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## On the Preparation of Disymmetrized Tris(Hydroxymethyl) Methanol Equivalents

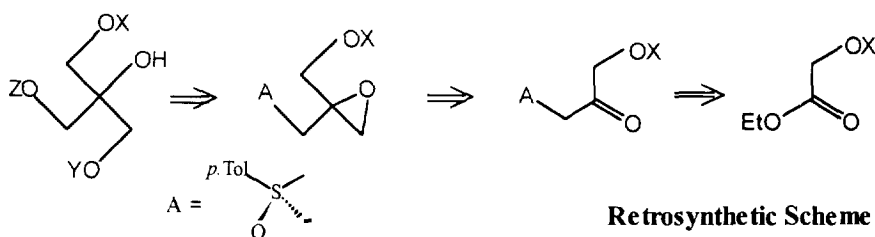
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**Abstract:** Synthetic equivalents, 1,1-bis-hydroxymethyl methylene oxides **7**, **18**, of trisubstituted carbinol derivatives such as the disymmetrized tetrahedral tris(hydroxymethyl) methanol **17** have been obtained in enantiomerically pure form from (*R*)-methyl-*p*-tolylsulfoxide, glycolic acid ethyl ester and diazomethane.

Optically active tertiary alcohols are widespread structural units in natural substances of biological significance.<sup>1</sup> However, the number and availability of these chiral units are limited and, as a consequence, substantial efforts are currently devoted to their synthesis by both biological<sup>2</sup> and chemical methods.<sup>3</sup>

Compounds showing a  $C_{3V}$  structural symmetry are highly desirable for their versatility as chiral synthons. In fact, they can in principle give rise to different structures in both enantiomeric forms depending on the sequence order followed in using the appropriate reagents on any single arm of the molecule<sup>4</sup>. We thought it would be possible to synthesise a  $C_{3V}$  structure unit for the synthesis of chiral tertiary alcohols by the route shown below in the retrosynthetic scheme.



Work in our laboratory on the development of efficient routes for the asymmetric synthesis of selectively fluorinated molecules<sup>5,6</sup> has led to an interesting observation: diazomethane transfers the methylene across the C=O bond of  $\beta$ -keto- $\gamma$ -fluorosubstituted sulfoxides with high efficiency and high facial selectivity to give the corresponding methylene oxides.<sup>7,8</sup>

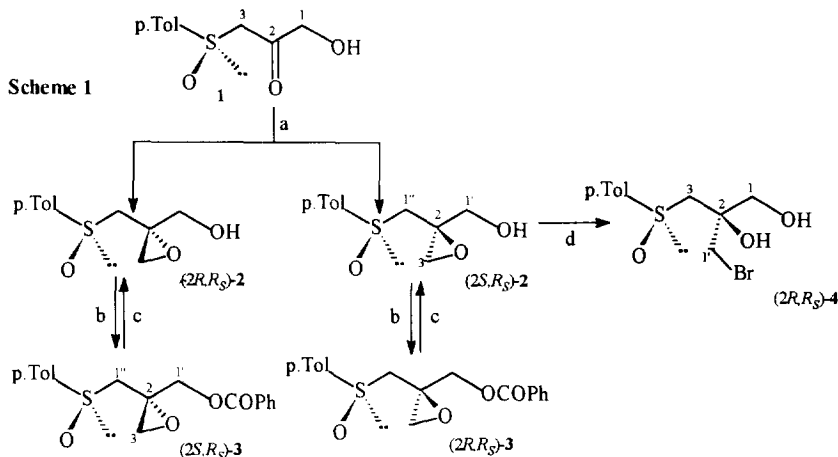
Following procedures similar to those described for fluorinated synthons, both (*R*<sub>S</sub>)- and (*S*<sub>S</sub>)-1-hydroxy-3-*p*-tolylsulfinyl-acetone **1** can be synthesized from glycolic acid and methyl-*p*-tolylsulfoxide. The action of diazomethane on the chiral ketone (*R*<sub>S</sub>)-**1** gives the corresponding methylene oxides **2**, although with lower diastereoselection than on the fluorinated substrates.<sup>8b</sup> Separation of both diastereoisomeric forms, (*2R,R*<sub>S</sub>)- and (*2S,R*<sub>S</sub>)-**2**, and elaboration at the carbon bearing the chiral auxiliary sulfinyl group afforded the corresponding methylene oxides, synthetic equivalents of the title compound, tris(hydroxymethyl)methanol derivatives, as shown in the Retrosynthetic Scheme.

## RESULTS AND DISCUSSION

The ethyl ester of the glycolic acid was used as starting material: the reaction with two moles of the lithium derivative of (*R*)-methyl-*p*-tolylsulfoxide gave (*R<sub>S</sub>*)-1-hydroxy-3-*p*-tolylsulfinyl-propan-2-one **1** in 70% isolated yield.

The carbon skeleton of the target compounds was completed by reacting diazomethane on the ketone moiety. An ether solution of the reagent was added dropwise to both methanolic and ether solutions of **1**. The reaction occurred smoothly but with low diastereoselection, giving mixtures of oxiranes (*R*)/(*S*)-**2** in a comparable ratio (1.0 : 2.3 in methanol and 1.0 : 2.9 in diethyl ether).

The two diastereoisomers could not be easily separated, neither by fractional crystallization nor chromatography. Among the attempts of derivatization of the hydroxyl moiety with different protecting groups to obtain separable compounds [trimethylsilyl chloride, dimethyl-*t*-butyl silyl chloride, benzyl bromide to give the corresponding ethers, benzoic acid and both (*R*)- and (*S*)-phenylpropionic acids to give the esters], only the esterification with benzoic acid afforded two diastereoisomeric benzoates **3** that could be obtained in enantiomerically pure form by flash chromatography. A basic hydrolysis at controlled pH to avoid the oxirane ring opening allowed enantiomerically pure hydroxymethyl oxiranes (*2R,R<sub>S</sub>*)-**2** and (*2S,R<sub>S</sub>*)-**2** to be obtained deriving, respectively, from esters (*2S,R<sub>S</sub>*)-**3** and (*2R,R<sub>S</sub>*)-**3**, as shown in Scheme 1.



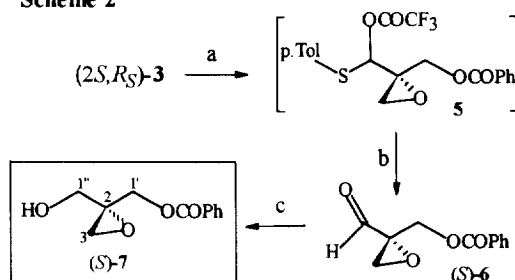
**Reagents and conditions:** a)  $\text{CH}_2\text{N}_2$ , MeOH or  $\text{Et}_2\text{O}$ ; b) DCC, DMAP,  $\text{PhCOOH}$ ,  $\text{CH}_2\text{Cl}_2$ ; c) NaOH, MeOH; d)  $\text{CuBr}_2$ , LiBr, THF,  $0^\circ\text{C}$ .

To establish the absolute configuration of the reported compounds, an X-ray analysis was performed on the bromohydrin **4**, a crystalline stable compound (Scheme 1). Starting from (*2S,R<sub>S</sub>*)-**2** (the minor component of the diastereoisomeric mixture) and using dilithium tetrabromocuprate<sup>9</sup> as a *non*-acidic source of nucleophilic bromine, the compound (*2S,R<sub>S</sub>*)-**4** was obtained in crystalline form from isopropyl ether (see experimental).

