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On the Synthesis of Optically Pure Monofluorocyclohexanol Derivatives by the Fluorinated Sulfoxide Chiron Route

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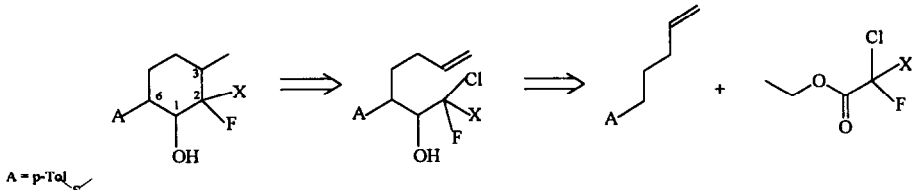
Abstract: *Monofluorocyclohexanols 1 are obtained in optically pure form through radical cyclization of gem-chlorofluoroheptenols 2 which derive from the condensation of α-lithium derivative of sulfoxide 3 on racemic ethyl chlorofluoroacetate 4, and hydride-promoted reduction of the intermediate ketones 5. Some considerations on the stereochemical course of the radical promoted cyclization reaction follow.*

The synthesis of selectively fluorinated chiral molecules is an important area of research.[1] Two routes are generally followed for the construction of target molecules: the stereo controlled fluorination of complex multi-functionalised compounds[2] or the asymmetric total synthesis from fluorinated chirons[3]. Microbial transformations of easily available prochiral fluorinated substrates or reactions of chiral reagents on simple prochiral fluorine-containing substrates to generate fluorinated molecules bearing a chiral auxiliary group have been utilised to prepare the required fluorinated chirons.[4]

Scheme 1



1 : X=H **2** : X=H **3** **4** : X=H

1' : X=F **2'** : X=F **4'** : X=F

1": X=Cl **2"**: X=Cl **4"**: X=Cl

In previously reported studies some *gem*-difluoro **1'**,[5] as well as some *gem*-chlorofluoro multi-functionalised cyclohexane derivatives **1"**,[6] have been synthesized by the second route (Scheme 1). In those cases the key step for the construction of the carbocyclic framework has been the intramolecular trapping of α-fluoroalkyl radicals deriving from chlorodifluoro-**2'** and dichlorofluoroheptenols **2"**, respectively, on the terminal vinyl group. Monofluorocyclohexanols **1** had been obtained from **1"** through reductive dechlorination reaction at the geminally chlorofluoro-substituted carbon atom, or from **2"** through a one-step process of intramolecular radical cyclization and reductive dechlorination[6].

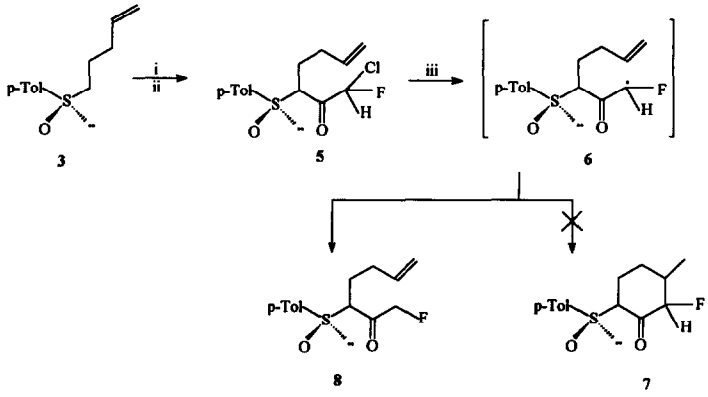
In the present paper, monofluorocyclohexane derivatives **1** have been synthesized through intramolecular trapping of monofluoroalkyl radicals obtained from *gem*-chlorofluoroheptenols **2**, which derived from the condensation of α-lithium derivative of sulfoxide **3** on racemic ethyl chlorofluoroacetate **4** and the hydride-promoted reduction of the thus formed intermediate ketones **5**. The herewith described procedure differs from those previously reported because the radical is generated on a carbon containing hydrogen and fluorine and we were interested in checking if a different asymmetric induction in respect with those previously described could be achieved for newly formed stereocenters.

Results and Discussion

The required substrates **5** and **2** for the radical cyclization were obtained as usual. The lithium derivative of 5-[(4-methylphenyl)sulfinyl]pent-1-ene (**3**) was reacted with racemic ethyl chlorofluoroacetate (**4**) in tetrahydrofuran (THF) at -60°C. The β-ketosulfoxide **5** was obtained in pure form after flash chromatography as a mixture of diastereoisomers (80% overall yield) (Scheme 2).

Four diastereoisomers were expected to be formed, because a new stereogenic carbon atom was created during the carbon-carbon forming reaction and racemic ethyl chlorofluoroacetate was used. In order to obtain a mixture enriched in a single diastereoisomer, the mono-anion α to the sulphinyl group or the α,γ-bis-anion were generated in basic conditions and some different quenching procedures followed to give back compounds **5**. As shown by NMR analyses performed on crude mixtures, only minor changes in the ratio of the diastereoisomers were achieved; anyway, a single diastereoisomer was always prevailing (see Experimental).

Scheme 2

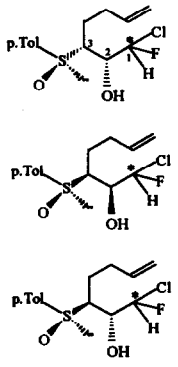


i) LDA, THF, -60 °C; ii) **4**, THF, -78 °C; iii) Bu_3SnH, hν, benzene, 35 °C.

We expected the fluorocyclohexanone derivatives **7** to be obtainable through the radical-promoted cyclization methodology applied directly to the diastereoisomeric mixture of **5** (Scheme 2) and to equilibrate the formed diastereoisomers through basic treatment of ketones **7**. For this purpose, the crude mixture of ketones **5** was treated with tributyltin hydride in benzene under UV light irradiation. Unfortunately, only the mixture of the corresponding open-chain α-fluorocarbonyl compounds **8** formed in moderate yield through reduction of the intermediate radical **6**. As a consequence, we decided to reduce chlorofluoroketones **5** to the corresponding secondary alcohols **2**, although this procedure would produce a more complex mixture of diastereoisomers from which single ones should be separated. The crude mixture of ketones **5** was reduced both with sodium borohydride in methanol/aqueous ammonia solution and with diisobutyl aluminium hydride (DIBAL-H) in THF. In both cases, the secondary alcohols **2** were obtained in high yields and in a different relative ratio, depending on the experimental conditions adopted, as shown by HPLC analyses (see Experimental). To obtain single diastereoisomers **2**, reported on Figure 1, the mixture was submitted to flash chromatography on silica gel.

Fractional crystallization of eluted fractions followed. Derivatization with (*S*)-(+)-**2**-phenylpropionic acid (PPA) of some enriched fractions, separation by flash chromatography of the corresponding PPA esters **14** followed by basic hydrolysis furnished four optically pure alcohols: both (1*R/S*,2*R*,3*R*,R_S)- and both (1*R/S*,2*S*,3*S*,R_S)-**2**. The absolute configuration at C-1 carbon was not determined because it would have been lost during the following radical cyclization process.

