of the chloromercurio and sulphinylmethyl substituents on a couple of diastereoisomeric tetrahydropyrans **6** allowed us to obtain the corresponding 3-fluoro-2-hydroxymethyltetrahydropyrans **11**.

Olefinic cyclization processes leading to the formation of heterocyclic systems are of continuing interest. From a theoretical point of view they often allow the analysis of the role of stereoelectronic effects in determining reaction pathways to be undertaken, and in their application they are a powerful tool for the synthesis of complex and multifunctional systems.[2]

Three- to seven-membered rings containing oxygen, nitrogen and sulphur atoms have been obtained through the nucleophilic attack of the heteroatom on the activated double bond. Several electrophilic species have been employed to attain such an activation, *e.g.* halogens (mainly selenium species), protons, carbocations and metal cations [mainly mercury(II) salts].

As a part of our continuing interest in the asymmetric synthesis of selectively fluorinated compounds, we have studied and already reported on the iodocyclization[3] and mercuriocyclization[4] of several hydroxyalkenes carrying fluorine atoms.

In this paper we describe the mercuriocyclization of four homochiral heptenols **3**, the 3-fluoro-1-[(*p*-tolyl)sulphinyl]hept-5-en-2-ols **3a** and the 3-fluoro-6-methyl-1-[(*p*-tolyl)sulphinyl]-hept-5-en-2-ols **3b** having the (2*S*,3*S*,R_S) and (2*S*,3*R*,R_S) absolute configurations, to give the 3-fluoro-tetrahydrofurans **4** and -tetrahydropyrans **5** and **6**.

Some elaboration reactions of these compounds to give homochiral and selectively fluorinated oxygen heterocycles which do not contain mercury and sulphur are also reported.

Results and Discussion

Intramolecular Oxymercuriation Reactions.—The 3-fluoro-1-[(*p*-tolyl)sulphinyl]hept-5-en-2-ones **2a** having the 3*R*,R_S and 3*S*,R_S absolute configurations were obtained[5] through alkylation of the dilithium derivative of (*R*)-1-fluoro-3-[(*p*-tolyl)sulphinyl]acetone **1**[6] with 1-bromobut-2-ene (76% yield, 1:1 diastereoisomer ratio) (Scheme 1).

Similarly, the 6-methyl analogues (3*R*,R_S)- and (3*S*,R_S)-**2b** were formed when 1-bromo-3-methylbut-2-ene was used to alkylate the dianion of compound **1**.

Single diastereoisomers of the ketones **2a,b** were isolated in pure form through flash chromatography and were reduced with diisobutylaluminium hydride (DIBAL). The corresponding alcohols **3a,b** always having the *S* absolute configuration at the newly formed carbon stereocentre were formed in high yield and with complete diastereoselection.

The mercuriocyclization of these four alcohols was performed by using mercury(II) trifluoroacetate in tetrahydrofuran (THF) solution and the chloromercurio-substituted heterocycles **4–6** were isolated in enantiomerically and diastereoisomerically pure form after exchange of the trifluoroacetoxy group with chlorine (potassium chloride in aq. solution).

The cyclization of the two diastereoisomeric alcohols **3a** having the opposite absolute configuration at C-3 occurred in very high yield to give the tetrahydrofurans **4** and the tetrahydropyrans **5** with good regioselectivity (Scheme 2).

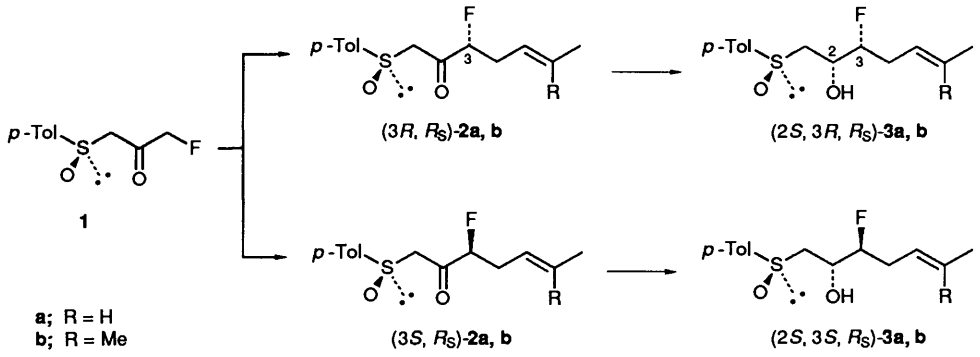
For both substrates the 5-*exo-trig*[7] process, leading to tetrahydrofurans **4**, was favoured with respect to the 6-*endo-trig* one, leading to tetrahydropyrans **5** [regioisomer ratio 6.7:3.3 for (2*S*,3*R*,R_S)-**3a** and 8.1:1.9 for (2*S*,3*S*,R_S)-**3a**]. The cyclization of the two diastereoisomeric alcohols **3b** having the (2*S*,3*R*,R_S) and (2*S*,3*S*,R_S) absolute configurations occurred with complete regioselectivity. Starting from both these alcoholic substrates the tetrahydropyrans **6** were exclusively formed through a 6-*endo-trig* process† (Scheme 3).

According to Baldwin's rules both the 5-*exo-trig* processes and the 6-*endo-trig* pathways are favoured. The regioselectivity observed in the cyclization of the Δ^4-alcohols **3a–c** may, however, be interpreted by considering the site of preferential localization of the positive charge in the intermediate mercurinium ion. According to Markovnikov, such localization occurs preferentially on the most substituted carbon, *i.e.* on C-5 for **3c** and on C-6 for **3b**, thus rationalizing the exclusive formation of tetrahydro-furans and -pyrans starting from compounds **3c** and **3b**, respectively.

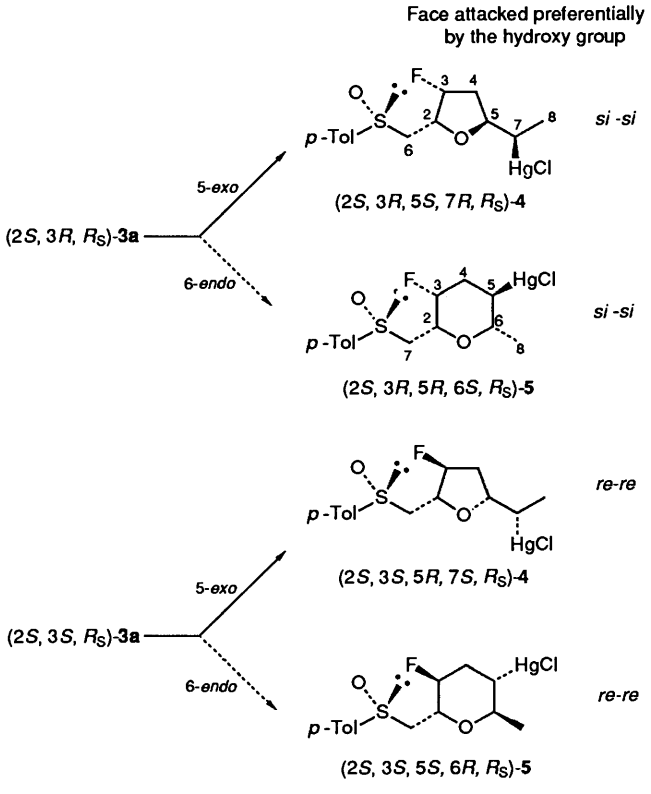
No such preferential localization operates for compound **3a**, which gives a mixture of 5- and 6-membered heterocyclic products.[8] Starting from (2*S*,3*R*,R_S)-**3a**, the prevailing diastereoisomers of the cyclization products **4** and **5** derived from attack of the hydroxy group on the *si-si* face of the olefinic double bond (de 50% for **4** and >95% for **5**). A similar preferential attack on the *si* face occurred in the cyclization of (2*S*,3*R*,R_S)-**3b,c** (de >95% for **6** and >95% for **7**).