It is noteworthy that the stereochemistries at C-2, (*R*) for the main and (*S*) for the minor diastereoisomer **2**, are consistent with the usually observed preference for the diazomethane attacking to one particular face of the starting ketone **1**. In fact, this particular behaviour has been observed for all the examined fluorinated substrates<sup>8b</sup> and also on  $\gamma$ -chloro- and  $\gamma$ -bromo- $\beta$ -keto-sulfoxides.<sup>10</sup>

To obtain the title compounds, the sulfinylmethyl group was transformed into hydroxymethyl *via* a Pummerer rearrangement, directly on the benzoyl-protected oxirane (*2S,R<sub>S</sub>*)-**3**, as shown in Scheme 2. The treatment with trifluoroacetic anhydride in acetonitrile at  $0^\circ\text{C}$  in the presence of *sym*-collidine gave the labile *p*-tolylthio-trifluoroacetoxy intermediate **5**, that was treated *in situ* with mercury(II) chloride to give the enantiomerically pure epoxy aldehyde (*S*)-**6**, isolated in 56% yield.

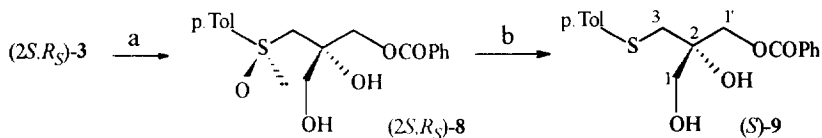
Scheme 2



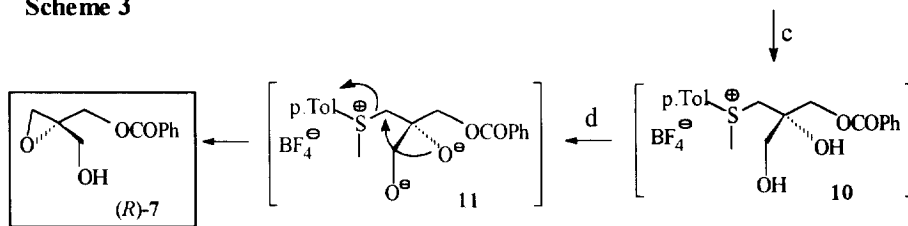
**Reagents and conditions:** a)  $(\text{CF}_3\text{CO})_2\text{O}$ , *sym*-collidine,  $\text{CH}_3\text{CN}$ ; b)  $\text{K}_2\text{CO}_3$ ,  $\text{HgCl}_2$ , 12h; or: r.t., 48h; c)  $\text{H}_2\text{O}$ ,  $\text{NaBH}_4$ .

The same compound (*S*)-6 was obtained from the intermediate 5 without adding any reagents, simply by leaving an acetonitrile solution of 5 under stirring for 48 hours. The spontaneously formed enantiomerically pure epoxy aldehyde 6 was isolated in 66% yield. Performing the same reactions on (*2R,R5*)-3, allowed the enantiomeric (*R*)-6 aldehyde to be obtained in comparable chemical yield.

The reduction of (*S*)-6, performed by adding an acetonitrile/water solution of sodium borohydride to the acetonitrile solution of the epoxy aldehyde, afforded (*S*)-2-benzoyloxymethyl-2-hydroxymethyl oxirane 7 in 85% yield. The enantiomeric purity degree of (*S*)-7 and of its enantiomer, obtained starting from (*R*)-6 and following the same procedure, was checked by  $^1\text{H}$  NMR spectra analyses of the corresponding lanthanide shift reagent complexes and of the (+)-(*S*)-phenylpropionic acid esters (see experimental).



Scheme 3



**Reagents and conditions:** a)  $\text{H}_2\text{O}/\text{HClO}_4/\text{THF}$ , r.t.; b)  $\text{NaI}$ ,  $(\text{CF}_3\text{CO})_2\text{O}$ ,  $\text{CH}_3\text{COCH}_3$ ,  $-40^\circ\text{C}$ ; c)  $(\text{CH}_3)_3\text{OBF}_4$ ,  $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{NO}_2$ ; d)  $\text{LiH}$ ,  $\text{DMF}$ .

To transform the same sulfynylmethyl/benzoyloxymethyl oxirane (*2S,R5*)-3 into the enantiomeric (*R*)-7 epoxide, the different reaction sequence shown on Scheme 3 was utilized. Acidic aqueous opening of the oxirane ring to give the sulfanyl diol 8, reduction of the sulfanyl moiety performed by sodium iodide and trifluoroacetic anhydride afforded (*S*)-3-benzoyloxy-2-[(4-methylphenyl)sulfonyl]methyl}-propan-1,2-diol 9. The sulfonium salt 10 was obtained by using trimethyloxonium fluoroborate as alkylating agent, while the alkoxy dilithium salt 11, formed by adding a double molar ratio of lithium hydride, spontaneously underwent to an intramolecular nucleophilic ring formation. The  $\text{S}_{\text{N}}2$  intramolecular reaction of the alkoxy anion on the carbon bearing the sulfonium ion afforded (*R*)-hydroxymethyl oxirane 7 in 65% yield. The enantiomeric purity was determined by esterifying 7 with (+)-(*S*)-phenylpropionic acid and analysing the  $^1\text{H}$  NMR spectra of

(*R/S*<sup>\*</sup>)-**12** (Figure 1) which showed that no racemization had occurred during the reaction. The *R* absolute configuration at C-2 was assigned from the opposite specific rotation value of **7** with respect to that of (*S*)-**7** obtained through the reaction sequence shown on Scheme 2. Moreover, esters **12** of the two hydroxymethyl epoxy compounds **7**, deriving from (*2S,R<sub>G</sub>*)-**3** following the two different procedures, were in a diastereoisomeric relationship as shown by their <sup>1</sup>H NMR spectra.

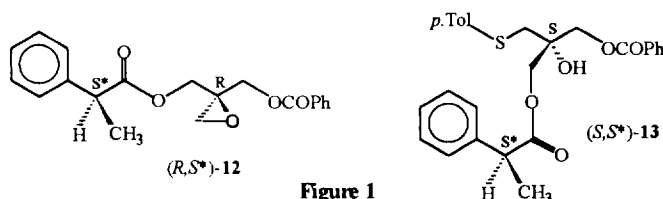
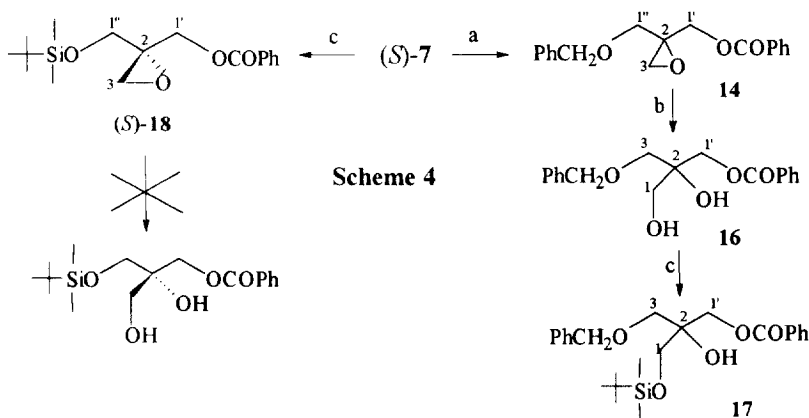


Figure 1

Similarly, the enantiomeric purity of (*R*)-**9** and (*S*)-**9**, obtained respectively from (*2R,R<sub>G</sub>*)-**3** and (*2S,R<sub>G</sub>*)-**3** through epoxide ring opening and reduction of the sulfinyl sulfur as shown in Scheme 3, was  $\geq 95\%$  as determined by <sup>1</sup>H NMR spectra analyses of their esters **13** with (+)-(*S*)-phenylpropionic acid as depicted in Figure 1 for (*S*)-**9**.

Finally, the protection of the hydroxyl moiety followed by the oxirane ring opening was necessary to obtain the title compound. As shown in Scheme 4, the silylation step, accomplished with dimethyl-*t*-butylsilyl chloride in pyridine gave the compound (*S*)-**18** in good chemical yield, but it was too labile under ring opening conditions, both basic and acid.



