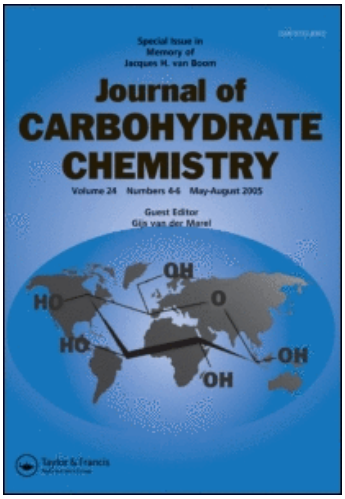

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Reaction of 2,3-*O*-Isopropylidene-D-Glyceraldehyde and Some Dialkyl and Diarylthiomethyl Sulfoxides: Stereochemical Aspects

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REACTION OF 2,3-*O*-ISOPROPYLIDENE-D-GLYCERALDEHYDE AND SOME DIALKYL AND DIARYLTHIOMETHYL SULFOXIDES: STEREOCHEMICAL ASPECTS

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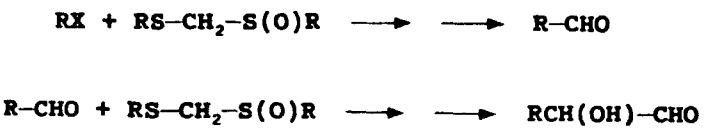
ABSTRACT

The reaction of 2,3-*O*-isopropylidene-**D**-glyceraldehyde with different dialkyl and diarylthiomethyl sulfoxides occurs with a high selectivity and produces the corresponding 1-alkyl(or 1-aryl)-sulfynil-1-alkyl(or 1-aryl) thio-3,4-*O*-isopropylidene-**D**-tetroses as pure diastereoisomers. We have determined the absolute configuration of the three chiral centers formed in these reactions.

INTRODUCTION

The alkyl-alkylthiomethyl sulfoxides has been used as alkylation agents in the synthesis of aldehydes[1] and α-hydroxyaldehydes,[2] as shown in the Scheme 1. These compounds have also been used to introduce a carbonyl group in a sugar derivative, by a Michael type reaction.[3]

In a previous work,[4] we described the reaction of 2,3-*O*-isopropylidene-**D**-glyceraldehyde **1**, with ethyl ethyl-thiomethyl sulfoxide **2** to give some **D**-erythrose and **D**-threose deri-

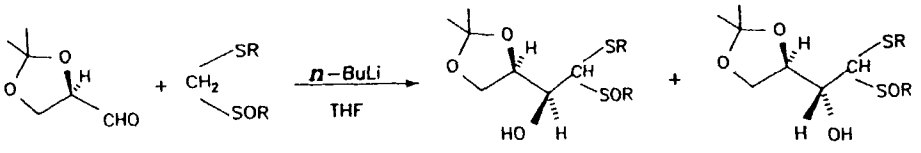


SCHEME 1

vatives by a way different from those previously reported,[5,6] and also described a study of the obtained sulfoxides. In addition, we have used this reaction to add a carbon atom to a derivative of 2,5-anhydro-D-mannose and employed the product in the synthesis of a C-glycofuranosylfuran derivative.[7] The product distribution observed in that reaction prompted us to use different dithioacetal *S*-oxides to study reaction stereoselectivity. Consequently, in some cases we used mixtures enriched in one of the enantiomers.

RESULTS AND DISCUSSION

The reaction of **1** with the lithium salt of racemic ethyl ethyl- **2**, methyl methyl- **3** and phenyl phenylthiomethyl sulfoxide **4**, and also with mixtures enriched in (+)-(*R*)-**2** and in (-)-(*S*)-**2**,[8] was carried out in a helium atmosphere at -78°C. In all of the reactions we obtained a mixture of diastereoisomers, mainly with the D-*erythro* configuration (Scheme 2).