In a complementary way the alcohols (2*S*,3*S*,R_S)-**3a,c**, having the opposite absolute configuration at the fluorinated carbon

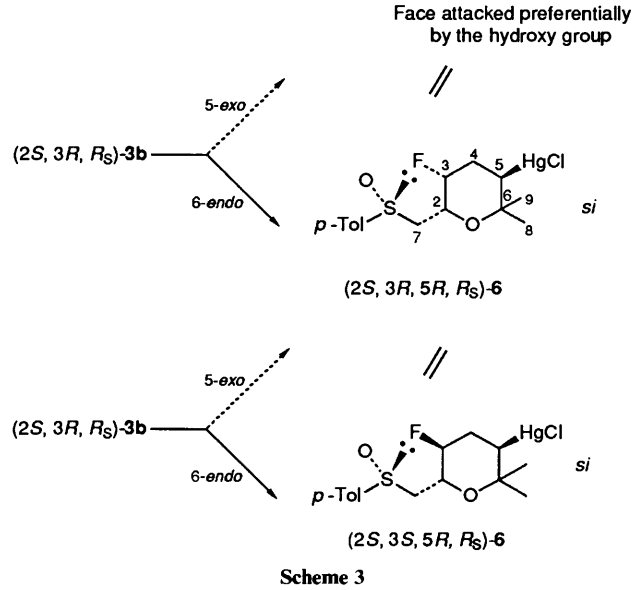
† We have already reported[4] how under the same reaction conditions both diastereoisomeric 3-fluoro-1-sulphinylhexenols **3c**, having opposite configurations at C-3, cyclize to give exclusively the tetrahydrofurans **7** through a 5-*exo-trig* process.



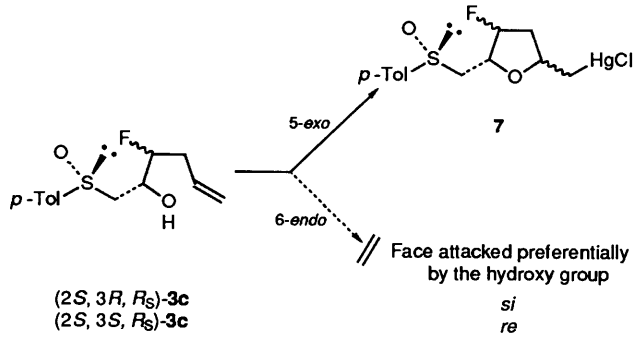
Scheme 1



Scheme 2



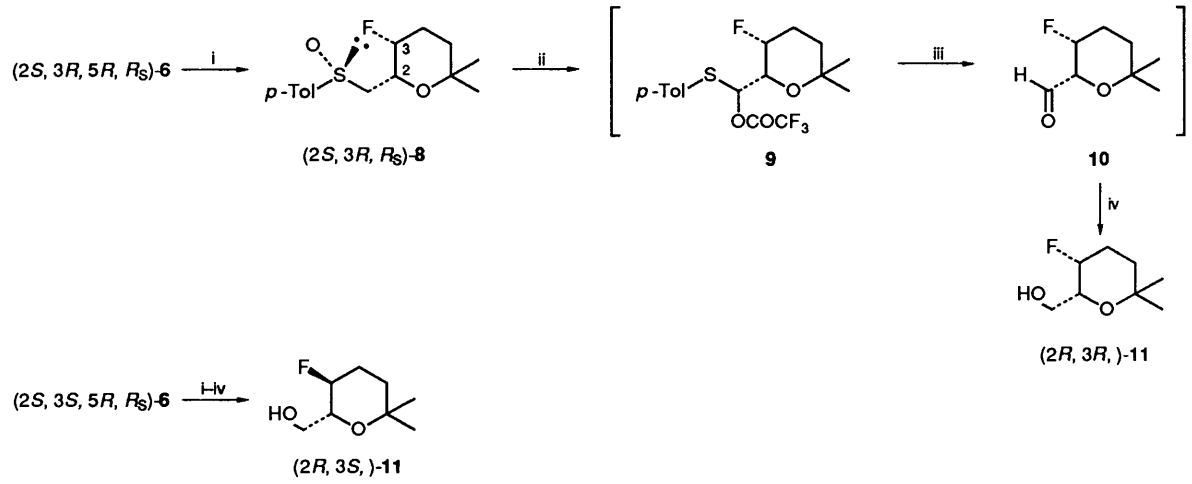
Scheme 3



with respect to the alcohols considered above, cyclized with a preferential entrance of the hydroxy group on the *re-re* and *re* face (de 15% for **4** and 67% for **7**), while the hydroxy group of (2*S*,3*S*,R_S)-**3b** entered by choice on the *si* face (de 53%). The data reported above suggest that the diastereoselection of the process is mainly determined by the configuration at C-3 (the atom which bears the highly electronegative fluorine substituent), the regioselectivity of the cyclization (5-*exo vs* 6-*endo* processes) playing a minor role. The formation of 3,5-*trans*-disubstituted products is favoured for both tetrahydro-furans and -pyrans, products **5** and **6**.

Elaboration of Tetrahydropyrans **6**.—In order to investigate the synthetic potentials of the mercurio-substituted heterocycles described above, we have studied some functional group elaborations of the chloromercurio and sulphinyl residues of the tetrahydropyrans **6** (Scheme 4). The reductive demercuriation of (2*S*,3*R*,5*R*,R_S)-**6** was performed in nearly quantitative yield with sodium borohydride. The (2*S*,3*R*,R_S)-3-fluoro-2-(p-tolylsulphinyl)methyl-tetrahydropyran **8** thus obtained was treated with trifluoroacetic anhydride (TFAA) and 2,4,6-trimethylpyridine to give the geminal trifluoroacetoxy-sulphenyl intermediate **9** through a clean Pummerer rearrangement. This masked aldehyde was not isolated but was unmasked *in situ* to give the tetrahydropyran-2-carbaldehyde **10**, which was directly reduced to the (2*R*,3*R*)-3-fluoro-2-hydroxymethyl-6,6-dimethyltetrahydrofuran **11**. A similar reaction sequence allowed us to obtain the epimer tetrahydropyran (2*R*,3*S*)-**11** in 64% overall yield starting from (2*S*,3*S*,5*R*,R_S)-**6**.

Stereostructural and Conformational Assignments.—All the compounds in this work presented spectral characteristics in accord with the proposed structures. The absolute configuration at the fluorinated stereocentre in the 3-fluoro-1-sulphinyl-heptenones **2a,b** was assigned from the well established correlation [9] existing between the relative stereochemistry at the sulphur and carbon stereocentres and the chemical-shift values of the CH_2SO methylene protons in the ^1H NMR spectra (Experimental section). The protons of the CH_2SO group are



Scheme 4 *Reagents and conditions:* i, $NaBH_4$–3 mol dm^{-3} NaOH–CH_2Cl_2, 0 °C; ii, TFAA–2,4,6-trimethylpyridine–MeCN, room temp.; iii, $HgCl_2$–MeCN, 0 °C, 2 h; iv, $NaBH_4$–MeCN, 0 °C

Table 1 Selected ^1H NMR chemical shifts (δ) and coupling constants (*J*/Hz) for compounds **4** in $CDCl_3$. Numbering as shown in Scheme 2.