Scheme 4

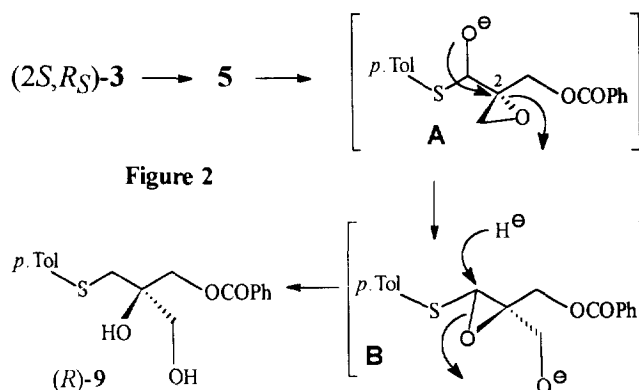
**Reagents and conditions:** a) NaH, THF, PhCH<sub>2</sub>Br, DMF, 0°C; b) H<sub>2</sub>O/HClO<sub>4</sub>/THF, r.t.; c) (CH<sub>3</sub>)<sub>3</sub>CSi(CH<sub>3</sub>)<sub>2</sub>Cl, Py.

On the other hand, as shown in Scheme 4, transformation of (*S*)-**7** into benzyloxy derivative **14**, opening of the oxirane ring in acidic medium and final protection of the primary hydroxy group of **16** by dimethyl-*t*-butylsilyl chloride in pyridine to give the disymmetrized tris(hydroxymethyl)methanol equivalent **17** was accomplished in good overall chemical yields, but with a significant loss of enantiomeric purity.

As confirmed by the use of the lanthanide shift reagent Eu(TFC)<sub>3</sub> on the benzyl/benzoyl protected oxirane **14**, the racemization process occurs during the benzylation step and is probably due to a Payne rearrangement<sup>11</sup> and/or to an intra-/intermolecular shift of the benzoyl protecting group towards a free hydroxy moiety, as suggested by the presence of small amount of the dibenzoyl derivative **15** in the crude reaction mixture.

Close examination of the conditions of the Pummerer rearrangement of sulfinyl oxiranes **3**, to obtain  $\alpha$ -methylenoxy aldehyde **6** and reduction to primary alcohol **7**, led to the following observation. When the

solution of the intermediate thio acetoxy derivative **5** was treated *in situ* with an acetonitrile/water solution of sodium borohydride, the *p*-tolylthio diol **9** was obtained in 50% yield as a mixture of epimers. The *R* absolute configuration at C-2 was always prevailing and, depending on reaction conditions, the *R/S* ratio was from 8 : 1 to 4 : 1. This implies that an inversion of configuration at C-2 had occurred during the transformation.



A tentative explanation is given on Figure 2: hydrolysis of the intermediate **5** in basic medium probably generates the alkoxy thio derivative **A**, which through a Payne rearrangement gives rise to structure **B**. The attacking hydride-releasing specie leads to the final compound **9** with a neat inversion of configuration at C-2.<sup>12</sup>

### STRUCTURAL ASSIGNMENTS

The <sup>1</sup>H and <sup>13</sup>C NMR spectra (experimental) of compounds **1-4** and **6-18** showed resonances which fully agree with the proposed structures. The values of 4.3-4.8 Hz observed for the geminal coupling constants of the C-2 protons were indicative of the presence of an oxirane ring in compounds **2, 3 and 6, 7 and 18**.

An ORTEP view of compound **4** is shown in Fig 1, while selected molecular dimensions are reported in Table 1. Bond lengths and angles fall in the expected range, except for the C(3)-Br distance which is 1.930(6) Å, significantly shorter than the literature mean value for a C(sp<sup>3</sup>)-Br bond (1.966 Å)<sup>13</sup>.

Table 1. Selected molecular dimensions of **4**

Bond lengths	[Å]	Bond angles	[°]	Torsion angles	[°]
Br-C(3)	1.930(6)	O(1)-S-C(11)	104.9(4)	C(11)-S-C(1)-C(2)	-176.8(5)
S-O(1)	1.506(7)	O(1)-S-C(1)	106.5(4)	S-C(1)-C(2)-C(3)	158.4(4)
S-C(11)	1.772(7)	C(11)-S-C(1)	98.2(3)	O(22)-C(2)-C(21)-O(21)	175.9(5)
S-C(1)	1.790(6)	C(2)-C(1)-S	113.0(4)	C(1)-C(2)-C(3)-Br	-172.7(4)
C(1)-C(2)	1.542(8)	O(22)-C(2)-C(21)	110.2(5)	O(1)-S-C(11)-C(12)	-157.4(6)
C(2)-C(21)	1.508(8)	O(22)-C(2)-C(1)	106.6(5)	C(1)-S-C(11)-C(12)	93.0(6)
C(2)-C(3)	1.537(8)	C(21)-C(2)-C(1)	113.0(5)	O(1)-S-C(11)-C(16)	19.5(7)
C(21)-O(21)	1.421(8)	O(22)-C(2)-C(3)	107.6(5)	C(1)-S-C(11)-C(16)	90.1(6)
C(2)-O(22)	1.431(8)	C(21)-C(2)-C(3)	112.4(5)		
O(21)-H(21)	0.677(69)	C(1)-C(2)-C(3)	106.7(4)		
O(22)-H(22)	0.711(64)	O(21)-C(21)-C(2)	107.5(5)		
		C(2)-C(3)-Br	113.5(4)		

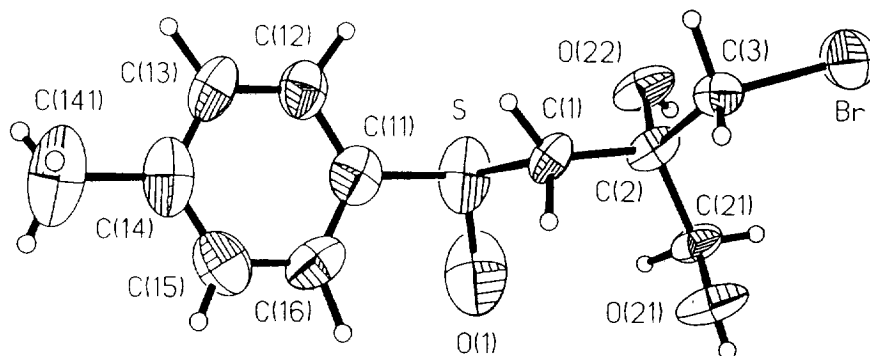


Fig. 3. ORTEP view of compound 4

The conformation of the molecule is characterized by an approximately *trans* sequence of the atoms C(11), S, C(1), C(2), C(3), Br, almost perpendicular to the phenyl ring. Comparison with other sulfoxide compounds with general structure  $R-S(=O)-CH_2-CXR_1R_2$  (in the present case:  $R = p$ -tol,  $R_1 = CH_2Br$ ,  $R_2 = CH_2OH$ ,  $X = OH$ ) where X is a -OR or -NR group,<sup>7b,14</sup> suggests that the conformation around the C(1)-C(2) bond may be influenced by stereoelectronic effects involving the S atom rather than by the steric requirements of  $R_1$  and  $R_2$  or by hydrogen bonding only. The common feature of nearly all of the related structures is the relative position of X to the sulfoxide group (see Fig. 4). A detailed investigation of this effect is presently in progress in our laboratories.

The packing projection of Fig. 5 shows that all hydrogen bonds are intermolecular and involve the sulfoxide oxygen and both the hydroxyl groups. The hydroxyl group on C(21) acts both as donor to the sulfoxide oxygen and as acceptor from the other hydroxyl group, forming a helicoidal structure along the c axis (see Table 2).

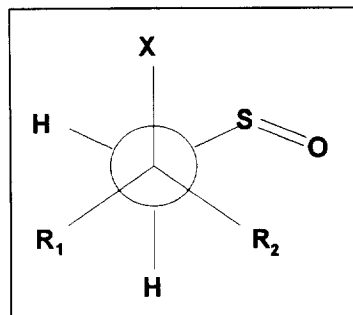


Fig. 4. Newman projection of a generic compound  $p$ -tol- $S(=O)-CH_2-CXR_1R_2$  in its commonly occurring conformation.