1 **2** (R=Et) **3** (R=Me) **4** (R=Ph) **5** (R=Et) **12** (R=Ph) **6,7,8,9** (R=Et) **10,11** (R=Me) **13,14,15** (R=Ph)

SCHEME 2

Using this reaction it is possible to obtain some **D**-erythrose and **D**-threose derivatives from **D**-glyceraldehyde, with stereoselectivity at the new chiral center. The fact that **D**-erythrose derivatives are mainly obtained can be explained by Felkin's theory.[9] Following this hypothesis, the attack of the nucleophilic reactant occurs on the more stable conformation of the aldehyde **1** and passes through the transition state shown in Figure 1, where the oxygen atom linked to the carbon atom next to the carbonyl group is placed in a position perpendicular to the π system.

According to this model, the product or products formed primarily will have the *R* configuration at C-2 (**D**-*erythro*), while the minor products will have the *S* configuration at the corresponding atom (**D**-*threo*). As the nucleophilic reactant used has a chiral center at the sulphur atom of the sulfoxide group and a new one is generated at the carbon atom C-1, eight stereoisomers, four with a **D**-*erythro* configuration and four with a **D**-*threo* configuration, can be produced.

In the condensation reaction between 2,3-*O*-isopropylidene-**D**-glyceraldehyde **1** and the racemic mixture of ethyl ethylthiomethyl sulfoxide **2**, we have obtained five out of the eight possible diastereoisomers (**5-9**), which are included in Table 1 with their relatives yields (**Y**), their specific optical rotations ($[\alpha]_D$) and their acid hydrolysis product (**Hyd**). In this Table are also indicated the yields of the same diastereoisomers when the reaction was carried out with mixtures enriched in (+)-(*R*)-**2** (**Y+**) or in (-)-(*S*)-**2** (**Y-**) enantiomers.

The reaction of the aldehyde **1** with racemic methyl methylthiomethyl sulfoxide **3** produces only two diastereoisomers, **10** and **11**, whose relative yields (**Y**), specific optical rotation values ($[\alpha]_D$) and hydrolysis products (**Hyd**) are included in Table 1. From the reaction between the aldehyde **1** and the racemic phenyl phenylthiomethyl sulfoxide **4** we have isolated four products (**12-15**), whose characteristics are also shown in Table 1.

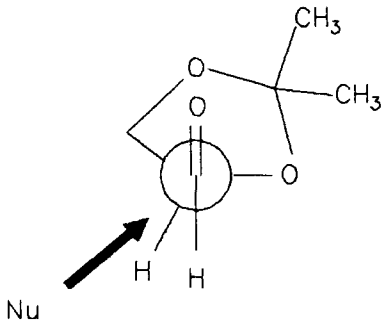


FIGURE 1

TABLE 1. Yields, specific optical rotation values and hydrolysis products of compounds **5** to **15**.

Compound	Y[a]	Y(+)[b]	Y(−)[c]	$[\alpha]_D$	Hyd
5	4	9	——	——	**D**-*threo*.
6	56	28	66	-16.7	**D**-*eryth*.
7	11	——	14	-176.8	**D**-*eryth*.
8	9	15	4	+170.6	**D**-*eryth*.
9	20	48	16	+14.7	**D**-*eryth*.
10	80	——	——	-64.3	**D**-*eryth*.
11	20	——	——	+22.8	**D**-*eryth*.
12	8	——	——	-190.0	**D**-*threo*.
13	29	——	——	-35.9	**D**-*eryth*.
14	47	——	——	+97.2	**D**-*eryth*.
15	16	——	——	+151.4	**D**-*eryth*.

a. Product Yield for reactions with racemic mixture of **2**.
b. Product Yield for reactions with mixtures enriched in (+)-(*R*)-**2**.
c. Product Yield for reactions with mixtures enriched in (−)-(*S*)-**2**.

To determine the configuration of the new chiral centers we performed a hydrolysis of products **5-15** in acidic medium. Paper chromatography of hydrolysis products, in comparison with authentic samples, indicates that **5** and **12** produce **D**-threose, while all the others yield **D**-erythrose, showing that in the first case, the configuration of the carbon atom C-2 is *S* (**D**-*threo*), while in all the others the configuration is

R (**D**-*erythro*). In this way we established that the condensation reaction produced mainly the **D**-erythrose derivatives in all the studied cases, according to the mechanism applying the Felkin's model.