Proton	(2*S*,3*R*,5*R*,7*S*)	(2*S*,3*R*,5*S*,7*R*)	(2*S*,3*S*,5*R*,7*S*)	(2*S*,3*S*,5*S*,7*R*)
2β	4.31	4.64	4.65	4.82
3	5.00 (β)	5.11 (β)	5.09 (α)	5.12 (α)
4α	2.02	2.50	1.68	2.43
4β	2.51	1.81	2.47	2.09
5	4.36 (β)	4.59 (α)	4.56 (β)	4.42 (α)
6a	3.06	3.01	3.00	2.81
6b	3.03	2.97	2.70	2.72
7	3.15	3.02	3.22	3.02
8	1.44	1.48	1.43	1.46
J[a]				
2β,3α			1.5	1.4
2β,3β	2.7	3.0		
2β,6a	*b*	4.1	4.2	5.6
2β,6b	*b*	8.2	9.1	8.5
2β,F	*b*	27.4	26.9	18.7
3α,4α			5.1	5.6
3α,4β			1.1	1.7
3α,F			53.2	53.5
3β,4α	1.0	0.9		
3β,4β	5.5	3.8		
3β,F	53.6	52.8		
4α,4β	15.0	13.7	13.9	15.0
4α,5α		5.2		8.2
4α,5β	5.8		10.8	
4α,F	30.8	18.2	37.0	32.5
4β,5α		10.5		5.2
4β,5β	8.2		4.5	
4β,F	33.6	40.5	19.8	27.9
5α,7		5.8		5.5
5β,7	4.7		5.0	
6a,6b	*b*	13.2	12.9	13.1
7,8	7.5	7.4	7.5	7.5

[a] The ^4J(5-H.F) and ^4J(6-H_2,F) range between 0 and 1.6 Hz. [b] Not assigned.

markedly anisochronous in the (3*R*,R_S)-diastereoisomers ($\Delta\delta_H$ 0.28 and 0.27 ppm) while they are nearly isochronous in the 3*S*,R_S ones. The absolute configuration at the hydroxylated stereocentre in the 3-fluoro-1-sulphinylheptenols **3a,b** was derived from analysis of some parameters of the ^1H and ^{19}F NMR spectra of these compounds (Experimental section) which allowed us to assign the relative stereochemistry of the fluorohydrin system. As already observed in related derivatives,[5] the *anti*-isomers (2*S*,3*S*,R_S)-**3a,b**[10] showed, with respect to the corresponding *syn*-isomers (2*S*,3*R*,R_S)-**3a,b**, the fluorine resonances at lower fields (δ_F −192.57 and −191.95 *vs.* −196.18 and −195.40), greater three-bond coupling constants between the C-2 and C-3 methine protons (5.8 and 5.9 *vs.* 2.8 and 2.9 Hz), lower three-bond couplings between 2-H and 3-F (11.6 and 11.8 *vs.* 22.3 and 22.1 Hz), and well resolved long-range couplings between 3-F and the C-1 methylene protons (1.6 and 0.7 *vs. ca.* 0 Hz).

The ^1H NMR resonances of the tetrahydro-furans **4** and -pyrans **5**, **6**, **8** and **11** have been completely assigned and are reported in Tables 1–3. These assignments were made mainly on the basis of the coupling patterns derived from ^1H NMR studies, supported by nuclear Overhauser effects (NOEs), extensive decoupling experiments, and chemical-shift criteria.

The tetrahydrofurans **4** were readily distinguished from the

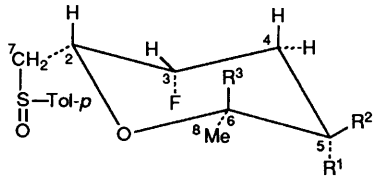
Table 2 Selected ^{1}H NMR chemical shifts (δ) for compounds **5**, **6**, **8** and **11** in $CDCl_3$. Numbering as shown in Schemes 2–4.

	5			**6**				**8**		**11**	
Proton	2*S*,3*R*,5*R*,6*S*	2*S*,3*S*,5*S*,6*R*	2*S*,3*S*,5*R*,6*S*	2*S*,3*R*,5*R*	2*S*,3*R*,5*S*	2*S*,3*S*,5*R*	2*S*,3*S*,5*S*	2*S*,3*R*	2*S*,3*S*	2*R*,3*R*	2*R*,3*S*
2β	4.15	4.47	3.99	4.29	4.27	4.19	4.26	4.22	4.12	3.70	3.58
3	4.41 (β)	4.44 (α)	4.08 (α)	4.38 (β)	4.48 (β)	4.10 (α)	4.33 (α)	4.39 (β)	4.14 (α)	4.54 (β)	4.37 (α)
4α	2.57	2.38	2.65	2.51	2.49	2.49	2.55	2.05	2.07	2.05	2.07
4β	2.32	2.45	2.35	2.42	2.56	2.38	2.51	1.85	1.89	1.81	1.84
5α	2.84		2.75	3.05		2.70		1.85	1.65	1.85	1.59
5β		2.94			2.66		3.05	1.37	1.70	1.36	1.64
6	4.00 (β)	4.20 (α)	3.92 (β)								
7a	3.00	3.01	3.20	2.95	3.03	3.17	3.19	3.01	3.19	3.80	3.79
7b	2.82	3.01	2.69	2.80	2.85	2.64	2.73	2.83	2.66	3.75	3.66
8	1.43	1.36	1.38	1.47	1.48	1.43	1.46	1.32	1.27	1.28	1.23
9				1.53	1.44	1.56	1.49	1.32	1.36	1.23	1.27

Table 3 Selected ^{1}H NMR coupling constants (*J*/Hz) for compounds **5** and **6** in $CDCl_3$. Numbering as shown in Schemes 2 and 3.

	5			**6**			
J	2*S*,3*R*,5*R*,6*S*	2*S*,3*S*,5*S*,6*R*	2*S*,3*S*,5*R*,6*S*	2*S*,3*R*,5*R*[a]	2*S*,3*R*,5*S*	2*S*,3*S*,5*R*	2*S*,3*S*,5*S*[a]
2β,3α		4.2	9.5			9.5	9.2
2β,3β	1.1			1.2	1.1		
2β,7a	10.5	*b*	*b*	9.6	10.5	1.9	3.2
2β,7b	2.4	*b*	10.2	2.6	2.4	10.2	8.2
2β,F	28.6	10.7	*b*	30.2	32.4	*b*	4.9
3α,4α		3.3	5.0			5.0	4.9
3α,4β		6.2	10.0			10.1	9.9
3α,F		47.8	48.0			*b*	48.0
3β,4α	3.2			3.1	3.2		
3β,4β	2.2			2.3	2.4		
3β,F	47.5			47.8	49.0		
4α,4β	14.5	14.5	*b*	15.0	*b*	*b*	13.4
4α,5α	3.8		*b*	4.4		4.1	
4α,5β		9.7			2.7		3.5
4α,F	10.7	28.0	*b*	12.6	*b*	*b*	6.1
4β,5α	13.6		*b*	13.5		13.8	
4β,5β		4.3			4.6		4.2
4β,F	41.5	*b*	*b*	41.8	*b*	*b*	11.2
5α,6β	11.0		10.9				
5α,8	<0.5		<0.5	0.8		0.8	
5α,F	<0.5		*b*	<0.5		1.2	
5β,6α		7.5					
5β,F		1.2			<0.5		3.4
6α,8		6.3					
6β,8	6.0		6.1				
7a,7b	13.2	*b*	13.1	12.8	13.2	12.8	12.8
7a,F	1.1	*b*	*b*	0.9	0.8	1.9	1.7
7b,F	<0.5	*b*	<0.5	<0.5	<0.5	<0.5	0.6

[a] Coupling constants obtained in [$^2H_6$]acetone. [b] Not assigned.



(2*S*,3*R*,5*R*,6*S*,R_S)-**5** $R^1 = R^3 = H$, $R^2 = HgCl$

(2*S*,3*R*,5*R*,R_S)-**6** $R^1 = H$, $R^2 = HgCl$, $R^3 = {}^9Me$

(2*S*,3*R*,5*S*,R_S)-**6** $R^1 = HgCl$, $R^2 = H$, $R^3 = Me$

Fig. 1 Preferred conformations for tetrahydropyrans **5** and **6** having C-2 and C-3 substituents *cis*-disposed

tetrahydropyrans **5**, since in the former class the 5-methine proton resonates at lower field than the corresponding proton in the latter class (δ 4.3–4.6 *vs.* 2.7–3.0). An analogous trend was observed for the C-5 carbon atom in the ^{13}C NMR spectra of the compounds obtained from (2*S*,3*R*,R_S)-**3a** (Experimental section). The assignment of the absolute configuration at C-5 in compounds **4** and **6**, and at C-5 and C-6 in compounds **5**, followed from the magnitude of the coupling constants of the protons of the five- and six-membered rings (Tables 1 and 3), from NOE results and from the fact that the absolute stereochemistries at C-2 and C-3 are fixed from their synthetic origin. The above data permit the assignment of the preferred conformation in the majority of compounds.