Figure 1

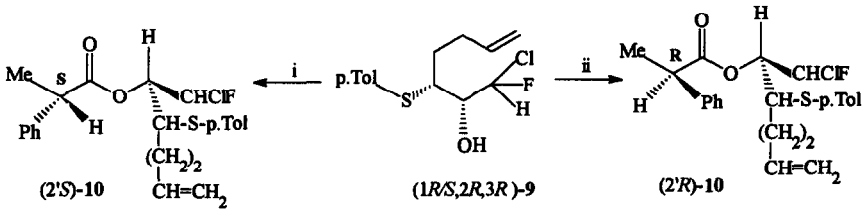


Compounds **2**	^{19}F NMR, δ	R_t, min.	R_F
1*R/S*,2*R*,3*R*,R_S	- 147.73	10.74	0.29
1*R/S*,2*R*,3*R*,R_S	- 147.46	11.18	0.29
1*R/S*,2*S*,3*S*,R_S	- 144.24	13.11	0.23
1*R/S*,2*S*,3*S*,R_S	- 147.94	14.31	0.23
1*R/S*,2*R*,3*S*,R_S	- 144.50	20.31	0.19
1*R/S*,2*R*,3*S*,R_S	- 144.54	21.60	0.19

The absolute configuration of the hydroxyl-bearing carbon of the four above mentioned diastereoisomers **2** was established as usual[7] by ^1H NMR studies performed on (*R*)-(-) and (*S*)-(+)-PPA esters **10**. In fact, for the (1*R/S*,2*R*,3*R*,R_S)-**2** pair, the protons of the pentenyl chain of (2'*S*)-**10** showed an up field shift (Δδ = 0.07 - 0.36 ppm) with respect to the corresponding protons of the (2'*R*)-**10** epimer, as a consequence of the shielding effect exerted by the phenyl group of the esterifying acid in the preferred conformation shown in Figure 2. An opposite behaviour was observed for the esters **10** obtained reacting the remaining pair of alcohols **2** with (*S*)-(+)- and (*R*)-(-)-PPA, thus indicating as *S* the absolute configuration at C-2. Another couple of heptenols, (1*R/S*,2*R*,3*S*,R_S)-**2**, was isolated as a one to one C-1 epimeric mixture. The chirality at C-2 and C-3 was readily assigned because they afforded, *inter alia*,[8] the same cyclic derivatives (1*S*,2*R*,3*R/S*,6*S*,R_S)-**1** obtained from the

corresponding dichlorofluoro analogs *via* dechlorination of the intermediate cyclohexanol (1*R*,2*S*,3*R*/*S*,6*S*,R_S)-**1''**, as already described.[6b]

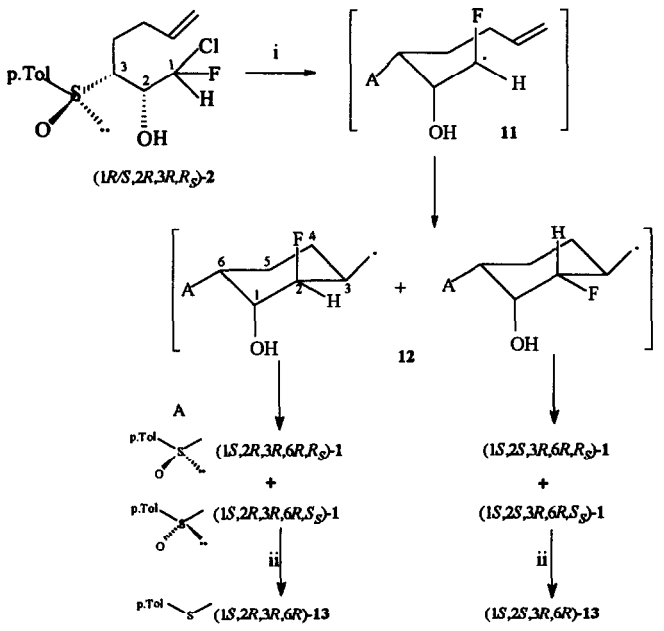
Figure 2



i) 4-DMAP, (*S*)-(+)-PPA, DCC, CH_2Cl_2, r.t.; ii) 4-DMAP, (*R*)-(-)-PPA, DCC, CH_2Cl_2, r.t.

Radical Cyclization Process. Heptenols **2** were treated with an excess of tributyltin hydride in degassed benzene. The energy required for bond breaking was supplied by irradiating the solution with a mercury discharge lamp with significant emission at 300 nm. The whole radical chain process was as shown in Scheme 3 for (1*R*/*S*,2*R*,3*R*,R_S)-**2**: hydrogen abstraction from tributyltin hydride generates a tributyltin radical, which through chlorine abstraction from the chlorofluoroalkyl group produces the fluoroalkyl radical **11**. This reactive electrophilic radical is intramolecularly trapped by the terminal vinyl group in a fast *exo-trig* cyclization, giving primary cyclohexylmethyl radicals **12** that, in turn, abstract a hydrogen atom from the stannane affording the products **1** and a tributyltin radical that propagates the chain reaction.

Scheme 3



i) Bu_3SnH, hv, benzene, 35 °C; ii) NaI, $(CF_3CO)_2O$, acetone, -40°C.

The open chain compounds **2** submitted to cyclization and the obtained fluorocyclohexanols **1** are reported in Table 1. From optically pure (1*R*/*S*,2*R*,3*R*,R_S)-2 (δ_F - 147.73), four cyclohexanols were formed (entry 1), but, surprisingly, two of them, (1*S*,2*R*,3*R*,6*R*,S_S)- and (1*S*,2*S*,3*R*,6*R*,S_S)-**1**, had opposite chirality at the sulphur atom since they showed ^1H and ^{19}F NMR spectra (Tables 2 and 3) identical with those exhibited by the known cyclohexanols (1*R*,2*S*,3*S*,6*S*,R_S)- and (1*R*,2*R*,3*S*,6*S*,R_S)-**1**[6] and opposite optical rotatory measurement values[9]. The stereochemistry of the remaining two cyclohexanols **1** was established as (1*S*,2*R*,3*R*,6*R*,R_S) and (1*S*,2*S*,3*R*,6*R*,R_S) because they gave, upon deoxygenation, the same pair of thio derivatives **13** obtained from the above-cited C-2 epimers (S_S)-**1**. Therefore, they must differ each other only in the chirality at the fluorinated C-2 carbons. Comparable results were observed from the optically pure (2*S*,3*S*)-**2** alcohols: four cyclohexanols were formed in both the examples (entries 2 and 3), the F_{ax}/F_{eq} ratio being similar and the only difference being the degree of the racemization at the sulphinyl sulphur atom, *i.e.* the (R_S)/(S_S) ratio. The stereochemical determination on these compounds was straightforward, since they presented identical ^1H and ^{19}F NMR spectra with those exhibited by the enantiomeric products of entry 1.

From the one to one 1*R* to 1*S* mixture of (2*R*,3*S*)-**2** (entry 4), eight products were formed, four of them being here again the corresponding products of epimerization at sulphur. As already mentioned, two of the main products, (1*S*,2*R*,3*R*,6*S*,R_S)- and the (3*S*)-**1** analogue, were identified by comparison with known compounds,[6b] while the stereochemistry of the two remaining cyclohexanols was assigned as (1*S*,2*S*,3*S*,6*S*,R_S) and (1*S*,2*S*,3*R*,6*S*,R_S) by inspection of appropriate ^1H, ^1H and ^1H, ^{19}F coupling constants. In fact, the values exhibited by H-1β, H-6α (10.0 and 10.1 Hz), H-5β, H-6α (11.0 and 11.5 Hz), H-1β, F-2α (29.0 and 27.0 Hz) and H-3, F-2α (34.5 and 11.5 Hz) indicate that the two cyclohexane rings preferentially assume a chair conformation in which the hydroxyl and the p.tolylsulphinyl groups are *trans* diequatorially disposed and H-3 and F-2α are, respectively, *trans* diaxially and *gauche* disposed.