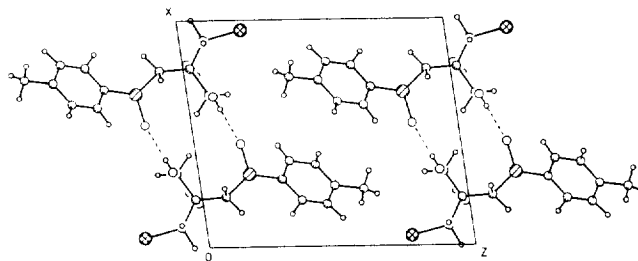


Fig. 5. Packing diagram of 4

Table 2. Hydrogen bond lengths and angles

Distance H..O [Å]		Angle OH..O [°]		Symmetry transformations used to generate equivalent atoms:	
O1 - H21O*1	1.932 (0.071)	O1 - H21O*1 - O21*1	176.96 ( 7.14)	*1	-x+1, y-1/2, -z+2
O21 - H22O*2	2.152 (0.071)	O21 - H22O*2 - O22*2	142.78 ( 6.92)	*2	x, y+1, z
H21O - O1*3	1.932 (0.071)	O21 - H21O - O1*3	176.96 ( 7.18)	*3	-x+1, y+1/2, -z+2
H22O - O21*4	2.152 (0.071)	O22 - H22O - O21*4	142.78 ( 6.92)	*4	x, y-1, z

## CONCLUSIONS

In the present paper it was shown that starting from the same (*R*<sub>G</sub>)-methyl-*p*-tolylsulfoxide and following different strategies, both enantiomeric disymmetrized synthetic equivalents (S)- and (R)-7 could be obtained in enantiomerically pure form. Loss of enantiomeric purity was observed only in the last steps, directed towards the obtainment of the true disymmetrized tris(hydroxymethyl) methanol derivative 15.<sup>15</sup>

## EXPERIMENTAL

**General Details.** <sup>1</sup>H, and <sup>13</sup>C NMR spectra were recorded on a Bruker AC 250L spectrometer. [α]<sub>D</sub> Values were obtained on a Jasco DIP-181 polarimeter. Melting points are uncorrected and were obtained on a capillary apparatus. Flash chromatographies were performed with silica gel 60 (60-200 μm, Merck) and preparative TLC separations were performed on Merck 60F<sub>254</sub> precoated plates. All reactions were monitored by TLC performed on analytical Merck silica gel 60F<sub>254</sub> TLC plates. Tetrahydrofuran (THF) was freshly distilled from sodium and diisopropylamine was distilled from calcium hydride and stored on 4Å molecular sieves. In other cases, commercially available reagent-grade solvents and reagents were employed without purification.

**Determination of the enantiomeric purity of the obtained compounds. General procedures. Lanthanide Shift Reagents Method.** Two sorts of experiments were made with the lanthanide shift reagent {tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphorate], europium (III) derivative}, [Eu(TFC)<sub>3</sub>]: first, on the artificial racemic mixtures and, second, on the presumed optically active compounds. The progressive addition of Eu(TFC)<sub>3</sub> to the racemic compounds gave rise to mixtures of diastereoisomeric complexes: the signals of the two α protons on the benzoate aromatic ring ranging between 7.95 and 8.10 ppm always showed a downfield shift and a contemporary splitting into doublets. On the homochiral compounds, the addition of Eu(TFC)<sub>3</sub> at the same concentrations affording the splitting on the racemic mixtures, gave only comparable downfield shift, but no splitting was observed.

**Esterification with Chiral Acid Method.** As for the lanthanide shift reagents method, the below described procedure was applied both to the artificial racemic mixtures and to the presumed enantiomerically pure compounds. Neat (+)-(*S*)-phenylpropionic acid (1.0 mmol) was added to a solution of the examined compounds (1.1 mmol) and DCC (1.0 mmol) in methylene chloride (8.0 ml). After 5 min., dimethylaminopyridine (0.1 mmol) was added and a white precipitate formed. After filtration, the crude containing the (*S*<sup>\*</sup>)-phenylpropionic esters was submitted to <sup>1</sup>H NMR analysis, in comparison with a sample obtained, following the same procedure, from a 1 : 1 artificial epimeric mixture. In all the examined cases, the phenylpropionic esters were obtained as the only reaction products and in yields ≥ 95%.

**Synthesis of 1-hydroxy-3-[(4-methylphenyl)sulfinyl]propan-2-one 1.** To a stirred solution of diisopropylamine (6.6 ml, 46.8 mmol) in THF (45 ml) cooled at -40°C under nitrogen, a 2.5 M solution in *n*-hexane of *n*-butyllithium (18.4 ml, 46.8 mmol) was added dropwise. LDA was cooled at -60°C and a solution

of methyl-*p*-tolylsulfoxide (3g, 19.4 mmol) in THF (25 ml) was added dropwise. Then the yellow solution was cooled at  $-70^{\circ}\text{C}$  and a solution of glycolic acid ethyl ester (2.75 ml, 29.0 mmol) in THF (3.0 ml) was added. After quenching with a saturated aqueous ammonium chloride solution, the organic products were extracted with ethyl acetate (3 x 50 ml), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give a residue that was purified by crystallization (*n*-hexane / ethyl acetate 1 : 1). White crystals of **1** were obtained in 60% yield:  $R_f$  0.35 (chloroform / ethyl acetate 4 : 6);  $[\alpha]_D^{20} + 234.1$  (c 1.0,  $\text{CHCl}_3$ ); m.p. 66.5-68.5 $^{\circ}\text{C}$ ; *Anal.* Calcd. for  $\text{C}_{10}\text{H}_{12}\text{O}_3\text{S}$ : C, 56.60; H, 5.66. Found: C, 56.67; H, 5.80.

**Synthesis of 2-hydroxymethyl-2-[(4-methylphenyl)sulfinyl]methyl oxiranes 2.** To a solution of sulfinyl hydroxy acetone **1** (3.0 g, 13.3 mmol) in methanol (50 ml) at  $0^{\circ}\text{C}$  was added portionwise an ethereal solution (c.a. 0.5 M) of diazomethane (80 ml). The reaction was complete in five minutes and a nitrogen gas flow was bubbled in, until the yellow solution was completely decoloured. Solvent was evaporated and the residue was purified by flash chromatography (*n*-hexane / ethyl acetate / isopropyl alcohol 3 : 7 : 1) to give in 42.7% yield a 1.0 : 2.3 mixture ( $^1\text{H}$  NMR analysis of the crude) of the diastereoisomeric oxiranes **2**. The same reaction, performed dissolving **1** in ethyl ether (50 ml) at the same temperature, gave in 6 hours a 1.0 : 2.9 diastereoisomeric mixture of **2** in 40.0% global yield.