In compound (2*S*,3*R*,5*R*,R_S)-**6**, having, as do the following two derivatives, the C-2 and C-3 substituents *cis*-disposed, the NOEs observed for 2-$H^β$ (12%) and 4-H at δ 2.42 (3%) upon irradiation of the 9-methyl protons at δ 1.53 indicate that these protons must be on the same β-face of the tetrahydropyran ring, as shown in Fig. 1.

The coupling constants of 41.8 and 13.5 Hz, observed between 3-$F^α$ and 4-$H^β$ and 4-$H^β$ and 5-H, are consistent with axial–axial relationships between these atoms, thus allowing the assignment of the chirality at C-5 as *R*. Similar NOE enhancements observed for 2-$H^β$ (12.5%) and 4-$H^β$ (2%) upon irradiation of 9-H_3, together with the values of 2.7 and 4.6 Hz observed between 4-$H^α$ and 5-H, and 4-$H^β$ and 5-H, indicate that in

compound (2*S*,3*R*,5*S*,R_S)-**6** the tetrahydropyran ring preferentially adopts the chair conformation shown in Fig. 1 in which the 5-HgCl grouping is α-axially disposed. It follows that the chirality at C-5 is *S*.

In compound (2*S*,3*R*,5*R*,6*S*,R_S)-**5** the coupling constants of 41.5, 13.6 and 11.0 Hz observed between 3-F$^{\alpha}$ and 4-H$^{\beta}$ at δ 2.32, 4-H$^{\beta}$ and 5-H, and 5-H and 6-H are again indicative of axial–axial relationships between these atoms. The chiralities at C-5 and C-6 are therefore *R* and *S*, respectively.

In the two C-5 epimers (2*S*,3*S*,5*R*,R_S)- and (2*S*,3*S*,5*S*,R_S)-**6**, having, as do the following two derivatives, the C-2 and C-3 substituents *trans*-disposed, the NOEs observed between 2-H$^{\beta}$ and 9-H_3 (8.5 and 12%, respectively), and 9-H_3 and 4-H at δ 2.38 and 2.51 (2.5 and 2%, respectively) indicate that these protons are *cis*-disposed. Moreover, the vicinal couplings observed between 2-H$^{\beta}$ and 3-H$^{\alpha}$, 3-H$^{\alpha}$ and 4-H$^{\beta}$, 4-H$^{\beta}$ and 5-H (^3J 9.5, 10.1 and 13.8 Hz) in the former compound and those observed between 2-H$^{\beta}$ and 3-H$^{\alpha}$, 3-H$^{\alpha}$ and 4-H$^{\beta}$, and 4-H$^{\beta}$ and 5-H (^3J 9.2, 9.9 and 4.2 Hz) in the latter require that both epimers preferentially adopt the chair conformation depicted in Fig. 2 in which the C-5 substituent is, respectively, β-equatorially and α-axially disposed. It follows that the chirality at C-5 is *R* and *S*, respectively.

An analogous conformation was found for the tetrahydropyran ring of (2*S*,3*S*,5*R*,6*S*,R_S)-**5** as evidenced by the axial–axial couplings of 9.5, 10.0 and 10.9 Hz observed between 2-H$^{\beta}$ and 3-H$^{\alpha}$, 3-H$^{\alpha}$ and 4-H$^{\beta}$, and 5-H$^{\alpha}$ and 6-H$^{\beta}$. These data permit the assignment of the chirality at C-5 and C-6 as *R* and *S*.

In compound (2*S*,3*S*,5*S*,6*R*,R_S)-**5** the NOEs observed between 6-H and 7-H_2^{α} (1.5%) and between 6-H and 4-H at δ 2.38 (1%) indicate that these protons are on the same α-face of the ring, thus allowing the assignment of the chirality at C-6 as *R*. In addition, irradiation of the 8β-methyl protons caused enhancements of the signals for 2-H$^{\beta}$ (1.5%) and 4-H$^{\beta}$ (1%). These findings are in accord with a rapid equilibrium between the two chair conformations A and B shown in Fig. 2. Moreover, the couplings of 4.2 and 6.2 Hz observed between 2-H$^{\beta}$ and 3-H$^{\alpha}$, and 3-H$^{\alpha}$ and 4-H$^{\beta}$ indicate that the form B in which these two pairs of protons are *trans*-equatorially disposed is the preferred one. Finally, the couplings of 9.7 and 7.5 Hz, observed between 4-H$^{\alpha}$ and 5-H, and 5-H and 6-H$^{\alpha}$, indicate these protons are *trans*-disposed and hence that the chirality at C-5 is *S*.

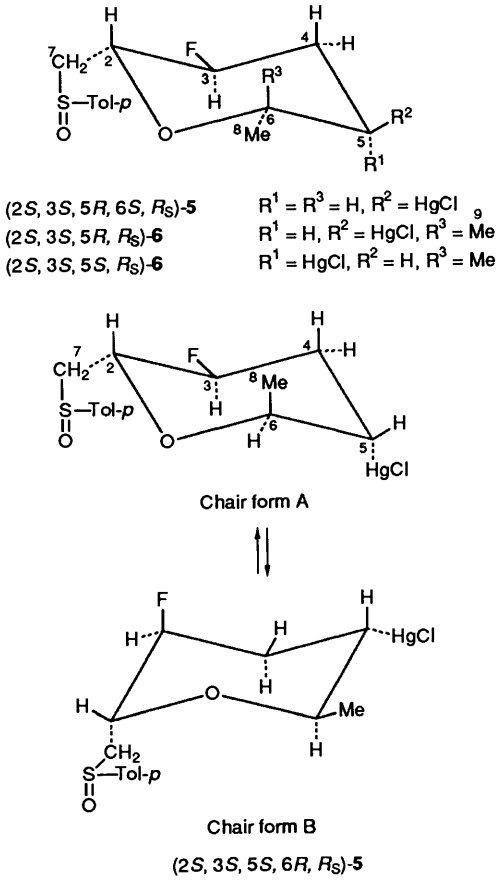


Fig. 2 Preferred conformations for tetrahydropyrans **5** and **6** having C-2 and C-3 substituents *trans*-disposed

In the tetrahydrofuran (2*S*,3*S*,5*S*,7*R*,R_S)-**4** the NOEs observed between 5-H and 6-H_2^{α} and *vice versa* (1 and 2.5%) require that these protons are *cis*-disposed. The chirality at C-5 is therefore *R*.

In compound (2*S*,3*R*,5*S*,7*R*,R_S)-**4** the NOE observed between 2-H$^{\beta}$ and the 4-H at δ 1.81 (1.5%) indicates that the two protons are both β-disposed. Moreover, 4-H$^{\beta}$ presented couplings of 40.5 and 10.5 Hz with 3-F$^{\alpha}$ and 5-H. Vicinal couplings of this magnitude can be associated with two pseudoaxial–pseudoaxial relationships, hence the preferred conformation of the tetrahydrofuran ring must be as shown in Fig. 3, with the C-5 substituent β-pseudoequatorially disposed. Thus the chirality at C-5 is *S*.

Analogously, the values of 37.0 and 10.8 Hz exhibited by the 4-H at δ 1.68 with 3-F$^{\beta}$ and 5-H, respectively, in compound (2*S*,3*S*,5*R*,7*S*,R_S)-**4** require the tetrahydrofuran ring preferentially to adopt the half-chair-like conformation shown in Fig. 3 in which these atoms are pseudoaxially disposed. It follows that the C-5 substituent is α-pseudoequatorially disposed and, as a consequence, that the chirality at C-5 is *R*.