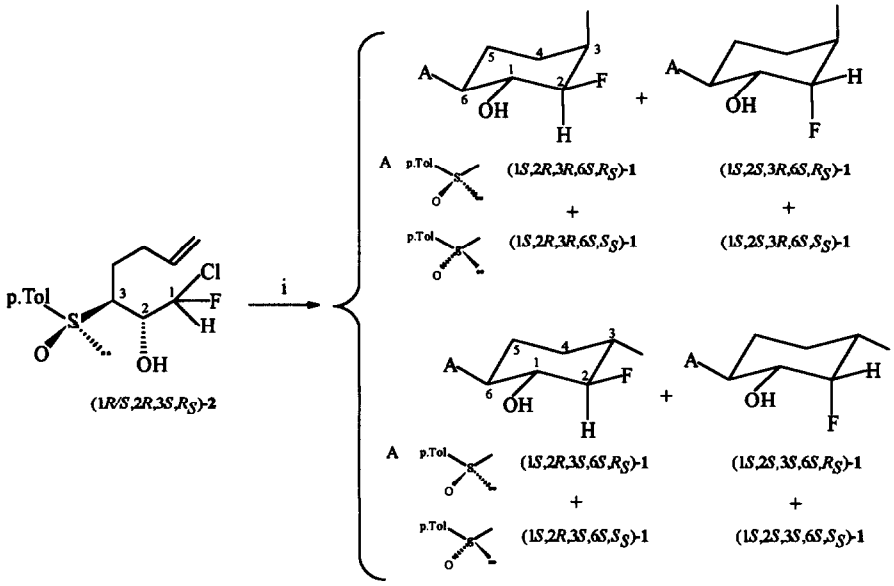
Table 1. Ratios and chemical yields of fluorocyclohexanols **1**.

Entry	Substrates **2** (^{19}F, δ)	Products **1**			Fax/Feq[a]	R_S/S_S Global ratio
		Carbon atom stereochemistries	Yield (%)			
			R_S	S_S		
1	1*R*/*S*,2*R*,3*R*,R_S (- 147.73)	1*S*,2*R*,3*R*,6*R*	33	14	2.5 : 1.0	2.1 : 1.0
		2*S*	12	7		
2	1*R*/*S*,2*S*,3*S*,R_S[b] (- 144.24)	1*R*,2*S*,3*S*,6*S*	25	16	2.1 : 1.0	1.3 : 1.0
		2*R*	9	11		
3	1*R*/*S*,2*S*,3*S*,R_S[c] (- 147.46)	1*R*,2*S*,3*S*,6*S*	20	20	2.0 : 1.0	1.0 : 1.2
		2*R*	7	13		
4	1*R*/*S*,2*R*,3*S*,R_S (- 144.50 /- 144.54)	1*S*,2*R*,3*R*,6*S*	14	2.5	1.0 : 1.0	5.7 : 1.0
		2*S*,3*R*	16	3		
		2*R*,3*S*	18	3		
		2*S*,3*S*	17	3		

[a]Referred to *threo/erythro* relationship with sulphinyl group. [b]Epimer at all carbons in respect to substrate of entry 1.

[c]Epimer at C-1 in respect to substrate of entry 2.

Scheme 4



i) Bu_3SnH, hv, benzene, 35 °C;

Some considerations could arise from the observed stereochemistries of the products **1**. First of all, entries 1, 2 and 3 show that the fluoroalkyl radical must approach the vinyl group through a folded-chain conformation to give the chair-like intermediate **11**, having the bulkier sulfinyl substituent in a *quasi*-equatorial position. In order to avoid 1,3-diaxial interactions[10] with *pseudo*-axial hydroxyl group, the incoming methyl group should choose a *pseudo*-equatorial orientation as shown on Scheme 3. Second, final compounds having the fluorine atom axially disposed, were predominant in respect with those having the fluorine equatorially disposed, their relative ratio being 2.5:1.0. and 2.1 : 1.0. The main diastereoisomers so obtained showed a 1,2-*cis* relationship between fluorine atom and methyl group. It is interesting to remind that compounds **1** obtained through reductive dechlorination of the corresponding *gem*-chlorofluoro derivatives **1"** and having the same C-1/C-6 relative stereochemistry, showed a preferential 1,2-*trans* relationship between the same groupings[6].

On the other hand, when substrates **2**, having a *threo* relationship between sulphinyl and hydroxyl groups were submitted to cyclization (entry 4), a lower diastereoselection was observed in the formation of the C-3 stereogenic centre, because the 1,3-diaxial interaction was lost in the intermediate analogue of **11**. Moreover, cyclohexanols **1** having the fluorine atom axially disposed were formed in similar ratio to the fluorine-equatorially-disposed ones.

In all examined cases, a certain degree of epimerization at sulphur occurred during the cyclization process. Though the photoracemization of sulfoxides is a well-known event,[11] any epimerization at sulphur had never been observed during cyclization of difluoroalkyl **2'** and chlorofluoroalkyl **2"** radicals. Probably, in the present case, the pyramidal inversion[11c] of sulfoxides occurred during the cyclization process involving the excited radical **11**. It differs from those already described,[6] leading to structures **1'** and **1"**, for the presence of the hydrogen atom on the radical carbon: a close approaching of the radical carbon to the stereogenic sulphur

atom may be more favourable in the present case. When the cyclic product (1*S*,2*R*,3*R*,6*R*,R_S)-**1** was submitted to the same reaction conditions employed for radical cyclization, no epimerization at sulphur was observed. Moreover, small amount of unreacted substrates **2**, epimers at sulphur, were isolated from the reaction mixture obtained upon treatment with tributyltin hydride: those observations are consistent with an epimerization event occurring on the reactive radical intermediates.

An intramolecular transfer of energy from the higher-energy-level radical to the sulfinyl group promoted by interactions with an electron lone pair[12] on the oxygen or on the sulphur atom should allow the epimerization process. The observed differences in the epimerization degree starting from (1*R/S*,2*R*,3*S*,R_S)-**2** (entry 4) should be due to a less efficient energy transfer that could result from conformational differences for these diastereoisomers during the cyclization process, or from faster and correspondingly less selective at C-2 ring closure.

Conclusion. Although during the radical cyclization of fluorochloro derivatives **2**, a certain degree of racemization at sulphur is observed, the resulting monofluoro cyclohexanols **1** are obtainable in optically pure form. From a synthetic point of view, this drawback can be overcome: it should be remembered that in further elaboration on derivatives **1**, the sulphinyl sulphur is generally lost.[5,6] It can be focused that the herewith described route and the one that starts from **4"** are complementary because the diastereoisomeric alcohols **2** and **2"**, having an *erythro* relationship between sulfinyl and hydroxyl groups, bring, as main products, to monofluorinated cyclohexanols **1** with identical configuration at the methyl-bearing carbon but opposite stereochemistry at the fluorine-bearing carbon atom.