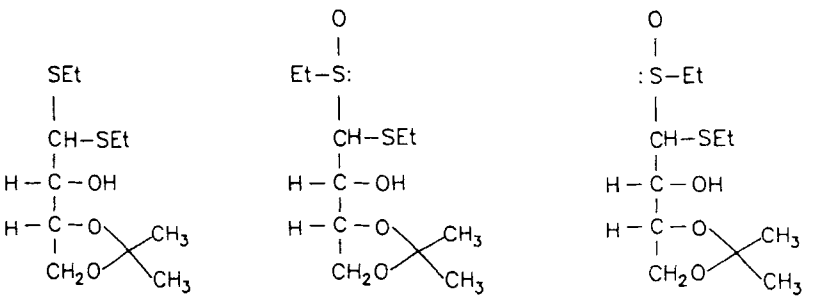
The sulphur atom configuration in the sulfoxide group is determined from products obtained by the reaction of aldehyde **1** with (+)-(*R*)-**2** and (-)-(*S*)-**2** enriched mixtures. When **1** reacts with (+)-(*R*)-**2**, products **5**, **6**, **8** and **9** are obtained in relative proportions of 9%, 28%, 15% and 48% respectively, as shown in Table 1 (**Y+**). However, the presence of compound **7** was not detected. In this regard, reaction of **1** with the racemic sulfoxide **2**, gives as major products **5**, **8** and **9**, indicating that all diastereoisomers that appear as major products have an R configuration at the sulphur atom of the sulfoxide group.

In the reaction of **1** with the mixture enriched in sulfoxide (-)-(*S*)-**2**, products **6**, **7**, **8** and **9** were isolated in relative proportions of 66%, 14%, 4% and 16%, respectively, (see **Y-** in Table 1) showing an increase in the proportions of diastereoisomers **6** and **7** compared to the experiment where the racemic mixture of sulfoxide **2** was used (see **Y+** in Table 1), indicating an *S* configuration at the sulphur atom in the sulfoxide group.

Based on the $[\alpha]_D$ values observed for the diastereoisomers **6**, **7**, **8** and **9** (Table 1), and following the method of optical comparison (10) we can assert:

- The contribution of the chiral centers C-2 and C-3 to the specific rotation of the four diastereoisomers is nearly the same. Such contribution is not signifiant since the value for the specific rotation of 3,4-*O*-isopropylidene-**D**-erythrose diethyl dithioacetal **16**, possessing a similar structure, is so small ($[\alpha]_D$ -1.4°).[11] As a consequence the observed specific rotation value for compounds **6**, **7**, **8** and **9** are mainly due to the contributions from the asymmetric centers C-1 and S*O (Fig. 2).

- The configuration at the sulfur atom in compounds **6** and **7** is the same, but opposite at their respective C-1 carbon.



16 **6,7** **8,9**

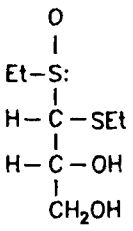
FIGURE 2

- Compounds **6** and **8** have an opposite configuration at S*O, but the same configuration at C-1.

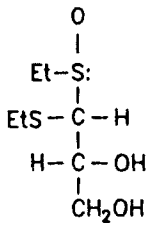
- Contributions from the chiral centers C-1 and S*O to specific rotation of compounds **6** and **9** have to be of opposite sign, according to the low value found (-16.7° and +14.7°, respectively). Both isomers differ in absolute configuration at the mentioned chiral centers.

- Contribution from chiral centers C-1 and S*O to the specific rotation of compounds **7** and **8** must have the same absolute value (negative in the first case and positive in the second one) because of the high value found (-176.8° and +170.6°, respectively). Both isomers also differ in configuration at the mentioned chiral centers.