In the last diastereoisomer, (2*S*,3*R*,5*R*,7*S*,R_S)-**4**, the NOE observed for 2-H$^{\beta}$ upon saturation of 4-H at δ 2.51 (1%) means that the two protons are on the same β-face of the ring. Moreover, the fact that 5-H showed a significant NOE to 4-H$^{\beta}$ (2%) but no effect to 4-H$^{\alpha}$ suggests that 5-H is on the β-face too and that the chirality of C-5 is *R*.

The absolute configuration at C-7 in the tetrahydrofurans **4** was assigned on the basis of the documented preference for *anti* attack in electrophilic addition of unstrained olefins by mercury(II) species.[11] The NOEs observed for 5-H$^{\beta}$ (4 and 4.5%, respectively) and 4-H_2 (1–3%) upon irradiation of the 8-methyl protons, and the lack of measurable NOEs between 4-H_2 and 7-H, together with the coupling-constant values of 4.7 and 5.0 Hz observed, respectively, between 5-H$^{\beta}$ and 7-H, suggest that in (2*S*,3*R*,5*R*,7*S*,R_S)- and (2*S*,3*S*,5*R*,7*S*,R_S)-**4** the chirality at C-7 is *S*, the preferred conformation of the C-5 side-chain around

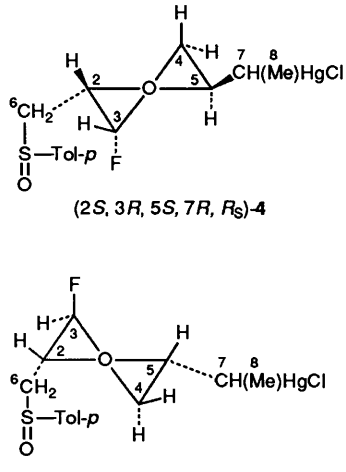


Fig. 3 Preferred conformations for the (2*S*,3*R*.5*S*,7*R*,R_S)- and (2*S*,3*S*,5*R*,7*S*,R_S)-tetrahydrofurans 4

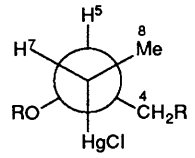


Fig. 4 Preferred conformation of the C-5 side-chain around the C5–C6 bond for the (2*S*,3*R*,5*R*,7*S*,R_S)- and (2*S*,3*S*,5*R*,7*S*,R_S)-tetrahydrofurans **4**

the C(5)–C(6) bond being as shown in Fig. 4. These results agree totally with the above chemical evidence.

Experimental

^1H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker CPX-300 or a Bruker AC 250L spectrometer. $SiMe_4$ was used as internal standard (δ_H and δ_C 0.00) for ^1H and ^{13}C nuclei while C_6F_6 was used as internal standard (δ_F −162.90) for ^{19}F nuclei. *J*-Values are given in Hz. NOE difference spectra were obtained by subtracting, alternatively, right-off resonance-free induction decays (FIDs) from right-on resonance-induced FIDs. NOE-Values reported in the text have only qualitative significance. $[\alpha]_D^{20}$-Values were obtained on a Jasco DIP-181 polarimeter. M.p.s are uncorrected and were obtained on a capillary apparatus. TLC was run on silica gel 60 F_{254} Merck. THF was freshly distilled from lithium aluminium hydride, and diisopropylamine was distilled from calcium hydride and stored over molecular sieves (4 Å). A 2.6 mol dm^{-3} solution of butyllithium in hexanes (Aldrich) was employed. In other cases commercially available reagent-grade solvents were employed without purification.

(R)-1-Fluoro-3-[(*p*-tolyl)sulphinyl]acetone **1** was obtained through acylation of (*R*)-methyl *p*-tolyl sulphoxide with ethyl fluoroacetate as already described.[6] **CAUTION:** It must be noted that ethyl fluoroacetate and compounds which upon decomposition may release fluoroacetic acid are potentially very toxic and should be handled with care inside a hood. The ratio of the diastereoisomeric chloromercurio compounds was established by HPLC on a Hibar Prepacked Column RT-Lichrosorb Si 60 (5 μm) (Merck).

Synthesis of (3R)- *and* (3S)-3-*Fluoro*-1-[(R)-(p-*tolyl*)-*sulphinyl*]*hept*-5-*en*-2-*one* **2a**.—A solution of LDA [prepared from diisopropylamine (8.00 cm^3, 56.19 mmol) and a solution of butyllithium (22.40 cm^3, 56.10 mmol)] in THF (60 cm^3) was cooled to −78 °C and treated dropwise at −60 °C with a solution of (R_S)-**1** (5.00 g, 23.36 mmol) in THF (80 cm^3). 1-Bromobut-2-ene (3.30 cm^3, 28.00 mmol) neat was added to the yellow solution of the α-sulphinyl anion at −78 °C. After the mixture had been stirred for 5 min at −78 °C, saturated aq. ammonium chloride was added. Extraction with ethyl acetate and removal of solvent under reduced pressure gave a residue (7.00 g). Compounds (3*R*)- and (3*S*)-**2a** were isolated by flash chromatography (hexane–ethyl acetate, 6:4) in 1:1 ratio as yellow pale liquids: *compound* (3*R*,R_S)-**2a** (2.38 g, 38%) (Found: C, 62.6; H, 6.3. $C_{14}H_{17}FO_2S$ requires C, 62.69; H, 6.34%); $[\alpha]_D^{20}$ +128° (*c* 1.1, $CHCl_3$); $\delta_H(CDCl_3)$ 7.57 and 7.34 (4 H, m, ArH), 5.54 (1 H, dtq, *J* 15.0, 6.2 and 1.3, 6-H), 5.29 (1 H, dtq, *J* 15.0, 6.8 and 1.5, 5-H), 4.72 (1 H, ddd, *J* 48.4, 6.8 and 4.4, 3-H), 4.17 (1 H, dd, *J* 14.5 and 3.4, 1-H^a), 3.89 (1 H, dd, *J* 14.5 and 2.7, 1-H^b), 2.45 (2 H, m, 4-H_2), 2.42 (3 H, br s, Ar*Me*) and 1.63 (3 H, ddt, *J* 6.2, 1.5 and 1.2, 7-H_3); *compound* (3*S*,R_S)-**2a** (2.38 g, 38%) (Found: C, 62.7; H, 6.4%); $[\alpha]_D^{20}$ +179° (*c* 0.9, $CHCl_3$), $\delta_H(CDCl_3)$ 7.57 and 7.35 (4 H, m, ArH), 5.59 (1 H, dtq, *J* 15.0, 6.3 and 1.3, 6-H), 5.37 (1 H, dtq, *J* 15.0, 6.8 and 1.5, 5-H), 4.72 (1 H, ddd, *J* 48.5, 7.0 and 4.6, 3-H), 4.03 (2 H, m, 1-H_2), 2.47 (2 H, m, 4-H_2), 2.42 (3 H, br s, Ar*Me*) and 1.67 (3 H, ddt, *J* 6.3, 1.5 and 1,2, 7-H_3).