Experimental

General Details. ^1H and ^{19}F NMR spectra were recorded on a Bruker AC 250L spectrometer; chemical shifts are in ppm (δ), tetramethylsilane 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. $[\alpha]_D$ Values were obtained on a Jasco DIP-181 polarimeter. Melting points are uncorrected and were obtained on a capillary apparatus. Flash chromatographies were performed on silica gel 60 (60-200 μm, Merck) and preparative TLC separations were performed on Merck $60F_{254}$ precoated plates. All reactions were monitored by TLC performed on analytical Merck silica gel $60F_{254}$ TLC plates. Run times were determined on a Waters 600E HPLC instrument, using Lichrosorb Si60 (5 μm) prepacked columns (Merck) and HPLC-grade ethyl acetate and hexane (Merck) as eluents. Tetrahydrofuran (THF) was freshly distilled from lithium aluminium hydride and diisopropylamine was distilled from calcium hydride and stored on 4Å molecular sieves. Benzene was refluxed and distilled from sodium and stored over molecular sieves (4Å); in other cases, commercially available reagent-grade solvents and reagents were employed without purification. The synthesis of compound **3** was already described[13].

Synthesis of 1-Chloro-1-fluoro-3-[(4-methylphenyl)sulfinyl]hept-6-en-2-one (5). A solution of **3** (5.00g, 24.0mmol) in dry THF (25ml) was added dropwise to a stirred solution of lithium diisopropylamide (LDA, 28.8mmol) in THF (20 ml) at -65°C. After 5 min a solution of ethyl chlorofluoroacetate (**4**, 5.10g, 36.1 mmol) in THF (10 ml) was added at the same temperature. After 5 min. the reaction mixture was quenched at -65°C adding a saturated aqueous solution of ammonium chloride (100 ml). The pH was adjusted to *ca.* 3 with 2

N hydrochloric acid, and ethyl acetate was used for extraction (3x50 ml). The combined organic layers were washed with a saturated aqueous solution of sodium chloride and dried over anhydrous sodium sulfate. Evaporation at reduced pressure and flash chromatography of the residue (eluent: 7:3 hexane/ethyl acetate) gave a mixture of the diastereoisomeric ketosulfoxides **5** (80% overall yield) whose HPLC analysis (9:1 hexane/ethyl acetate, 1.0 ml/min) gave: 21.70 min (49%, two broad peaks), 24.23 min (43%) and 27.59 min (8%); ^{1}H NMR ($CDCl_3$): 1.6-2.3 (4H, m, H_2-4 + H_2-5), 2.4-2.5 (3H, brs, CH_3), 4.0-4.5 (1H, m, H-3), 4.9-5.2 (2H, m, H_2-7), 5.5-5.9 (1H, m, H-6), 5.8-6.6 (1H, d,H-1, J~50 Hz), and 7.1-7.6 (4H, m, ArH); ^{19}F: - 147.96, - 148.16, - 149.92, and - 151.35 (1F, d,J~50 Hz, F-1).

Equilibration of the Diastereoisomeric Ketones 5 by Formation of the Corresponding Mono- and Bis-anions. To a stirred solution of the mixture of ketones **5** (50 mg, 0.165 mmol; ^{19}F signal vs ratio: -147.9/-148.2/-149.9/-151.3 = 1.49/1.00/2.49/1.82) in anhydrous THF (5 ml), a solution of LDA (0.198 mmol or 0.397 mmol) in THF (2 ml) was added at once at -70°C. After periods of time varying from 2 min to 30 min the reaction mixture was quenched at *ca.* -50°C adding a saturated aqueous solution of ammonium chloride (10 ml). ^{19}F NMR Analysis of the mixture obtained from mono-anion showed in all cases poor modification of the diastereoisomers ratio. From α,γ-bis-anion quenching, after 2 min, a slightly modified ratio was observed (1.86/1.00/5.05/4.36). Alternatively, to a solution of ketones **5** (50 mg, 0.165 mmol) in THF a solution of LDA (0.297 mmol) in THF was added and quenched in 45 min by slowly adding at *ca.* -30°C a solution of butanol in THF. After the same work-up described above, ^{19}F NMR analysis showed again a slightly modified ratio (2.14/1.00/5.33/4.76).

Attempted Photolytic Radical Cyclization of the Mixture of Ketones 5. A solution of the mixture of ketones **5** obtained as above described (100mg, 0.33mmol) and tributyltin hydride (0.39mmol) in oxygen-free benzene (5ml) in a Pyrex tube was irradiated with a 350 nm lamp in a Rayonet apparatus at 35°C. After evaporation of the solvent, acetonitrile (5ml) was added and the solution was washed with hexane (3x5 ml). Acetonitrile was removed at reduced pressure and the residue was purified by flash chromatography (7:3 hexane/ethyl acetate). After short reaction times (from 30 min to 1 h) ^{1}H and ^{19}F NMR analysis of the purified reaction products revealed the presence of 1-fluoro-3-[(4-methylphenyl)sulfinyl]hept-6-en-2-one **8** (20% yield) along with some unreacted starting material and unidentified decomposition products. After longer reaction times (from 1 hour to 5 hours) only decomposition products could be revealed.

Reduction of the Ketones 5 to the Corresponding Alcohols 1-Chloro-1-fluoro-3-[(4-methylphenyl)sulfinyl]hept-6-en-2-ols (2). *Reduction with Sodium Borohydride.* A suspension of sodium borohydride (69 mg, 1.82 mmol) in 3 ml of a 9:1 (v/v) mixture of methanol and 30% aqueous ammonia was dropped into the mixture of ketones **5** (0.50g, 1.65mmol), dissolved in the same solvent mixture (5ml), at 0°C under nitrogen atmosphere. After 10 min, an aqueous solution of hydrochloric acid was added until pH 4 was reached. After methanol evaporation, extraction with ethyl acetate (3x20ml) and anhydrification, the mixture of diastereoisomeric alcohols **2** (71.5% global yield) was submitted to HPLC and NMR analyses, showing the presence of, respectively, seven peaks and eight products: R_t: 9.68 min; (δ_F: - 142.81 and - 143.53 ppm), 20.0%; 10.74 min (δ_F: - 147.73 ppm), 16.7%; 11.18 min (δ_F:- 147.46 ppm), 10.0%; 13.11 min (δ_F:- 144.24 ppm), 11.2%; 14.31 min (δ_F: - 147.94 ppm), 16.6%; 20.31 min (δ_F: - 144.50 ppm), 18.2%; 21.6 min (δ_F:- 144.54 ppm), 7.0%.

Reduction with DIBAL-H. A 1 *N* solution of DIBAL-H in hexane (12.7ml, 12.7mmol) was added dropwise to a stirred solution of the mixture of ketones **5** (3.2g, 10.6 mmol) in THF (15 ml) at -60°C under