**Isolation of the enantiomerically pure oxiranes 2.** The above described mixture of oxiranes **2** (2.0 g, 8.33 mmol) was dissolved in dichloromethane (100 ml) under nitrogen atmosphere at  $0^{\circ}\text{C}$  and dicyclohexylcarbodiimide (1.9 g, 9.22 mmol) was added. After 5 min., dimethylaminopyridine (108 mg, 0.88 mmol) and benzoic acid (1.1 g, 9.29 mmol) were added. After 4.30 hours the reaction was complete and the slurry was concentrated up to half the volume, the white precipitate was filtered, the clear organic phase washed with acidic (HCl) water (5 ml), dried over anhydrous sodium sulfate and concentrated to give a residue that was purified by flash chromatography (*n*-hexane / ethyl acetate 3 : 7) to give: the ester of the major diastereoisomer (2*S*)-**3** oxirane in 61.3% yield from **1**:  $R_f$  0.32 (in the same solvents);  $[\alpha]_D^{20} + 157.4$  (c 1.0,  $\text{CHCl}_3$ ); m.p. 70-72 $^{\circ}\text{C}$  (isopropyl ether); Mass (C.I.): 331 ( $\text{M}^+ + 1$ , 100%), 191 ( $\text{M}^+ - \text{PhCOO}^+ - \text{H}_2\text{O}$ , 10%); IR (KBr)  $\text{cm}^{-1}$ : 1715 ( $\nu\text{C}=\text{O}$ ), 1280, 1250, 1050, 860; *Anal.* Calcd. for  $\text{C}_{18}\text{H}_{18}\text{O}_4\text{S}$ : C, 65.43; H, 5.49. Found: C, 65.49; H, 5.50 and the ester of the minor diastereoisomer (2*R*)-2-benzoyloxymethyl-2-[(4-methylphenyl)sulfinyl]methyl oxirane **3** in 26.7% yield from **1**:  $R_f$  0.35 (in the same solvents);  $[\alpha]_D^{20} + 136.2$  (c 0.8,  $\text{CHCl}_3$ ); m.p. 73-74 $^{\circ}\text{C}$  (isopropyl ether); Mass (C.I.): 331 ( $\text{M}^+ + 1$ , 100%), 191 ( $\text{M}^+ - \text{PhCOO}^+ - \text{H}_2\text{O}$ , 10%); IR (KBr)  $\text{cm}^{-1}$ : 1715 ( $\nu\text{C}=\text{O}$ ), 1280, 1250, 1050, 860. The benzoyl derivatives (2*S*)-**3** and (2*R*)-**3** (1.0 g, 3.03 mmol) were separately added to a 0.025% in pound methanolic solution (22 ml) of sodium hydroxide at  $10^{\circ}\text{C}$  and after 1.5 hours the esters **3** had completely reacted. Buffered solutions of citric acid were added up to pH 5, methanol was evaporated and the residues were purified by flash chromatography (*n*-hexane / ethyl acetate 1 : 4). From (2*S*)-**3**, (2*R*)-**2** (major diastereoisomer) was obtained in 65.0% yield:  $R_f$  0.35 (in the same mixture of solvents);  $[\alpha]_D^{20} + 280.8$  (c 0.4,  $\text{CHCl}_3$ ); clear oil; Mass (C.I.): 227 ( $\text{M}^+$ , 100%), 209 ( $\text{M}^+ - \text{H}_2\text{O}$ , 10%). From (2*R*)-**3**, (2*S*)-**2** (minor diastereoisomer) was obtained in 64.5% yield:  $R_f$  0.35 (in the same solvents);  $[\alpha]_D^{20} + 171.0$  (c 1.0,  $\text{CHCl}_3$ ); m.p. 77-78 $^{\circ}\text{C}$  (isopropyl ether); IR (KBr)  $\text{cm}^{-1}$ : 3400 ( $\nu\text{O-H}$ ), 1210, 1050, 1030, 810; *Anal.* Calcd. for  $\text{C}_{11}\text{H}_{14}\text{O}_3\text{S}$ : C, 58.38; H, 6.23. Found: C, 58.26; H, 6.25.

**Synthesis of 3-[(4-methylphenyl)sulfinyl]-2-bromomethyl-1,2-diol 4. General Procedure.** Cupric bromide (740 mg, 3.33 mmol), dried overnight at  $100^{\circ}\text{C}$  *in vacuo*, was suspended in THF (5 ml) at  $0^{\circ}\text{C}$  and anhydrous lithium bromide (580 mg, 6.66 mmol) was added. After 2 min., the slurry became orange and then converted in clear solution. At  $20^{\circ}\text{C}$  oxirane **2** (500 mg, 2.08 mmol) in THF (5 ml) was added dropwise. After 3 hours, starting compound **2** had completely disappeared and the solution was concentrated up to half the volume and directly poured into a silica gel packed chromatography column and eluted in *n*-hexane / ethyl acetate 3 : 7. From (2*R*)-**2**, the bromo derivative (2*S*)-**4** was obtained in 85% yield:  $[\alpha]_D^{20} + 159.8$  (c 1.0,  $\text{CHCl}_3$ ); m.p. 82 - 84 $^{\circ}\text{C}$  (isopropyl ether); Mass (C.I.): 309 ( $\text{M}^+ + 1$ , 100%), 263 ( $\text{M}^+ - \text{CO}_2$ , 5%), 227 ( $\text{M}^+ - \text{Br}^+$ , 10%); *Anal.* Calcd. for  $\text{C}_{11}\text{H}_{15}\text{O}_3\text{BrS}$ : C, 43.01; H, 4.92. Found: C, 43.05; H, 4.90. From (2*S*)-**2**, the bromo derivative (2*R*)-**4** was obtained in 79.2% yield:  $[\alpha]_D^{20} + 166.5$  (c 1.4,  $\text{CHCl}_3$ ); m.p. 108.5 - 110.5 $^{\circ}\text{C}$  (isopropyl ether); Mass (C.I.): 307 ( $\text{M}^+ - 1$ , 100%), 263 ( $\text{M}^+ - \text{CO}_2$ , 5%), 227 ( $\text{M}^+ - \text{Br}^+$ , 35%); IR (KBr)



cm<sup>-1</sup>: 3320 (νO-H), 1120, 1035, 1030, 810; *Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>O<sub>3</sub>BrS: C, 43.01; H, 4.92. Found: C, 43.07; H, 4.89. (2*R*)-**4** was used for the determination of absolute configuration at C-2 by X-ray analysis.

**X-Ray structural analysis of the bromohydrin (2*R*,*R*<sub>S</sub>)-**4**.** White crystals of **4**, suitable for X-ray analysis were obtained by crystallization from isopropyl ether. Diffraction data were collected on a Siemens P4 diffractometer, with graphite monochromated Cu-Kα radiation. The selected crystal had the dimension of 0.12 x 0.13 x 0.68 mm. Crystal data are: C<sub>11</sub>H<sub>15</sub>O<sub>3</sub>SBr, f.w. 307.20, monoclinic, space group P2<sub>1</sub>, a=10.512(2), b=5.101(1), c=12.228(2) Å, β=97.86(3)°, V=649.5(2) Å<sup>3</sup>, Z=2, D<sub>c</sub>=1.571 Mg/m<sup>3</sup>, μ=5.752 mm<sup>-1</sup>, F(000)=312

Intensity data were collected using the θ-2θ scan technique, in the range 3<θ<55°. 1587 independent reflections were collected. 3 Standard reflections were measured every 250 reflections and showed no significant decay. The data were corrected for Lorentz and polarization effects, while no absorption correction was applied. The structure was solved using the SHELXTL<sup>16</sup> program and refined by full-matrix least squares on F<sup>2</sup> values with SHELXL-93.<sup>17</sup> Non hydrogen atoms were refined with anisotropic temperature factors. The hydroxyl hydrogens were located by difference-Fourier map, and refined isotropically, while the other hydrogens were included at calculated positions and refined in the riding mode. The final value of the residual R and wR2 were respectively 0.0504 and 0.1305 for 1513 reflections with I>2σ(I). The highest peak in final difference-Fourier map was 0.45 eÅ<sup>-3</sup>. Flack's x parameter<sup>18</sup> was refined giving a value of -0.02(5), consistent with a very reliable determination of the absolute configuration of **4** which is S(*R*), C2(*R*).

**Synthesis of (S)-2-benzoyloxymethyl-2-formyl oxirane 6. Method a.** To a solution of sulfinyl oxirane (2*S*,*R*<sub>S</sub>)-**3** (2.5 g, 8.11 mmol) and *sym*-collidine (2.38 ml, 17.8 mmol) in acetonitrile (15 ml) at 0°C under nitrogen atmosphere, trifluoroacetic anhydride (2.27 ml, 16.2 mmol) in the same solvent (8.5 ml) was added dropwise. Neat potassium carbonate was added up to pH 7, then a solution of mercury(II) chloride (6.6 g, 24.3 mmol) in acetonitrile (20 ml) was added dropwise and stirring was continued at room temperature overnight. The formed pale yellow precipitate was filtered and the clear yellow solution (pH = 5.5) was concentrated at reduced pressure. The residue was purified by flash chromatography (*n*-pentane / ethyl ether 4 : 1) and (*S*)-**6** was obtained in 56% yield: R<sub>f</sub> 0.35; [α]<sub>D</sub><sup>20</sup> + 28.9 (c 1.0, CHCl<sub>3</sub>); [α]<sub>365</sub><sup>20</sup> + 197.8 (c 2.3, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 3.22 and 3.30 (2H, d, *J* = 4.7 Hz, CH<sub>2</sub>O), 4.60 and 4.90 (2H, d, *J* = 12.6 Hz, CH<sub>2</sub>OCO), 7.4-8.1 (5H, m, ArH), 9.05 (1H, s, CHO). The same procedure, applied to (2*R*,*R*<sub>S</sub>)-**3**, allowed the obtainment of (*R*)-**6** in 62% yield: [α]<sub>D</sub><sup>20</sup> - 28.3 (c 0.6, CHCl<sub>3</sub>); [α]<sub>365</sub><sup>20</sup> - 193.0 (c 2.3, CHCl<sub>3</sub>); spectral data were identical to those of the above described (*S*)-**6** aldehyde.