Synthesis of (3R)- *and* (3S)-3-*Fluoro*-6-*methyl*-1-[(R)-(p-*tolyl*)*sulphinyl*]*hept*-5-*en*-2-*one* **2b**.—In the same way starting from 1-bromo-3-methylbut-2-ene (6.48 cm^3, 56.04 mmol) a residue (10.0 g) was isolated which, after flash chromatography (hexane–ethyl acetate, 3:2) gave, in 1:1 ratio, as yellow pale liquids: *compound* (3*R*,R_S)-**2b** (4.74 g, 36%) (Found: C, 63.4; H, 6.8. $C_{15}H_{19}FSO_2$ requires C, 63.83; H, 6.74%); $[\alpha]_D^{20}$ +182° (*c* 0.7, $CHCl_3$); $\delta_H(CDCl_3)$ 7.57 and 7.35 (4 H, m, ArH), 5.03 (1 H, br t, *J* 7.4, 5-H), 4.72 (1 H, ddd, *J* 49.0, 6.3 and 5.0, 3-H), 4.17 (1 H, dd, *J* 14.6 and 3.2, 1-H^a), 3.90 (1 H, dd, *J* 14.6 and 2.7, 1-H^b), 2.46 (2 H, m, 4-H_2), 2.42 (3 H, br s, Ar*Me*) and 1.67 and 1.56 (6 H, br s, 7- and 8-H_3); *compound* (3*S*,R_S)-**2b** (4.74 g, 36%) (Found: C, 63.5; H, 6.8%); $[\alpha]_D^{20}$ +141° (*c* 0.4, $CHCl_3$); $\delta_H(CDCl_3)$ 7.57 and 7.34 (4 H, m, ArH), 5.11 (1 H, br t, *J* 7.4, 5-H), 4.71 (1 H, dt, *J* 49.0 and 5.9, 3-H), 4.04 (2 H, m, 1-H_2), 2.52 (2 H, m, 4-H_2), 2.42 (3 H, br s, Ar*Me*) and 1.72 and 1.60 (6 H, br s, 7- and 8-H_3).

Synthesis of (2S,3S)- *and* (2S,3R)-3-*Fluoro*-1-[(R)-(p-*tolyl*)-*sulphinyl*]*hept*-5-*en*-2-*ol* **3a**.—A solution of (3*S*,R_S)-**2a** (0.90 g, 3.36 mmol) in THF (20 cm^3) was cooled to −60 °C and treated dropwise with a 1 mol dm^{-3} solution of DIBAL in hexane (3.36 cm^3, 3.36 mmol) at the same temperature. After the reaction mixture had been stirred for 10 min at −60 °C, saturated aq. ammonium chloride was added, followed by 10 mol dm^{-3} hydrochloric acid dropwise to pH 3. Extraction with ethyl acetate and flash chromatography of the residue (pentane–diethyl ether, 1:9) gave the *title compound* (2*S*,3*S*,R_S)-**3a** (0.73 g, 80%), m.p. 114–115 °C (from Et_2O) (Found: C, 62.0; H, 7.1. $C_{14}H_{19}FSO_2$ requires C, 62.22; H, 7.00%); $[\alpha]_D^{20}$ +244° (*c* 1.0, $CHCl_3$); $\delta_H(CDCl_3)$ 7.52 and 7.36 (4 H, m, ArH), 5.45 (dtq, *J* 15.0, 6.1 and 1.3, 6-H), 5.34 (1 H, dtq, *J* 15.0, 6.8 and 1.5, 5-H), 4.42 (1 H, dddd, *J* 47.4, 7.3, 5.8 and 4.5, 3-H), 4.35 (1 H, dd, *J* 3.9 and 0.7, 2-OH), 4.16 (1 H, ddddd, *J* 11.6, 9.5, 5.8, 3.9 and 1.8, 2-H), 3.15 (1 H, ddd, *J* 13.6, 9.5 and 0.7, 1-H^a), 2.83 (1 H, ddd, *J* 13.6, 1.8 and 1.6, 1-H^b), 2.5–2.1 (2 H, m, 4-H_2), 2.44 (3 H, br s, Ar*Me*) and 1.62 (3 H, ddt, *J* 6.1, 1.5 and 1.2, 7-H_3); $\delta_F(CDCl_3)$ −192.57.

Starting from (3*R*,R_S)-**2a** (0.90 g, 3.36 mmol), *compound* (2*S*,3*R*,R_S)-**3a** (0.77 g, 85%) was obtained, m.p. 126–127 °C (from Et_2O) (Found: C, 62.3; H, 7.1%); $[\alpha]_D^{20}$ +267° (*c* 0.9, $CHCl_3$); $\delta_H(CDCl_3)$ 7.53 and 7.36 (4 H, m, ArH), 5.56 (1 H, dtq, *J* 15.0, 6.2 and 1.3, 6-H), 5.38 (1 H, dtq, *J* 15.0, 6.8 and 1.5, 5-H), 4.29 (1 H, dddd, *J* 47.5, 7.8, 5.4 and 2.8, 3-H), 4.25 (1 H, ddddd, *J* 22.3, 10.3, 4.7, 2.8 and 1.9, 2-H), 3.60 (1 H, d, *J* 4.7, 2-OH), 3.18 (1 H, dd, *J* 13.3 and 10.3, 1-H^a), 2.72 (1 H, dd, *J* 13.3 and 1.9, 1-H^b), 2.5–2.2 (2 H, m, 4-H_2), 2.43 (3 H, br s, Ar*Me*) and 1.65 (3 H, ddt, *J* 6.2, 1.5 and 1.2, 7-H_3); $\delta_F(CDCl_3)$ −196.18.

Synthesis of (2S,3S)- *and* (2S,3R)-3-*Fluoro*-6-*methyl*-1-[(R)-(p-*tolyl*)*sulphinyl*]*hept*-5-*en*-2-*ol* **3b**.—A solution of (3*S*)-3-fluoro-6-methyl-1-[(R)-(*p*-tolyl)sulphinyl]hept-5-en-2-one **2b** (0.74 g, 2.60 mmol) in THF (16 cm^3) was cooled to −60 °C and treated dropwise with a 1 mol dm^{-3} solution of DIBAL in hexane (2.62 cm^3, 2.62 mmol) at the same temperature. After the reaction mixture had been stirred for 10 min at −60 °C, saturated aq. ammonium chloride was added, followed by 10 mol dm^{-3} hydrochloric acid to pH 3. Extraction with ethyl acetate and flash chromatography of the residue (hexane–ethyl acetate, 1:1) gave *compound* (2*S*,3*S*,R_S)-**3b** (0.63 g, 85%), m.p. 89–90 °C (from Et_2O) (Found: C, 63.3; H, 7.3. $C_{15}H_{21}FSO_2$ requires C, 63.38; H, 7.39%); $[\alpha]_D^{20}$ +97° (*c* 0.6, $CHCl_3$); $\delta_H(CDCl_3)$ 7.53 and 7.37 (4 H, m, ArH), 5.05 (1 H, tqq, *J* 7.2, 1.5 and 1.5, 5-H), 4.42 (1 H, dddd, *J* 48.0, 7.2, 5.9 and 5.0, 3-H), 4.40 (1 H, br, 2-OH), 4.17 (1 H, dddd, *J* 11.8, 9.5, 5.9 and 1.9, 2-H), 3.16 (1 H, ddd, *J* 13.7, 9.5 and 0.7, 1-H^a), 2.83 (1 H, ddd, *J* 13.7, 1.9 and 1.6, 1-H^b), 2.5–2.1 (2 H, m, 4-H_2), 2.44 (3 H, br s, Ar*Me*) and 1.67 and 1.57 (6 H, br s, 7- and 8-H_3); $\delta_F(CDCl_3)$

−191.95. Starting from (3*R*,R_S)-**2b** (0.33 g, 1.20 mmol), *compound* (2*S*,3*R*,R_S)-**3b** (0.30 g, 90%), m.p. 135–136 °C (from Et_2O) (Found: C, 63.35; H, 7.3%); $[\alpha]_D^{20}$ +107° (*c* 0.4, $CHCl_3$); $\delta_H(CDCl_3)$ 7.53 and 7.36 (4 H, m, ArH), 5.08 (1 H, tqq, *J* 7.2, 1.5 and 1.5, 5-H), 4.28 (1 H, dddd, *J* 47.5, 7.8, 5.4 and 2.9, 3-H), 4.24 (1 H, dddd, *J* 22.1, 10.4, 2.9 and 2.1, 2-H), 3.50 (1 H, br, 2-OH), 3.19 (1 H, dd, *J* 13.5 and 10.5, 1-H^a), 2.72 (1 H, dd, *J* 13.5 and 2.0, 1-H^b), 2.6–2.2 (2 H, m, 4-H_2), 2.43 (3 H, br s, Ar*Me*) and 1.69 and 1.62 (6 H, br s, 7- and 8-H_3); $\delta_F(CDCl_3)$ −195.40.