nitrogen. A saturated aqueous solution of ammonium chloride (50ml) was added, pH was adjusted to *ca.* 3 with 2 *N* hydrochloric acid and extraction was performed with ethyl acetate (3x50ml). After washing of the combined organic phases with a saturated aqueous solution of sodium chloride, drying over anhydrous sodium sulphate, and solvent evaporation, by HPLC and NMR analyses of the crude (7:3 hexane/ethyl acetate, 1.0 ml/min) six compounds were detected: δ_F: - 147.73 ppm, 27.0%; - 147.46 ppm, 8.0%; - 144.24 ppm, 27.0%; - 147.94 ppm, 5.6%; - 144.50 ppm, 16.4%; - 144.54 ppm, 16.0%. By TLC (7:3 cyclohexane/ethyl acetate) of the crude only three spots (R_F : 0.29, 0.23 and 0.19) were detectable. By flash chromatography (6:4 cyclohexane/ethyl acetate) the three different fractions (R_F 0.29, 840 mg, solid; R_F 0.23, 726 mg, oil; R_F 0.19, 650 mg, oil; in global yield 70%) were isolated. HPLC analysis showed that each fraction was a mixture of two compounds. R_F 0.29 fraction (3.4:1.0 mixture of R_t 10.74 / R_t 11.18 min) was crystalized (isopropyl ether) giving a 9:1 ratio enriched mixture that was used as starting material for the cyclization reaction (see below). R_F 0.23 fraction (4.8 : 1.0 mixture of R_t 13.11 / R_t 14.31 min) were separated and submitted to cyclization in optically pure form. R_F 0.19 fraction (1.0 : 1.0 mixture of R_t 20.31 / R_t 21.60 min) was used as mixture of the two alcohols epimer at C-1; ^{1}H NMR ($CDCl_3$): 1.4-2.3 (2 x 4H, m, H_2-4 and -5), 2.43 (2 x 3H, brs, ArMe), 2.93 and 3.08 (2 x 2H, m, H-3), 4.21 (2 x 1H, m, H-2), 4.45 and 4.55 (2 x 1H, broad signal, OH-2), 4.8-5.0 (2 x 2H, m, H_2-7), 5.50 (2 x 1H, m, H-6), 6.40 and 6.46 (2 x 1H, dd, J = 50.0 and 5.1 and 49.6 and 5.1 Hz, H-1) and 7.3-7.6 (2 x 4H, m, ArH); ^{19}F ($CDCl_3$): - 144.50 and - 144.54 (2 x 1F, m, F-1).

Isolation of Optically Pure Alcohols 2 Via the Corresponding PPA Esters 14. General Procedure. 4-Dimethylaminopyridine (14.3mg, 0.117mmol) was added to a dichloromethane solution (2.5ml) of the mixture of two alcohols **2** (355mg, 1.17 mmol), (+)-(*S*)-PPA (175µl, 1.28mmol) and dicyclohexylcarbodiimide (264mg, 1.28mmol). After 30 min at room temperature, the dicyclohexylurea was filtered and washed with hexane. The dried residue was purified by flash chromatography (8:2 cyclohexane/ethyl acetate) to give the two diastereoisomeric esters **14** in optically pure form. From (1*R/S*,2*R*,3*R*,*R*$_S$)-**2** couple (R_F = 0.29 in 7/3 cyclohexane/ethyl acetate; ^{19}F: -147.73.and.-147.46), the following esters were obtained: R_F 0.40; ^{1}H NMR ($CDCl_3$): 1.56 (3H,d,J=7.1 Hz,H_3-3'), 1.5 -2.1 (4H,m,H_2-4 and H_2-5), 2.40 (3H,brs,ArCH_3), 2.98 (1H,ddd,J=7.7,4.6 and 2.9 Hz,H-3), 3.79 (1H,q,J=7.1 Hz,H-2'), 4.90 and 4.95 (2H,m,H_2-7), 5.49 (1H,m,H-6), 5.55 (1H,ddd,J=18.3, 3.0 and 2.9 Hz,H-2), 6.06 (1H,dd,J=50.4 and 3.0 Hz,H-1), and 7.5-7.3 (9H,m,ArH); ^{19}F: - 147.26 (1F, brdd, J=50.4 and 18.3 Hz,F-1). R_F 0.35; ^{1}H NMR ($CDCl_3$): 1.56 (3H, d, J=7.1 Hz, H_3-3'), 1.4 - 2.0 (4H, m, H_2-4 and H_2-5), 2.41 (3H, brs, ArCH_3), 2.86 (1H, ddd, J=7.2, 5.1 and 3.7 Hz, H-3), 3.81 (1H, q, J=7.1 Hz,H-2'), 4.85 and 4.93 (2H, m, H_2-7), 5.42 (1H, m, H-6), 5.69 (1H, ddd, J=15.5, 4.3 and 3.7 Hz, H-2), 6.02 (1H, dd, J=49.3 and 4.3 Hz ,H-1), and 7.2 - 7.5 (9H, m, ArH); ^{19}F: - 148.18 (1F, brdd, J=49.3 and 15.5 Hz ,F-1). The same procedure was employed for the (1*R/S*,2*S*,3*S*,*R*$_S$)-**2** couple (R_F = 0.23 in 7/3 cyclohexane/ethyl acetate; ^{19}F: - 144.24 and - 147.94), which was esterified with both (+)-(*S*)- and (-)-(*R*)-PPA. All the four PPA esters **14** were isolated in optically pure form and immediately hydrolysed to obtain the two optically pure alcohols **2**, or deoxygenated to the corresponding thio derivatives **10** (see below).

Saponification of the Esters 14. General Procedure. NaOH (4.4mg, 0.11mmol) was added to a methanolic solution (1 ml) of the ester **14** (40mg, 0.092 mmol) and after 30 min solvent was evaporated, than the crude mixture was dissolved in ethyl acetate (3ml) and washed with 5% aqueous solution of hydrochloric acid (3x3ml). The organic phase was dried as usual and concentrated to give a residue which was purified by flash chromatography (65:35 cyclohexane/ethyl acetate) to give: (1*R/S*,2*R*,3*R*,*R*$_S$)-**2**, R_t 10.74 min. (major isomer); $[\alpha]_D^{20}$ + 203.0 (*c* 0.2, $CHCl_3$); m.p. 82-84 °C (isopropyl ether); ^{1}H NMR ($CDCl_3$): 2.0-2.6 (4H, m,

H_2-4 and H_2-5), 2.44 (3H, br s, Me), 2.79 (1H, dddd, J = 9.9, 3.9, 1.7 and 1.5 Hz, H-3), 4.22 (1H, dddd, J = 11.1, 5.8, 2.1 and 1.5 Hz, H-2), 4.42 (1H, dd, J = 2.1 and 1.7 Hz, OH-2), 5.13 and 5.14 (2H, m, H_2-7), 5.80 (1H, m, H-6), 5.99 (1H, dd, J = 50.4 and 5.8 Hz, H-1), 7.38 and 7.46 (4H, m, Ar-H); ^{19}F NMR ($CDCl_3$): - 147.73 (1F, br dd, J = 50.4 and 11.1 Hz, F-1), and (1*R/S*,2*R*,3*R*,*R*$_S$)-**2**, R_t 11.18 min. (minor diastereoisomer); [α]$_D^{20}$ + 157.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 1.9 - 2.6 (4H,m,H_2-4 and H_2-5), 2.46 (3H,brs,CH_3), 2.73 (1H,dddd,J=9.9, 4.1, 1.5 and 1.4 Hz, H-3), 4.32 (1H,dddd,J=13.1, 6.8,2.0 and 1.5 Hz, H-2), 4.60 (1H,d,J=2.0 Hz, OH-2), 5.12 and 5.13 (2H,m,H_2-7), 5.76 (1H,m,H-6), 5.94 (1H,dd,J=50.9 and 6.8 Hz, H-1), and 7.39 and 7.49 (4H,m,ArH); ^{19}F: - 147.46 (1F,brdd,J=50.9 and 13.1 Hz, F-1). Analogously, the esters of the other alcohols gave: major isomer, (1*R/S*,2*S*,3*S*,*R*$_S$)-**2** (R_t = 13.11 min) which showed: [α]$_D^{20}$ + 256 (*c* 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 1.7-2.0 (4H, m, H_2-4 and -5), 2.44 (3H, brs, ArMe), 2.86 (1H, br signal, OH-2), 2.98 (1H, m, H-3), 4.52 (1H, ddd, J = 9.2, 5.4, and 3.1 Hz, H-2), 4.86 and 4.92 (2H, m, H_2-7), 5.50 (1H, m, H-6), 6.25 (1H, dd, J = 49.7 and 5.4 Hz, H-1), 7.37 and 7.49 (4H, m, ArH); ^{19}F ($CDCl_3$): - 144.24 (1F, dd, J = 49.7 and 9.2 Hz, F-1); and minor isomer (1*R/S*,2*S*,3*S*,*R*$_S$)-**2** (R_t = 14.31 min) which showed ^{1}H NMR ($CDCl_3$): 1.7-2.0 (4H, m, H_2-4 and -5), 2.44 (3H, brs, ArMe), 2.99 (1H, m, H-3), 3.35 (1H, br signal, OH-2), 4.41 (1H, ddd, J = 15.1, 5.3 and 3.2 Hz, H-2), 4.89 and 4.93 (2H, m, H_2-7), 5.51 (1H, m, H-6), 6.20 (1H, dd, J = 50.4 and 5.3 Hz, H-1), 7.37 and 7.51 (4H, m, ArH); ^{19}F ($CDCl_3$): - 147.94 (1F, dd, J = 50.4 and 15.1 Hz, F-1).