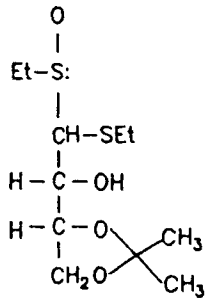
Finally, we determined the absolute configuration at C-1 in compounds **6** to **9** from a comparative study of the specific rotations of the mentioned compounds with those of the four diastereoisomers having similar structure (Fig. 3), i.e.,2*R*-1-ethylsulfinyl-1-ethylthio-2,3-dihydroxypropane(**17-20**), whose absolute configurations have been determined by X-Ray diffraction.[12] The specific rotation values and the absolute configurations deduced for compounds **6-9** are shown in Table 2.



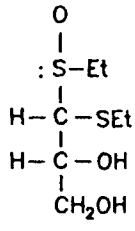
(1*S*)-(*S*)-17



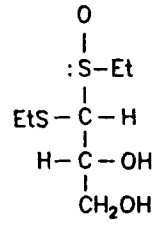
(1*R*)-(*S*)-18



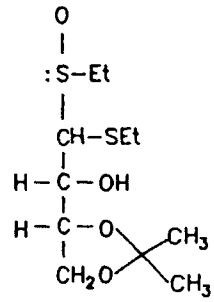
(1*S*)-(*S*)-6
(1*R*)-(*S*)-7



(1*S*)-(*R*)-19



(1*R*)-(*R*)-20

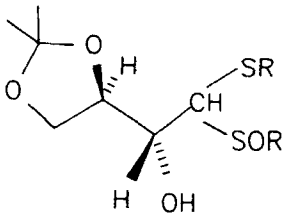


(1*S*)-(*R*)-8
(1*R*)-(*R*)-9

FIGURE 3

TABLE 2. Absolute configurations and specific optical rotation values for compounds of Fig.3

Prod.	Configuration C-2,C-1,S-O	$[\alpha]_D$
6	*R,S,S*	-16.7
7	*R,R,S*	-176.8
8	*R,S,R*	+170.6
9	*R,R,R*	+14.7
17	*R,S,S*	-13.8
18	*R,R,S*	—
19	*R,S,R*	+141.3
20	*R,R,R*	+54.2



13,14,15 (R=Ph)

FIGURE 4

TABLE 3. Absolute configurations and specific optical rotation values for compounds of Fig.4

Prod.	Configuration C-2,C-1,S-O	$[\alpha]_D$
13	*R,R,S*	-35.9
14	*R,S,S*	+97.2
15	*R,R,R*	+151.4

When the attached group at the sulfoxide is phenyl instead of alkyl (**13**, **14** and **15**, Fig.4), the specific rotation of the corresponding dithioacetal **21** is very high ($[\alpha]_D$ +164.7°). According to this value, the contribution of the chiral centers C-2 and C-3, in the sulfoxides, must be high. By a similar analysis as above, we propose the configurations shown in Table 3.

EXPERIMENTAL

Solvents used were dried over anhydrous sodium or magnesium sulphate, and evaporated under reduced pressure at temperature below 40 °C. Paper chromatography analysis (descending technique) was performed on Whatman Nº1 paper,

using as eluents 1-butanol-pyridine-water mixtures, 5:3:2 (solvent A), 15:4:3 (solvent B) and 15:5:6 (solvent C) and detection was done with silver nitrate.[13] **D**-threose and **D**-erythrose used for comparison were synthesized.[14] TLC was performed on glass plates coated with Silica Gel G (Merck), spots being detected with iodine vapors or by charring with sulphuric acid in ethanol (10%). Column chromatography was performed using Silica Gel Merck 60 (70-230 mesh).

Melting points were determined with a Gallenkamp MFB-595 device, and optical rotations were measured at room temperature with a 141 Perkin-Elmer or an Atago "POLAX" polarimeter.

^{1}H NMR spectra for solutions in $CDCl_3$ were measured using a Bruker WP-80-SY or an AM-300 spectrometer. Chemical shift values are expressed in ppm (δ), relative to TMS as the internal reference; signal multiplicities are noted as s, singlet; d, doublet; t, triplet; dd, double doublet; q, quartet and m, multiplet. Active hydrogens of some compounds were exchanged with deuterium oxide. The enantiomeric ratios were determined by measuring the ^{1}H NMR spectra taken in the presence of the chiral shift reagent Eu(tfc)$_3$, Europium(III)-tris[3-(trifluoromethylhydroxymethylene)-d-camphorate], employing a Bruker WH-200 or a Bruker WP-80-SY spectrometer.