Synthesis of (2S,3S,5R,7S,R_S)- *and* (2S,3S,5S,7R,R_S)-5-(1-*Chloromercurioethyl*)-3-*fluoro*-2-(p-*tolylsulphinylmethyl*)*tetrahydrofuran* **4** *and of* (2S,3S,5S,6R,R_S)- *and* (2S,3S,5R,6S,R_S)-5-*Chloromercurio*-3-*fluoro*-6-*methyl*-2-(p-*tolylsulphinylmethyl*)-*tetrahydropyran** **5**.—A solution of mercury(II) trifluoroacetate (0.51 g, 1.19 mmol) in anhydrous THF (5 cm^3) was added to a solution of (2*S*,3*S*,R_S)-**3a** (0.27 g, 1.00 mmol) in the same solvent (5 cm^3) at 0 °C and the mixture was stirred for *ca.* 10 min until the starting product was completely used up (TLC; hexane–ethyl acetate, 1:1). Aq. potassium chloride (0.12 g, 1.61 mmol, 1 cm^3) was then added, after which the mixture was stirred for 10 min, diluted with water (10 cm^3), and extracted with dichloromethane (3 × 10 cm^3). The combined extracts were dried (Na_2SO_4), and evaporated under reduced pressure. Benzene (2 cm^3) was added to the residue and was then evaporated off. Flash chromatography (ethyl acetate–hexane, 53:47) gave, in order, *compound* (2*S*,3*S*,5*R*,7*S*,R_S)-**4** (0.38 g, 75.2%), m.p. 178–180 °C (from EtOAc) (Found: C, 33.6; H, 3.7. $C_{14}H_{18}ClFHgSO_2$ requires C, 33.30; H, 3.57%); $\delta_C(CDCl_3)$ 96.23 (dd, $^1J_{C,F}$ 182.3, C-3), 82.75 (d, C-5), 79.33 (dd, $^2J_{C,F}$ 28.2, C-2), 61.92 (dt, $^3J_{C,F}$ 9.2, C-6), 53.25 (d, C-7), 40.90 (dt, $^2J_{C,F}$ 19.8, C-4) and 16.61 (q, C-8); $[\alpha]_D^{20}$ +137.5° (*c* 1.0, $CHCl_3$); *compound* (2*S*,3*S*,5*R*,6*S*,R_S)-**5** (0.04 g, 8.1%), m.p. 183–185 °C (from EtOAc) (Found: C, 33.5; H, 3.6%); $[\alpha]_D^{20}$ +119.7° (*c* 0.7, $CHCl_3$); *compound* (2*S*,3*S*,5*S*,6*R*,R_S)-**5** (0.05 g, 10.9%), m.p. 162–163 °C (from EtOAc) (Found: C, 33.4; H, 3.6%); $[\alpha]_D^{20}$ +74° (*c* 1.4, $CHCl_3$); *compound* (2*S*,3*S*,5*S*,7*R*,R_S)-**4** (0.03 g, 5.8%), m.p. 160–161 °C (from EtOAc) (Found: C, 33.4; H, 3.6%); $[\alpha]_D^{20}$ +155.4° (*c* 1.0, $CHCl_3$). The diastereoisomeric ratios and the t_R-values were determined by HPLC (hexane–ethyl acetate, 1:4); (2*S*,3*S*,5*R*,7*S*,R_S)-**4**, t_R 5.06 min; (2*S*,3*S*,5*R*,6*S*,R_S)-**5**, t_R 5.48 min; (2*S*,3*S*,5*S*,6*R*,R_S)-**5**, t_R 6.82 min; (2*S*,3*S*,5*S*,7*R*,R_S)-**4**, t_R 7.42 min. ^1H NMR data are reported in Tables 1–3.

Synthesis of (2S,3R,5S,7R,R_S)- *and* (2S,3R,5R,7S,R_S)-5-(1-*Chloromercurioethyl*)-3-*fluoro*-2-(p-*tolylsulphinylmethyl*)-*tetrahydrofuran* **4** *and of* (2S,3R,5R,6S,R_S)-5-*Chloromercurio*-3-*fluoro*-6-*methyl*-2-(p-*tolylsulphinylmethyl*)*tetrahydropyran** **5**.—The same procedure, applied to (2*S*,3*R*,R_S)-**3a** gave, after flash chromatography (hexane–ethyl acetate, 1:1), in order: *compound* (2*S*,3*R*,5*S*,7*R*,R_S)-**4** (0.25 g, 50.3%), m.p. 166–167 °C (from EtOAc) (Found: C, 33.4; H, 3.6%); $\delta_C(CDCl_3)$ 94.79 (dd, $^1J_{C,F}$ 183.1, C-3), 82.22 (d, C-5), 75.55 (dd, $^2J_{C,F}$ 19.1, C-2), 58.26 (dt, $^3J_{C,F}$ 9.2, C-6), 52.95 (d, C-7), 41.41 (dt, $^2J_{C,F}$ 21.4, C-4) and 16.89 (q, C-8); $[\alpha]_D^{20}$ +127.3° (*c* 0.5, $CHCl_3$); *compound* (2*S*,3*R*,5*R*,6*S*,R_S)-**5** (0.17 g, 33%), m.p. 75–77 °C (from EtOAc) (Found: C, 33.6; H, 3.7%); $\delta_C(CDCl_3)$ 87.91 (dd, $^1J_{C,F}$ 180.1, C-3), 76.87 (d, C-6), 72.04 (dd, $^2J_{C,F}$ 18.5, C-2), 60.78 (dt, $^3J_{C,F}$ 3.1, C-7), 50.53 (d, C-5), 35.09 (dt, $^2J_{C,F}$ 22.1, C-4) and 24.52 (q, C-8); $[\alpha]_D^{20}$ +111.0° (*c* 1.6, $CHCl_3$); *compound* (2*S*,3*R*,5*R*,7*S*,R_S)-**4** (0.08 g, 16.7%), m.p. 174–175 °C (from EtOAc) (Found: C, 33.3; H, 3.6%); $\delta_C(CDCl_3)$ 94.62 (dd, $^1J_{C,F}$ 183.1, C-3), 82.14 (d, C-5), 75.97 (dd, $^2J_{C,F}$ 19.8, C-2), 57.42 (dt, $^3J_{C,F}$ 6.1, C-6), 53.92 (d, C-7), 40.03 (dt, $^3J_{C,F}$ 20.6, C-4) and 16.50 (q, C-8); $[\alpha]_D^{20}$ +121° (*c* 0.6, $CHCl_3$). The diastereoisomeric ratios and the t_R-values were determined by HPLC (hexane–ethyl acetate, 1:4): (2*S*,3*R*,5*S*,7*R*,R_S)-**4**, t_R 8.05 min; (2*S*,3*R*,5*R*,6*S*,R_S)-**5**, t_R 11.70 min; (2*S*,3*R*,5*R*,7*S*,R_S)-**4**, t_R 14.87 min. ^1H NMR data are reported in Tables 1–3.