Reduction of Sulfinyl Alcohols 2 to the Corresponding Thio Alcohols 1-Chloro-1-fluoro-3-[(4-methylphenyl)thio]hept-6-en-2-ols (9). Trifluoroacetic anhydride (160µl, 1.15mmol) was added dropwise to a solution of (1*R/S*,2*R*,3*R*,*R*$_S$)- **2** (major diastereoisomer, R_t = 10.74 min) (70mg, 0.23mmol) and sodium iodide (103 mg, 0.69 mmol) in acetone (4 ml) at -40°C under nitrogen atmosphere. After quenching with a saturated aqueous solution of sodium sulphite and sodium hydrogen carbonate, acetone was removed and the aqueous layer was extracted with ethyl acetate (3x10ml). The combined organic layers were dried as usual and the solvent was evaporated. Flash chromatography of the residue (9:1 hexane/ethyl ether) gave the thio alcohol (1*R/S*,2*R*,3*R*)-**9** in 90% yield: [α]$_D^{20}$ +23.45 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 1.64 and 1.95 (2H, m, H_2-4), 2.29 and 2.44 (2H, m, H_2-5), 2.34 (3H, br s, Me), 2.48 (1H, d, J = 5.3 Hz, OH-2), 3.16 (1H, br ddd, J = 10.3, 6.0 and 3.3 Hz, H-3), 3.91 (1H, dddd, J = 7.3, 6.0, 5.3 and 4.5 Hz, H-2), 5.02 and 5.08 (2H, m, H_2-7), 5.80 (1H, m, H-6), 6.49 (1H, dd, J = 49.4 and 4.5 Hz, H-1), 7.12 and 7.32 (4H, m, ArH); ^{19}F: -143,58 (1F,brdd,J = 49.4 and 7.3 Hz,F-1); the same procedure,on the minor diastereoisomeric alcohol **2** (R_t = 11.18 min.), gave: ^{1}H NMR ($CDCl_3$): 1.5-2.6 (4H, m, H_2-4 and -5), 2.34 (3H, brs, ArMe), 2.66 (1H, d, J = 4.5 Hz, OH-2), 3.27 (1H, ddd, J = 10.5, 6.1 and 3.2 Hz, H-3), 3.78 (1H, dddd, J = 17.9, 6.1, 4.5 and 4.2 Hz, H-2), 5.02 and 5.08 (2H, m, H_2-7), 5.80 (1H, m, H-6), 6.43 (1H, dd, J = 50.3 and 4.2 Hz, H-1), 7.12 and 7.32 (4H, m, ArH); ^{19}F: - 148.98 (1F, dd, J = 50.3 and 17.9 Hz, F-1).

Synthesis of the Phenylpropionic Esters 10 of Alcohols 9. 4-(Dimethylamino)pyridine (1.3mg, 0.0104mmol) was added to a dichloromethane solution (1.5ml) of the thio alcohol (1*R/S*,2*R*,3*R*)-**9** (30mg, 0.104mmol), (*S*)-(+)-PPA (15.6µl, 0.114 mmol) and dicyclohexylcarbodiimide (23.5mg, 0.114mmol). After 30 min at room temperature the dicyclohexylurea was removed by filtration and washed with hexane. The solvent was evaporated and the residue was flash chromatographed (97:3 hexane/ethyl acetate) to give (*S*)-(+)-2-phenyl propionate **10** of the thio alcohol (1*R/S*,2*R*,3*R*)-**9**: (1*R/S*,2*R*,3*R*,2'*S*)-**10**: ^{1}H NMR ($CDCl_3$): 1.19 and 1.40 (2H, m, H_2-4), 1.52 (3H, d, J = 7.1 Hz, H_3-3'), 2.11 and 2.22 (2H, m, H_2-5), 2.32 (3H, br s, ArMe), 3.07 (1H, ddd, J = 10.2, 7.4 and 3.2 Hz, H-3), 3.78 (1H, q, J = 7.1 Hz, H-2'), 4.92 and 4.93 (2H, m, H_2-7), 5.30 (1H, ddd, J = 9.0, 7.4 and 3.4 Hz, H-2), 5.52 (1H, m, H-6), 6.60 (1H, dd, J = 48.8 and 3.4 Hz, H-1), 7.0-7.4 (9H, m, ArH);

^{19}F: -144.02 (1F, brdd, J = 48.8 and 9.0 Hz, F-1).The reaction performed on the same thio-alcohol **9** by using (*R*)-(-)-2-phenylpropionic acid afforded the diastereoisomeric ester **10**: (1*R/S*,2*R*,3*R*,2'*R*)-**10**: ^1H NMR ($CDCl_3$):1.52 (3H, d, J = 7.2 Hz, H_3-3'), 1.55 and 1.63 (2H, m, H_2-4), 2.32 (3H, br s, ArMe), 2.24 and 2.37 (2H, m, H_2-5), 3.19 (1H, ddd, J = 10.3, 6.5 and 3.4 Hz, H-3), 3.73 (1H, q, J = 7.2 Hz, H-2'), 5.00 and 5.02 (2H, m, H_2-7), 5.29 (1H, ddd, J = 9.2, 6.5 and 3.8 Hz, H-2), 5.69 (1H, m, H-6), 6.47 (1H, dd, J = 48.8 and 3.8 Hz, H-10), and 7.0-7.4 (9H, m, ArH); ^{19}F: -144.46 (1F, br dd, J = 48.8 and 9.2 Hz, F-1). From the minor thio derivative (1*R/S*,2*R*,3*R*)-**9** and (*S*)-(+)-PPA, (1*R/S*,2*R*,3*R*,2'*S*)-**10** was obtained in 95% yield : ^1H NMR ($CDCl_3$): 1.20 and 1.35 (2H, m, H_2-4), 1.55 (3H, d, J = 7.1 Hz, H_3-3'), 2.09 and 2.25 (2H, m, H_2-5), 2.32 (3H, brs, ArMe), 3.10 (1H, ddd, J = 10.2, 8.2 and 3.4 Hz, H-3), 3.83 (1H, q, J = 7.1 Hz, H-2'), 4.89 and 4.90 (2H, m, H_2-7), 5.18 (1H, ddd, J = 20.5, 8.2 and 2.9 Hz, H-2), 5.48 (1H, m, H-6), 6.61 (1H, dd, J = 49.5 and 2.9 Hz, H-1) and 7.0-7.5 (9H, m, ArH); analogously, from (*R*)-(-)-PPA, (1*R/S*,2*R*,3*R*,2'*R*)-**10** was obtained in 90% yield: ^1H NMR ($CDCl_3$): 1.50 and 1.60 (2H, m, H_2-4), 1.57 (3H, d, J = 7.2 Hz, H_3-3'), 2.23 and 2.35 (2H, m, H_2-5), 2.33 (3H, brs, ArMe), 3.20 (1H, ddd, J = 10.2, 7.3 and 3.5 Hz, H-3), 3.83 (1H, q, J = 7.2 Hz, H-2'), 4.99 and 5.00 (2H, m, H_2-7), 5.20 (1H, ddd, J = 19.0, 7.3 and 3.5 Hz, H-2), 5.66 (1H, m, H-6), 6.46 (1H, dd, J = 49.0 and 3.5 Hz, H-1) and 7.0-7.5 (9H, m, ArH).