**Method b.** Starting from (2*S*,*R*<sub>S</sub>)-**3**, the acetonitrile yellow solution of **5** was stirred at room temperature for 48 hours under nitrogen atmosphere. A TLC monitoring showed that aldehyde **6** spontaneously formed. After usual work-up, (*S*)-**6** was isolated in 66% yield.

**Synthesis of (S)-2-benzoyloxymethyl-2-hydroxymethyl oxirane 7.** A solution of (*S*)-**6** (1.67 g, 8.11 mmol) in acetonitrile (10 ml) was treated dropwise with a solution of sodium borohydride (460 mg, 12.1 mmol) dissolved in acetonitrile (4.0 ml) and water (0.1 ml). The reaction was complete in 10 min., then the reaction mixture was dried over anhydrous sodium sulfate, filtered, concentrated to dryness and the residue was purified by flash chromatography (*n*-hexane / ethyl acetate 4 : 1). The product (*S*)-**7** was obtained in 85% yield: [α]<sub>D</sub><sup>20</sup> + 3.9 (c 0.6, CHCl<sub>3</sub>); [α]<sub>365</sub><sup>20</sup> + 8.1 (c 0.6, CHCl<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ: 49.23 (t, C-3), 57.92 (s, C-2), 61.59 (t) and 64.56 (t) (C-1' and C-1"), 128.50 (d), 129.42 (s), 129.75 (d), 133.40 (d) (ArC), and 166.38 (s, CO<sub>2</sub>); Mass (C.I.): 209 (M<sup>+</sup>, 100%), 191 (M<sup>+</sup> - H<sub>2</sub>O, 5%), 105 (C<sub>6</sub>H<sub>5</sub>CO<sup>+</sup>, 20%); *Anal.* Calcd. for C<sub>11</sub>H<sub>12</sub>O<sub>4</sub>: C, 63.45; H, 5.81. Found: C, 63.40; H, 5.79. The same procedure, applied to (*R*)-**6** gave (*R*)-**7** in 80% yield: [α]<sub>D</sub><sup>20</sup> - 3.1 (c 1.0, CHCl<sub>3</sub>); [α]<sub>365</sub> - 8.7 (c 1.0, CHCl<sub>3</sub>). The enantiomeric purity of **7** was checked following both the described methods: the <sup>1</sup>H NMR spectrum of the europium complex with the chiral epoxy alcohol (*S*)-**7** showed downfield shift and no splitting, whilst the same analyses on the artificial mixture of diastereoisomeric complexes showed both downfield shift and peaks splitting. Following the second method, from enantiomerically pure (*S*)-**7**, the crude containing the (*S*,*S*<sup>\*</sup>) epoxy phenylpropionic/benzoic diester **17** showed <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.51 (3H, d, *J* = 7.2 Hz, CH<sub>3</sub>CHPh), 2.77 and 2.85 (2H, d, *J* = 4.6 Hz, CH<sub>2</sub>O), 3.76 (1H,

q,  $J = 7.2$  Hz,  $\text{CH}_3\text{CHPh}$ ), 4.20 and 4.42 (2H, d,  $J = 12.3$  Hz,  $\text{CH}_2\text{OCO}$ ), 4.22 and 4.37 (2H, d,  $J = 12.3$  Hz,  $\text{CH}_2\text{OCO}$ ), 7.2-8.1 (10H, m, ArH), whilst the same crude containing the (*S/R,S\**)-diesters **12** from the artificial racemic mixture showed  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.51 (6H, d,  $J = 7.2$  Hz,  $2\text{CH}_3\text{CHPh}$ ), 2.77, 2.79, 2.84 and 2.85 (H, d,  $J = 4.6$  Hz,  $2\text{CH}_2\text{O}$ ), 3.75 and 3.76 (2H, q,  $J = 7.2$  Hz,  $2\text{CH}_3\text{CHPh}$ ), 4.20, 4.22, 4.28, 4.29, 4.36, 4.37, 4.41 and 4.42 (8H, d,  $J = 12.3$  Hz,  $4\text{CH}_2\text{OCO}$ ), 7.2-8.1 (20H, m, 2ArH).