The ^{13}C NMR spectra were recorded with a Bruker AM-300 spectrometer. IR spectra were measured using a 782 Perkin-Elmer, a 408 Shimadzu or a Nicolet FTIR-20-SX spectrometer.

Elemental analyses were determined with a Carlo Erba Elemental Analyzer 1106.

Synthesis of Formaldehyde Diphenyl Dithioacetal.[15] Thiophenol (66 g, 0.6 mmol) was added to a stirred mixture of paraformaldehyde (9 g, 0.3 mmol) in concentrated hydrochloric acid (50 mL) at 25 °C, and the stirring was continued for 4 h. The organic layer was separated, the aqueous phase was extracted with chloroform, the extracts

were combined, dried and concentrated, and the residue was chromatographed (hexane). The final product was a white solid (21 g, 30%) mp 37.2-38.0 °C, lit.[16] 39.5-40 °C; ^{1}H NMR ($CDCl_3$) δ 4.3 (2H, s, CH_2), 7.2-7.6 (10H, m, aromatic protons).

Synthesis of Phenyl Phenylthiomethyl Sulfoxide 4.[15] Hydrogen peroxide (2.23 mL, 30 %) was added to a solution of formaldehyde diphenyl dithioacetal (5.1 g, 21.9 mmol) in acetic acid (10 mL), and the resulting solution cooled in an ice-salt bath. After 7 h, methylene chloride (10 mL) was added, the solution was neutralized with potassium carbonate, and the mixture filtered. The filtrate was dried over anhydrous sodium sulphate, concentrated, and the residue was chromatographed, (hexane-ethyl acetate, 1:1). A colorless liquid was obtained (4.79 g, 88%): ^{1}H NMR ($CDCl_3$) δ 4.08 (2H, s, CH_2), 7.26-7.83 (10H, m, aromatic protons); IR (KBr) 3050, 3000, 2900, 1580, 1480, 1440, 1085, 1045, 1025, 740 and 690 cm^{-1}.

Anal. Calcd for $C_{13}H_{12}OS_2$: C, 62.90; H, 4.87. Found: C, 62.73; H, 5.00.

Synthesis of (+)-(R)-Ethyl Ethylthiomethyl Sulfoxide. (+)-(R)-2. Titanium (IV) isopropoxide $Ti(OiPr)_4$ (4.47 mL, 15 mmol) and (+)-(*R,R*)-diethyl tartrate (5.13 mL, 30 mmol) were dissolved in methylene chloride (150 mL) under a helium atmosphere at 25 °C.[17] Water was added (0.27 mL, 15 mmol), and the mixture was stirred until it became homogeneous. Freshly distilled formaldehyde diethyl dithioacetal[15] (2.04 g, 15 mmol) was added, the mixture was cooled (-40 °C) and a solution of *t*-butyl hydroperoxide (7.5 mL, 2M) in methylene chloride was added. After 24 h at -40 °C, water (30 mL) was added to the cooled solution. The gelatinous mixture was stirred for one h while the temperature was allowed to rise to 20 °C. After filtration, the filtrate was extracted with methylene chloride, the organic extracts were combined, washed successively with 1M sodium hydroxide and brine, dried, concentrated and the residue chromatographed

(diethyl ether) to give the desired product as a pale yellow liquid (1.6 g, 70% yield): $[\alpha]_D$ +89.9° (*c* 1.90, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.22-1.47 (6H, 2t, J= 7.5 Hz, $SCH_2\underline{CH_3}$, $SOCH_2\underline{CH_3}$), 2.59-3.15 (4H, m, $SC\underline{H_2}CH_3$, $SOC\underline{H_2}CH_3$), 3.7 (2H, s, $C\underline{H_2}$-). The enantiomeric excess (60%) was determined by ^{1}H NMR spectroscopy in the presence of $Eu(tfc)_3$, and the R configuration of the sulfoxide was established as described.[17]