Synthesis of (2S,3S,5R,R_S)- *and* (2S,3S,5S,R_S)-5-*Chloromercurio*-3-*fluoro*-6,6-*dimethyl*-2-(p-*tolylsulphinylmethyl*)-*tetrahydropyran** **6**.—The same procedure, applied to (2*S*,3*S*,R_S)-**3b** gave, after flash chromatography (hexane–ethyl acetate, 55:45), in order: *compound* (2*S*,3*S*,5*R*,R_S)-**6** (0.39 g, 76.7%), m.p. 157–159 °C (from EtOAc) (Found: C, 34.6; H, 3.95. $C_{15}H_{20}ClFHgSO_2$ requires C, 34.71; H, 3.85%); $\delta_C(CDCl_3)$ 90.50 (dd, $^1J_{C,F}$ 184.6, C-3), 76.11 (s, C-6), 66.98 (dd, $^2J_{C,F}$ 24.4, C-2), 60.95 (dt, $^3J_{C,F}$ 2.2, C-7), 57.54 (dd, $^3J_{C,F}$ 7.6, C-5), 33.13 (dt, $^2J_{C,F}$ 18.3, C-4), 32.52 (q, C-8) and 25.16 (q, C-9); $[\alpha]_D^{20}$ +159° (*c* 1.1, $CHCl_3$); *compound* (2*S*,3*S*,5*S*,R_S)-**6** (0.12 g, 23.3%), m.p. 156–157 °C (from EtOAc–Et_2O, ~1:1) (Found: C, 34.6; H, 3.8%); $\delta_C(CDCl_3)$ 90.51 (dd, $^1J_{C,F}$ 183.1, C-3), 76.31 (s, C-6), 67.36 (dd, $^2J_{C,F}$ 24.4, C-2), 61.15 (dt, $^3J_{C,F}$ 2.2, C-7), 60.84 (dd, $^3J_{C,F}$ 9.2, C-5), 34.87 (q, C-8), 32.47 (dt, $^2J_{C,F}$ 19.8, C-4) and 23.07 (q, C-9); $[\alpha]_D^{20}$ +121° (*c* 1.0, $CHCl_3$). The diastereoisomeric ratios and the t_R-values were determined by HPLC (hexane–ethyl acetate, 1:4): (2*S*,3*S*,5*R*,R_S)-**6**, t_R 4.52 min; (2*S*,3*S*,5*S*,R_S)-**6**, t_R 5.61 min. ^1H NMR data are reported in Tables 2 and 3.

Synthesis of (2S,3R,5R,R_S)- *and* (2S,3R,5S,R_S)-5-*Chloromercurio*-3-*fluoro*-6,6-*dimethyl*-2-(p-*tolylsulphinylmethyl*)-*tetrahydropyran** **6**.—The same procedure applied to (2*S*,3*R*,R_S)-**3b** gave, after flash chromatography (hexane–ethyl acetate, 1:4), in order: *compound* (2*S*,3*R*,5*R*,R_S)-**6** (0.50 g, 96.6%), m.p. 172–174 °C (from acetone) (Found: C, 35.0; H, 3.9%); $\delta_C(CDCl_3)$ 87.79 (dd, $^1J_{C,F}$ 180.1, C-3), 75.93 (s, C-6), 65.90 (dd, $^2J_{C,F}$ 19.8, C-2), 60.75 (dt, $^3J_{C,F}$ 3.0, C-7), 54.79 (d, C-5), 33.25 (q, C-8), 31.99 (dt, $^3J_{C,F}$ 21.4, C-4) and 24.55 (q, C-9); $[\alpha]_D^{20}$ +129° (*c* 0.7, $CHCl_3$); *compound* (2*S*,3*R*,5*S*,R_S)-**6** (0.02 g, 3.4%), m.p. 178–179 °C (from acetone) (Found: C, 34.85; H, 3.9%); $\delta_C(CDCl_3)$ 85.46 (dd, $^1J_{C,F}$ 176.2, C-3), 72.08 (s, C-6), 71.99 (dd, $^2J_{C,F}$ 18.3, C-2), 62.84 (dt, $^3J_{C,F}$ 6.5, C-7), 31.15 (q, C-8), 30.11 (t, C-5), 25.15 (dt, $^2J_{C,F}$ 22.1, C-4) and 21.32 (q, C-9); $[\alpha]_D^{20}$ +112° (*c* 0.6, MeOH). The diastereoisomeric ratios and the t_R-values were determined by HPLC (hexane–ethyl acetate, 1:4): (2*S*,3*R*,5*R*,R_S)-**6**, t_R 7.68 min; (2*S*,3*R*,5*S*,R_S)-**6**, t_R 9.29 min. ^1H NMR data are reported in Tables 2 and 3.

Synthesis of (2S,3R,R_S)- *and* (2S,3S,R_S)-3-*Fluoro*-6,6-*dimethyl*-2-(p-*tolylsulphinylmethyl*)*tetrahydropyran** **8**.—To a solution of (2*S*,3*R*,5*R*,R_S)-**6** (2.00 g, 3.87 mmol) in dichloromethane (55 cm^3) (sparged with Ar for 30 min) at 0 °C was added dropwise a solution of $NaBH_4$ (0.24 g, 5.73 mmol) in 3 mol dm^{-3} aq. sodium hydroxide (55 cm^3). Metallic mercury precipitated out immediately. The reaction mixture was stirred for 30 min at 0 °C, acetic acid was added dropwise to pH 6, the mercury(0) was filtered off, and extraction of the filtrate with dichloromethane, evaporation of the extract under reduced pressure, and crystallization of the residue (Pr^i_2O) gave *compound* (2*S*,3*R*,R_S)-**8** (0.92 g, 85%), m.p. 129–131 °C (from Pr^i_2O) (Found: C, 63.3; H, 7.2. $C_{15}H_{21}FSO_2$ requires C, 63.38; H, 7.39); $[\alpha]_D^{20}$ +216° (*c* 1.0, $CHCl_3$). ^1H NMR data are reported in Table 2.

The same procedure, applied to (2*S*,3*S*,5*R*,R_S)-**6**, afforded, after flash chromatography of the residue (hexane–ethyl acetate, 3:2), *compound* (2*S*,3*S*,R_S)-**8** (0.99 g, 90%), m.p. 97–99 °C (from Pr^i_2O) (Found: C, 62.9; H, 7.3%); $[\alpha]_D^{20}$ +248° (*c* 1.0, $CHCl_3$). ^1H NMR data are reported in Table 2.

* Non-systematic nomenclature, retained to provide consistency in numbering schemes of the ring systems.

Synthesis of (2R,3R)- *and* (2R,3S)-3-*Fluoro*-2-*hydroxymethyl*-6,6-*dimethyltetrahydropyran* * **11**.—To a solution of (2*S*,3*R*,R_S)-**8** (0.47 g, 1.65 mmol) and 2,4,6-trimethylpyridine (0.44 cm^3, 3.30 mmol) in acetonitrile (15 cm^3) at −20 °C was added dropwise a solution of TFAA (0.34 cm^3, 2.48 mmol) in THF (4 cm^3). After the starting product had been completely consumed (TLC; hexane–ethyl acetate, 3:2) solid K_2CO_3 (to pH 7–8) and a solution of mercury(II) chloride (0.62 g, 2.30 mmol) in acetonitrile (4 cm^3) were added to the reactants at 0 °C and the reaction mixture was stirred at the same temperature for 2 h. The white, precipitated mercury(II) sulphide was then filtered off, the solution was cooled at 0 °C and a suspension of $NaBH_4$ (0.14 g, 3.30 mmol) in acetonitrile (10 cm^3) was added dropwise at the same temperature. Acetic acid was then added to pH 3–4, acetonitrile was evaporated off under reduced pressure, the residue was diluted with ethyl acetate–water, and the organic phase was separated. Flash chromatography (hexane–ethyl acetate, 3:7) gave *compound* (2*R*,3*R*)-**11** (0.15 g, 55%), m.p. 36–37 °C (from Et_2O) (Found: C, 59.2; H, 9.1. $C_8H_{15}FO_2$ requires C, 59.26; H, 9.26%); $[\alpha]_D^{20}$ +11° (*c* 0.7, $CHCl_3$). ^1H NMR data are reported in Table 2.

The same procedure, applied to (2*S*,3*S*,R_S)-**8** gave, after flash chromatography ($CHCl_3$–EtOAc, 3:7) (2*R*,3*S*)-**11** (0.17 g, 64%), m.p. 52–53 °C (from Pr^i_2O) (Found: C, 59.35; H, 9.2%); $[\alpha]_D^{20}$ +59° (*c* 1.0, $CHCl_3$); $[\alpha]_{Hg365}^{20}$ +173° (*c* 1.0, $CHCl_3$). ^1H NMR data are reported in Table 2.

* See note on p. 1321.

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