Reduction of Sulfinyl Esters 14 to the Corresponding Thio Esters 10. *General Procedure.* Trifluoroacetic anhydride (160µl, 1.15mmol) was added to a solution of ester **14** (100mg, 0.23mmol) and sodium iodide (103 mg, 0.69 mmol) in acetone (4 ml) kept at -40°C under nitrogen atmosphere. An excess of a saturated aqueous solution of sodium sulphite and sodium hydrogen carbonate was added, acetone was removed under reduced pressure and the aqueous layer was extracted with ethyl acetate (3x10ml). The combined organic layers were dried as usual and the solvent was evaporated. Flash chromatography of the residue (9:1 pentane/ethyl ether) gave the thio ester **10.** The reaction was performed on the four pure esters (1*R/S*,2*S*,3*S*,*R*$_S$,2'*R/S*)-**14** deriving from alcohols **2** (R_t =13.11 and 14.31 min.). The ^1H NMR spectra of the four esters **10** so obtained were identical to the appropriate thio esters deriving from the (1R/S,2R,3R)-**9** alcohols, this fact implying an enantiomeric relationship at all carbons.

Photolytic Radical Cyclization of 2. General Procedure. Alcohol **2** (97mg, 0.32mmol), in oxygen-free benzene (5 ml), and added of tributyltin hydride (128µl, 0.47mmol) was irradiated in a Pyrex tube for 20 h under a 300 nm lamp in a Rayonet apparatus, at 35°C. Benzene was evaporated, acetonitrile (5ml) was added and the solution was washed with hexane (3x5ml). After acetonitrile removal, flash chromatography of the residue (cyclohexane/ethyl acetate varying from 7:3 to 4:6) or purification by using precoated silica gel plates (layer thickness 0.5-2.0 mm), from (1*R/S*,2*R*,3*R*,*R*$_S$)-**2**, the four obtained cyclohexanols were separated in optically pure form: (1*S*,2*R*,3*R*,6*R*,*R*$_S$)-**1** (70mg, 33%yield); R_F (6:4 cyclohexane/ethyl acetate) 0.32; $[\alpha]_D^{20}$ + 57.0° (*c* 0.2, $CHCl_3$); m.p. 170-173°C (isopropylether); (1*S*,2*R*,3*R*,6*R*,*S*$_S$)-**1** (30mg, 14%yield); R_F (6:4 cyclohexane/ethyl acetate) 0.22; $[\alpha]_D^{20}$ - 42.3 (*c* 0.3, $CHCl_3$); (1*S*,2*S*,3*R*,6*R*,*R*$_S$)-**1** (25mg, 12%yield); R_F (6:4 cyclohexane/ethyl acetate) 0.15; $[\alpha]_D^{20}$ + 150.0 (*c* 0.2, $CHCl_3$); (1*S*,2*S*,3*R*,6*R*,*S*$_S$)-**1** (15mg, 7%yield); R_F (6:4 cyclohexane/ethyl acetate) 0.125; $[\alpha]_D^{20}$ - 67.1 (*c* 0.2, $CHCl_3$), along with: (1*R/S*,2*R*,3*R*,*S*$_S$)-**2** (20mg, 7%yield); R_F (6:4 cyclohexane/ethyl acetate) 0.38 ; $[\alpha]_D^{20}$ - 249.0 (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): 1.2 - 2.0 (4H, m, H_2-4 and H_2-5), 2.44 (3H, brs, CH_3), 2.98 (2H, m, H-3 and OH-2), 4.51 (1H, m, H-2), 4.85 and 4.91 (2H, m, H_2-7), 5.50 (1H, m, H-6), 6.25 (1H, dd,J = 49.7 and 5.5 Hz, H-1), 7.36 and 7.50 (4H, m, ArH); ^{19}F: -144.24 (1F, brdd, J = 49.7 and 18.2 Hz,F-1), (2*R*,3*R*,*R*$_S$)-1-fluoro-3-[(4-methylphenyl)sulfinyl]hept-6-en-2-ol **15** (22mg, 10.3%yield), and traces of unreacted starting material. ^1H And ^{19}F NMR data of cyclohexanols **1**

Table 2· Selected ^{1}H and ^{19}F NMR chemical shifts (δ) of cyclohexanols **1** and **13**

	(1*S*,2*R*,3*R*,6*R*,R_S)-**1**	(1*S*,2*R*,3*R*,6*R*,S_S)-**1**	(1*S*,2*S*,3*R*,6*R*,R_S)-**1**	(1*S*,2*S*,3*R*,6*R*,S_S)-**1**	(1*S*,2*R*,3*R*,6*R*)-**13**	(1*S*,2*S*,3*R*,6*R*)-**13**
H-1	4.35	4.68	4.64	4.03	3.82	4.04
H-2	4.33	4.51	3.83	3.87	4.58	3.96
H-3	2.08	2.03	2.25	2.15	1.95	2.14
H-4α	1.68	1.55	1.86	1.93	1.53	~1.75
H-4β	1.42	1.23	0.96	0.97	1.45	1.04
H-5α	2.40	2.02	2.09	2.05	1.66	~1.75
H-5β	1.89	1.18	1.45	1.92	1.77	~1.75
H-6	2.51	2.69	2.35	2.45	3.40	3.04
H-7	0.98	0.98	1.01	1.01	1.01	1.01
OH	5.07	4.26	3.53	2.61	2.64	2.48
F	-207.86	-207.74	-190.49	-190.67	-208.76	-188.38

Table 3. Selected NMR coupling constants (J/Hz) of cyclohexanols **1** and **13**