**Synthesis of (*S*)-2-[[4-(4-methylphenyl)sulfinyl]methyl]-3-*O*-benzoyl-propan-1,2,3-triol **9**. Method a.**

To a solution of (*2S,R<sub>S</sub>*)-**3** (2.0 g, 6.49 mmol) in a 1 : 1 THF /  $\text{H}_2\text{O}$  mixture (20 ml), 2.0 ml of perchloric acid were added at  $40^\circ\text{C}$ . After 48 hours at the same temperature, the solvents were evaporated and the residue was purified by flash chromatography (*n*-hexane / ethyl acetate 3 : 7) to give (*2S,R<sub>S</sub>*)-2-[[4-(4-methylphenyl)sulfinyl]methyl]-3-*O*-benzoyl-propan-1,2,3-triol **8** in 62% yield:  $R_f$  0.35;  $[\alpha]_{\text{D}}^{20} + 111.4$  (c 0.7,  $\text{CHCl}_3$ ); m.p.  $175 - 177^\circ\text{C}$  (ethyl acetate);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.42 (3H, brs, Me), 2.90 and 3.20 (2H, brd,  $J = 13.7$  Hz,  $\text{CH}_2\text{S}$ ), 3.62 (1H, t,  $J = 6.5$  Hz,  $\text{CH}_2\text{OH}$ ), 3.78 (2H, d,  $J = 6.5$  Hz,  $\text{CH}_2\text{OH}$ ), 4.42 (1H, s, OH), 4.45 and 4.53 (2H, d,  $J = 11.5$  Hz,  $\text{CH}_2\text{OCO}$ ), 7.3-8.1 (9H, m, ArH). To a stirred slurry of sodium iodide (880 mg, 5.86 mmol) and (*2S,R<sub>S</sub>*)-**8** (636 mg, 1.95 mmol) in acetone (10 ml) stirred under nitrogen atmosphere, a solution of trifluoroacetic anhydride (1.36 ml, 9.76 mmol) in the same solvent (5.0 ml) was added at  $-40^\circ\text{C}$ . The reaction was quenched with saturated aqueous solutions of sodium sulfite / sodium hydrogen carbonate and the organic layer was extracted with ethyl acetate (3x5 ml), dried over anhydrous sodium sulfate and concentrated to give a residue that, upon flash chromatographic purification in *n*-hexane / ethyl acetate 1 : 1, gave (*S*)-**9** in 95% yield:  $R_f$  0.35;  $[\alpha]_{\text{D}}^{20} + 4.3$  (c 0.9,  $\text{CHCl}_3$ );  $[\alpha]_{365} + 19.1$  (c 0.9,  $\text{CHCl}_3$ ); m.p.  $55.6 - 58.6^\circ\text{C}$  (ethyl ether / ethyl acetate 4 : 1); *Anal.* Calcd. for  $\text{C}_{18}\text{H}_{20}\text{O}_4\text{S}$ : C, 65.04; H, 6.06. Found: C, 64.96; H, 6.05. The same procedure was applied to (*2R,R<sub>S</sub>*)-**3**, giving (*2R,R<sub>S</sub>*)-**8** in 58% yield:  $R_f$  0.35 (*n*-hexane / ethyl acetate 2 : 3);  $[\alpha]_{\text{D}}^{20} + 129.7$  (c 0.4,  $\text{CHCl}_3$ ); m.p.  $168 - 170^\circ\text{C}$  (ethyl acetate);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.40 (3H, s, Me), 3.05 and 3.13 (2H, d,  $J = 12.5$  Hz,  $\text{CH}_2\text{S}$ ), 3.16 (1H, brt,  $J = 6.0$  Hz,  $\text{CH}_2\text{OH}$ ), 3.85 and 3.96 (2H, brdd,  $J = 11.8$  and  $6.0$  Hz,  $\text{CH}_2\text{OCO}$ ), 4.19 (1H, brs, OH), 4.47 and 4.49 (2H, d,  $J = 11.2$  Hz,  $\text{CH}_2\text{OCO}$ ), 7.30-8.05 (9H, m, ArH). The sulfinyl diol **8** was then reduced to sulfenyl diol following the above described procedure and affording (*R*)-**9** in 90% yield:  $[\alpha]_{\text{D}}^{20} - 3.9$  (c 0.3,  $\text{CHCl}_3$ );  $[\alpha]_{365} - 18.8$  (c 0.3,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  spectrum was superimposable to that of the (*S*)-**9** enantiomer. The enantiomeric purity of the described thio compounds **9** was checked by esterification with (+)-(*S*)-phenylpropionic ester. In particular, the ester (*S,S\**)-**18** of (*S*)-**9** showed the following  $^1\text{H NMR}$  spectrum: 1.49 (3H, d,  $J = 7.0$  Hz,  $\text{CH}_3\text{CHPh}$ ), 2.26 (3H, s,  $\text{ArCH}_3$ ), 2.77 (1H, brs, OH), 3.10 (2H, s,  $\text{CH}_2\text{S}$ ), 3.70 (1H, q,  $J = 7.0$  Hz,  $\text{CH}_3\text{CHPh}$ ), 4.13 and 4.23 (2H, d,  $J = 11.5$  Hz,  $\text{CH}_2\text{OCO}$ ), 4.14 and 4.28 (2H, d,  $J = 11.5$  Hz,  $\text{CH}_2\text{OCO}$ ), 6.98-7.98 (14H, m, ArH), whilst the esters (*S/R,S\**)-**18** obtained from an artificial racemic mixture of **9** showed the following signals:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.48 and 1.49 (6H, d,  $J = 7.0$  Hz,  $2\text{CH}_3\text{CHPh}$ ), 2.24 and 2.26 (6H, s,  $2\text{ArCH}_3$ ), 2.77 (2H, brs, 2OH), 3.03 and 3.08 (2H, d,  $J = 13.8$  Hz,  $\text{CH}_2\text{S}$ ) and 3.10 (2H, s,  $\text{CH}_2\text{S}$ ), 3.70 and 3.72 (2H, q,  $J = 7.0$  Hz,  $2\text{CH}_3\text{CHPh}$ ), 4.13 and 4.23 (2H, d,  $J = 11.5$  Hz,  $\text{CH}_2\text{OCO}$ ), 4.14 and 4.28 (2H, d,  $J = 11.5$  Hz,  $\text{CH}_2\text{OCO}$ ) and 4.20 (4H, s,  $2\text{CH}_2\text{OCO}$ ), 6.96-7.98 (28H, m, 2ArH). The (*R*)-**9** enantiomer was esterified with the same (*S*)-phenylpropionic acid:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.48 (3H, d,  $J = 7.0$  Hz,  $\text{CH}_3\text{CHPh}$ ), 2.24 (3H, s,  $\text{ArCH}_3$ ), 2.77 (1H, s, OH), 3.03 and 3.08 (1H, d,  $J = 13.8$  Hz,  $\text{CH}_2\text{S}$ ), 3.72 (1H, q,  $J = 7.0$  Hz,  $\text{CH}_3\text{CHPh}$ ), 4.20 (4H, s,  $2\text{CH}_2\text{OCO}$ ), 6.96-7.90 (14H, m, ArH).

**Method b.** A solution of sodium borohydride (460 mg, 12.1 mmol) in acetonitrile (4.0 ml) and water (0.1 ml) was added dropwise to the yellow solution of the intermediate **5**, obtained from (*2S,R<sub>S</sub>*)-**3** following the above mentioned procedure. The starting compound disappeared in two hours, giving rise to a product having lower  $R_f$ . The yellow solution was concentrated to dryness and purified by flash chromatography (*n*-hexane / ethyl acetate 2 : 3) to give **9** in 50% yield. Checking its enantiomeric purity through esterification with chiral acid method, it was evident that the resulting  $^1\text{H NMR}$  spectrum was consistent with a 8 : 1 = (*R,S\**) / (*S,S\**) mixture of diastereoisomeric phenylpropionic esters **13**.

**Table 3.** <sup>1</sup>H chemical shifts (ppm) and coupling constants (Hz) values for oxiranes **2**, **3** and **7**, **14**, **18** in CDCl<sub>3</sub>.

Proton <sup>a</sup>	(2 <i>R</i> )- <b>2</b>	(2 <i>S</i> )- <b>2</b>	(2 <i>R</i> )- <b>3</b>	(2 <i>S</i> )- <b>3</b>	<b>7</b>	<b>14</b>	<b>18</b>
<b>3a</b>	3.02	2.83	3.16	3.07	3.00	2.92	2.89
<b>3b</b>	2.96	2.64	2.98	3.01	2.91	2.86	2.85
<b>1'a</b>	3.76	3.85	4.56	4.85	4.61	4.62	4.57
<b>1'b</b>	3.72	3.81	4.27	4.43	4.43	4.46	4.44
<b>1''a</b>	3.47	3.18	3.51	3.35	3.91	3.72	3.88
<b>1''b</b>	2.82	3.01	2.98	2.85	3.82	3.72	3.82
<b>OH</b>	3.05	3.48			2.10		
<b>J<sub>3a,3b</sub></b>	4.3	4.5	4.3	4.3	4.7	4.7	4.8
<b>J<sub>1'a,1'b</sub></b>	11.6	12.0	12.4	12.5	12.2	12.1	12.0
<b>J<sub>1''a,1''b</sub></b>	13.9	13.8	13.8	13.5	12.5	b	11.3

<sup>a</sup>The aromatic protons resonate between 7.2 and 8.1 ppm. Moreover, the 1''-methylene protons of compounds **14** resonate at 4.59 ppm, the methyl protons of compounds **2** and **3** resonate at 2.43 and 2.42 ppm and the *t*-butyl and the methyl protons of compound **18** resonate at 0.89 and 0.08 ppm. <sup>b</sup>Not assigned.

**Synthesis of (R)-2-benzoyloxymethyl-2-hydroxymethyl oxirane 7 from (S)-2-[(4-methylphenyl)sulfonyl]methyl-3-O-benzoyl-propan-1,2,3-triol 9.** To a solution of (*S*)-**9** (170 mg, 0.52 mmol) in a 1:1 mixture of CH<sub>2</sub>Cl<sub>2</sub> / CH<sub>3</sub>NO<sub>2</sub> (5.0 ml) neat trimethyloxonium fluoroborate (114 mg, 0.77 mmol) was added at -10°C under nitrogen. Then the mixture was warmed up to room temperature and after one hour, the starting material had completely disappeared. Solvents were removed under reduced pressure, DMF (4.0 ml) was added at 0°C and solid lithium hydride (10 mg, 1.04 mmol) was added. After two hours, the reaction mixture was slowly poured into a cooled saturated NH<sub>4</sub>Cl aqueous solution and extracted with ethyl ether (3 x 5 ml). After water removal on anhydrous sodium sulfate, solvent was evaporated and the residue was flash chromatographed (*n*-hexane / ethyl acetate 3 : 2) to give **7** in 65% yield: [α]<sub>D</sub><sup>20</sup> - 3.2 (c 0.7, CHCl<sub>3</sub>); <sup>1</sup>H NMR spectrum was identical to that of the above described enantiomer (*S*)-**7**. The enantiomeric purity of **7** was checked by esterification with the usual (*S*) chiral acid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.51 (3H, d, *J* = 7.2 Hz, CH<sub>3</sub>CHPh), 2.79 and 2.84 (2H, d, *J* = 4.6 Hz, CH<sub>2</sub>O), 3.75 (1H, q, *J* = 7.2 Hz, CH<sub>3</sub>CHPh), 4.28 and 4.36 (2H, d, *J* = 12.3 Hz, CH<sub>2</sub>OCO), 4.29 and 4.41 (2H, d, *J* = 12.3 Hz, CH<sub>2</sub>OCO), 7.2-8.1 (10H, m, ArH). The <sup>1</sup>H NMR spectrum of the phenylpropionic/benzoyl diester **12** revealed the presence of a single compound and the comparison with the <sup>1</sup>H NMR spectra of the esters **12** obtained from the artificial racemic mixture of oxiranes **7** and from the enantiomerically pure (*S*)-**7** (see above) confirmed the enantiomeric relationship between the two enantiomerically pure hydroxymethyl oxiranes **7**.

**Synthesis of 2-benzoyloxymethyl-2-benzoyloxymethyl oxirane 14.** To a suspension of sodium hydride (53 mg, 1.2 mmol), in freshly distilled THF (1.3 ml) at 0°C under argon atmosphere a solution of hydroxymethyl oxirane **7** (250 mg, 0.81 mmol) in DMF (1.0 ml) was added dropwise. The resulting grey slurry was poured into an ice/water bath and extracted with ethyl ether (3 x 1.0 ml). The combined organic layers were dried over sodium sulfate and evaporated under reduced pressure to give a residue that was submitted to flash chromatography (*n*-hexane / ethyl ether 4 : 1) to give the benzyl/benzoyl derivative **14** contaminated by a 10% of the corresponding dibenzoyl derivative **15** in 40% global yield. The two compounds were not separable and the symmetric achiral dibenzoyl derivative **15** was identified in mixture by its <sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>; δ: 3.02 (2H, s, H<sub>2</sub>-3), 4.50 and 4.65 (4H, d, *J* = 12.2 Hz, 2xCH<sub>2</sub>-2), and 7.43, 7.57 and 8.04 (10H, m, ArH). The enantiomeric purity of **14** was checked by using the lanthanide shift reagents: the <sup>1</sup>H NMR spectrum of the europium complex deriving from the artificial epimeric mixture of **14** showed identical behaviour (peaks splitting and downfield shift) to that of the same complex with the compounds **14** (6 : 4 epimeric mixture)

obtained from the above described reaction. The same reaction was performed on (*S*)-7 using Ag<sub>2</sub>O (116.6 mg, 0.503 mmol) instead of NaH, but the compared analyses of the two <sup>1</sup>H NMR spectra gave identical results.

**Table 4.** <sup>1</sup>H chemical shifts (ppm) and coupling constants (Hz) values for compounds **1**, **4**, **9**, **16** and **17** in CDCl<sub>3</sub>.

Proton <sup>a</sup>	<b>1</b>	( <i>2R</i> )- <b>4</b>	( <i>2S</i> )- <b>4</b>	<b>9</b>	<b>16</b>	<b>17</b>
<b>1a</b>	4.18	3.77	3.93	3.67	3.68	3.73
<b>1b</b>	4.18	3.77	3.88	3.62	3.68	3.68
<b>3a</b>	4.06	3.18	3.15	3.25	3.61	4.57
<b>3b</b>	3.79	3.02	3.08	3.25	3.61	4.57
<b>1'a</b>		3.73	3.72	4.41	4.60	3.60
<b>1'b</b>		3.58	3.59	4.34	4.56	3.53
<b>OH-1</b>	3.64	3.36	3.29	2.40	2.41	
<b>OH-2</b>		4.38	4.22	2.40	3.00	2.84
<i>J</i> <sub>1a,1b</sub>	b	b	11.6	11.5	b	10.0
<i>J</i> <sub>3a,3b</sub>	12.8	13.8	13.8	b	b	b
<i>J</i> <sub>1'a,1'b</sub>		10.7	10.8	11.5	11.8	12.0

<sup>a</sup>The aromatic protons resonate between 7.0 and 8.1 ppm. Moreover, the 1'-methylene protons of compounds **16** and **17** resonate at 4.42 and 4.40 ppm. <sup>b</sup>Not assigned.

**Synthesis of 2-benzoyloxymethyl-3-O-benzoyl-propan-1,2,3-triol 16.** A solution of the mixture (*2R*)-**14/15** (200 mg, *c.a.* 0.67 mmol) in THF (5 ml) was treated at 0°C with a 1 : 1 THF / H<sub>2</sub>O solution (3.5 ml) containing 10% mol. perchloric acid. The reaction was stirred at the same temperature for 10 hours, then a saturated aqueous solution of sodium bicarbonate was added up to pH 6.0, the organic layers were extracted with ethyl acetate, dried over anhydrous sodium sulfate, evaporated to dryness and the residue was purified by flash chromatography (*n*-hexane / ethyl acetate 7 : 3) to give **16** in 90% yield as a yellowish oil: *Anal.* Calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>5</sub>: C, 68.34; H, 6.37. Found: C, 68.32; H, 6.35.

**Synthesis of 2-benzoyloxymethyl-1-[O-(dimethyl-*t*-butyl)silyl]-3-O-benzoyl-propan-1,2,3-triol 17.** To a solution of **16** (55 mg, 0.18 mmol) in pyridine (0.5 ml) stirred under nitrogen at 0°C, neat dimethyl-*t*-butylsilyl chloride (50 mg, 0.33 mmol) was added. After 24 hours pyridine was removed under *vacuum* and the residue was purified by flash chromatography (*n*-hexane / ethyl acetate 4 : 1) to give **17** in 95% yield: <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ: - 1.84 [q, (CH<sub>3</sub>)<sub>2</sub>Si], 18.22 (s) and 25.81 (q) (*t*-buC), 63.95, 65.46, 70.58 and 73.62 (t, 4xCH<sub>2</sub>), 70.82 (s, C-2), 127.56 (d), 127.62 (d), 128.35 (d), 128.35 (d), 129.64 (d), 130.05 (s), 132.96 (d) and 137.82 (s) (ArC), and 166.40 (s, CO<sub>2</sub>); Mass (C.I.): 431 (M<sup>+</sup>, 78%), 413 (M<sup>+</sup> - H<sub>2</sub>O, 60%), 387 (M<sup>+</sup> - CO<sub>2</sub>, 20%), 373 (M<sup>+</sup> - C<sub>4</sub>H<sub>9</sub><sup>+</sup>, 90%), 309 (M<sup>+</sup> - PhCOO<sup>+</sup>, 15%), 91 (PhCH<sub>2</sub><sup>+</sup>, 100%), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 36%); *Anal.* Calcd. for C<sub>24</sub>H<sub>34</sub>O<sub>5</sub>Si: C, 66.94; H, 7.96. Found: C, 66.93; H, 7.98.

**Synthesis of (*S*)-2-benzoyloxymethyl-2-(dimethyl-*t*-butyl)silyloxymethyl oxirane 18.** To a solution of oxirane (*S*)-**7** (200 mg, 0.96 mmol) in pyridine (2 ml) at 0°C under argon atmosphere, neat dimethyl-*t*-butylsilyl chloride (180 mg, 11.53 mmol) was added. After 5 min., a white precipitate appeared and stirring was continued for 24 hours. After all starting material **7** had completely disappeared, the reaction mixture was poured into a chromatography column packed with silica gel and eluted in *n*-hexane / ethyl ether 9 : 1 to give **18** in 55% yield: [α]<sub>D</sub><sup>20</sup> + 1.15 (c 0.8, CHCl<sub>3</sub>); *Anal.* Calcd. for C<sub>17</sub>H<sub>26</sub>O<sub>4</sub>Si: C, 63.32; H, 8.13. Found: C, 63.77; H, 8.15.

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