	(1*S*,2*R*,3*R*,6*R*,R_S)-**1**	(1*S*,2*R*,3*R*,6*R*,S_S)-**1**	(1*S*,2*S*,3*R*,6*R*,R_S)-**1**	(1*S*,2*S*,3*R*,6*R*,S_S)-**1**	(1*S*,2*R*,3*R*,6*R*)-**13**	(1*S*,2*S*,3*R*,6*R*)-**13**
H-1,H-2	4.0	4.2	2.7	2.8	3.9	2.7
H-1,H-6	2.1	2.0	2.1	2.2	2.5	1.5
H-1,OH	1.7	1.5	2.0	1.7	1.8	a
H-2,H-3	1.9	1.8	10.7	10.7	2.2	10.8
H-3,H-4α	4.5	4.6	4.2	4.3	4.7	a
H-3,H-4β	12.7	12.3	12.5	13.0	12.1	a
H-3,H-7	7.0	6.7	6.5	6.5	7.0	6.5
H-4α,H-5α	4.0	4.0	4.2	4.0	4.0	a
H-4β,H-5α	13.3	13.0	13.3	13.0	12.8	a
H-5α,H-6	13.5	13.0	13.3	12.6	12.4	10.5
H-5β,H-6	3.4	3.7	4.1	4.4	4.5	a
H-1,F	5.2	3.5	9.1	8.7	5.0	9.5
H-2,F	47.1	47.0	46.8	46.6	46.8	47.0
H-3,F	38.6	38.5	8.5	8.5	38.2	a

[a] Not determined.

are reported in Tables 2 and 3. The global yield of the cyclization reaction resulted 66%. From (1*R/S*,2*S*,3*S*,*R*$_S$)-**2** (R_t 13.11 min) the four obtained cyclohexanols were analysed in mixture: (1*R*,2*S*,3*S*,6*S*,*R*$_S$)-**1** was obtained in 25%, (1*R*,2*S*,3*S*,6*S*,*S*$_S$)-**1** in 16%, (1*R*,2*R*,3*S*,6*S*,*R*$_S$)-**1** in 9% and (1*R*,2*S*,3*S*,6*S*,*S*$_S$)-**1** in 11% yield (60% global yield). The stereochemical attributions were made on the basis of the ^1H, ^{19}F NMR and analytical data in comparison with the products **1** obtained from (1*R/S*,2*R*,3*R*,*R*$_S$)-**2**. The same procedure was followed for the four products deriving from (1*R/S*,2*S*,3*S*,*R*$_S$)-**2** (R_t 14.31 min.) (see Table 1). From the mixture of the two C-1 epimers (1*R/S*,2*R*,3*S*,*R*$_S$)-**2**, eight products were obtained (65% global yield) and four of them were isolated in optically pure form. Among them, (1*S*,2*R*,3*S*,6*S*,*R*$_S$)-**1** (18% yield) and (1*S*,2*R*,3*R*,6*S*,*R*$_S$)-**1** (14% yield) presented spectroscopical, analytical and chemico-physical data identical to those of the same already described compounds;[6b] the remaining two showed the following properties: (1*S*,2*S*,3*R*,6*S*,*R*$_S$)-**1** (16% yield) $[\alpha]_D^{20}$ + 23.8 (*c* 0.2, $CHCl_3$); m.p. 172-174°C (isopropyl ether); ^1H NMR ($CDCl_3$): 0.93 (3H, d, J = 7.5 Hz, H_3-7), 1.1-1.9 (4H, m, H_2-4 and -5), 2.28 (1H, m, H-3), 2.43 (3H, brs, ArMe), 2.88 (1H, brddd, J = 11.5, 10.1 and 4.0 Hz, H-6), 3.66 (1H, d, J = 6.5 Hz, OH-1), 4.11 (1H, dddd, J = 27.0, 10.0, 6.5 and 2.3 Hz, H-1), 4.68 (1H, ddd, J = 49.6, 4.0 and 2.3 Hz, H-2), 7.33 and 7.47 (4H, m, ArH); ^{19}F: - 194.89 (1F, brddd, J = 49.6, 27.0 and 11.5 Hz, F-2); and (1*S*,2*S*,3*S*,6*S*,*R*$_S$)-**1** (17% yield) showed: $[\alpha]_D^{20}$ + 50.6 (*c* 0.2, $CHCl_3$) and ^1H NMR ($CDCl_3$): 1.12 (3H, d, J = 6.6 Hz, H_3-7), 1.1-1.8 (5H, m, H-3, H_2-4 and -5), 2.42 (3H, brs, ArMe), 2.88 (1H, brddd, J = 11.0, 10.0 and 5.8 Hz, H-6), 3.90 (1H, brs, OH-1), 3.93 (1H, m, H-1), 4.68 (1H, brd, J = 51.7 Hz, H-2), 7.34 and 7.46 (4H, m, ArH); ^{19}F: - 217.60 (1F, brddd, J = 51.7, 34.5 and 29.0 Hz, F-2). The ^{19}F NMR signals of the remaining four cyclohexanol derivatives **1**, having opposite chirality at the sulphur atom, resonated at δ: - 190.45 (brd, $J_{F,H}$ = 53.6 Hz), - 190.70 (brd, $J_{F,H}$ = 49.0 Hz), - 193.87 (ddd, J = 48.8, 22.8 and 11.2 Hz), - 216.78 (ddd, J = 51.3, 34.2 and 27.3 Hz).

Attempted Epimerization at Sulphur of (1S,2R,3R,6R,R$_S$)-1. A solution of the cyclohexanol (1*S*,2*R*,3*R*,6*R*,*R*$_S$)-**1** (2.3mg, 0.0085mmol) and tributyltin hydride (3.4 μl, 0.0128mmol) in oxygen-free benzene was introduced in a Pyrex tube and irradiated for 21 h as above described. By TLC (6:4 cyclohexane/ethyl acetate) only unchanged starting cyclohexanol **1** was detected.

Deoxygenating of Sulfinyl Cyclohexanols 1 to the Corresponding Thio Cyclohexanols 13. To a solution of cyclohexanol (1*S*,2*R*,3*R*,6*R*,*R*$_S$)-**1** (16mg, 0.059 mmol) and sodium iodide (35mg, 0.236mmol) in acetone (3ml) at -40°C under nitrogen atmosphere, a solution of trifluoroacetic anhydride (50μl, 0.354mmol) in the same solvent (0.5ml) was added. Quenching and work-up were performed as previously described, giving 13.5 mg (89.6% yield) of pure thio cyclohexanol (1*S*,2*R*,3*R*,6*R*)-**13**: $[\alpha]_D^{20}$ + 57.6 (c 1.0, $CHCl_3$), ^1H and ^{19}F NMR data are reported in Tables 2 and 3. On (1*S*,2*R*,3R,6*R*,*S*$_S$)-**1** the corresponding thio cyclohexanol **13** was obtained: $[\alpha]_D^{20}$ + 56.2 (*c* 0.8, $CHCl_3$) and superimposable ^1H and ^{19}F NMR spectra. Starting from the epimeric couple (1*S*,2*S*,3*R*,6*R*,*R*$_S$)- and (*S*$_S$)-**1**, (1*S*,2*S*,3*R*,6*S*)-**13** was the common product obtained: $[\alpha]_D^{20}$ + 26.1 (*c* 1.2, $CHCl_3$) from (*R*$_S$)-**1** and $[\alpha]_D^{20}$ + 25.2 (*c* 0.8, $CHCl_3$) from (*S*$_S$)-**1**. Both thio-cyclohexanols showed identical ^1H and ^{19}F NMR spectra (see Table 2 and 3). The same reaction was performed on the open-chain alcohol (1*R/S*,2*R*,3*R*,*S*$_S$)-**2** (see above). The thio alcohol showed identical physical and spectroscopic properties in respect with the thio alcohol (1*R/S*,2*R*,3*R*)-**9** *i.e.* $[\alpha]_D^{20}$ + 25.4 (*c* 1.2, $CHCl_3$) along with superimposable ^1H and ^{19}F NMR spectra.

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