Synthesis of (-)-(S)-ethyl Ethylthiomethylsulfoxide. (-)-(S)-2. The procedure used was similar to that applied to the synthesis of the (+)-(R)-2 isomer, but employing (-)-(*S,S*)-diethyl tartrate as the reactant. The product was purified by column chromatography (diethyl ether) and a pale yellow liquid (1.32 g, 58%) was obtained: $[\alpha]_D$ -72.3°(*c* 0.89, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.22-1.47 (6H, two t, J= 7.5 Hz, SCH2$\underline{CH_3}$, $SOCH_2$-$\underline{CH_3}$), 2.59-3.15 (4H, m, $SC\underline{H_2}CH_3$,$SOC\underline{H_2}CH_3$), 3.65 (2H, s, $C\underline{H_2}$). The enantiomeric excess (50%), and the S configuration was determined as in the case of the R isomer.

Reaction of 2,3-*O*-Isopropylidene-D-glyceraldehyde, 1, with Ethyl Ethylthiomethyl Sulfoxide, 2. *n*-BuLi (15% in hexane, 30 mL, 48 mmol) was slowly added at -70 °C to a stirred solution of **2**[18] (4.91 g, 32 mmol) in THF (21 mL). After 30 min, a solution of the the aldehyde **1** (19) (4.2 g, 32 mmol) in THF (10 mL) was added to the mixture. The reaction mixture was allowed to warm to room temperature and then poured into water (130 mL). The mixture was extracted several times with methylene chloride, the organic phases were dried and concentrated. The residue was chromatographed (gradient of diethyl ether-chloroform 1:1, - ether), to give five products isolated in order of elution as follows:

*1-(R)-ethylsulfinyl-1-ethylthio-3,4-O-isopropylidene-***D-***threose,* **5.** Colorless syrup (300 mg, 3%): $[\alpha]_D$ +34.8° (*c* 1.2, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.15-1.50 (12H, m, SCH2$\underline{CH_3}$, $SOCH_2$-$\underline{CH_3}$, $C(Me)_2$), 2.60-2.87 (2H, c, J= 7.5 Hz, $SC\underline{H_2}$-CH_3), 3.52 (1H, broad s, H-1), 3.87-4.05 (3H, m, H-

2, H-4, H-4'), 4.27 (1H, broad s, OH, disappears on deuteration), 4.61 (1H, dd, $J_{3,4}$=7 Hz, H-3); IR (KCl): 3300, 2990, 2940, 1455, 1375, 1269, 1210, 1155, 1125, 1069, 1005, 979, 889 and 750 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_4S_2$: C, 46.78; H, 7.85. Found: C, 46.70; H, 7.70.

(1S)-1-(S-ethylsulfinyl)-1-ethylthio-3,4-O-isopropylidene-D-erythrose, **6**. Solid (3.5 g, 39%): mp 85-86 °C (from hexane-carbon tetrachloride); $[\alpha]_D$ -16.7° (*c* 0.83, chloroform); ^1H NMR ($CDCl_3$) δ 1.20-1.05 (12H, m, $SCH2C\underline{H}_3$, $SOCH_2-C\underline{H}_3$, $C(Me)_2$), 2.62-2.90 (2H, c, J=7.5 Hz, $SC\underline{H}_2CH_3$), 2.85-3.13 (2H, c, J=7.5 Hz, $SOC\underline{H}_2CH_3$), 3.20 (1H, broad s, OH, disappears on deuteration), 3.87 (1H, broad s, H-1), 4.07-4.20 (2H, m, H-4, H-4'), 4.22-4.40 (2H, m, H-2, H-3); IR (KBr): 3307, 2980, 2934, 2877, 1461, 1388, 1377, 1261, 1210, 1146, 1124, 1097, 1073, 1029, 964, 842, 634 and 602 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_4S_2$: C, 46.78; H, 7.85. Found: C, 46.81; H, 8.10.

*(1R)-1-(S-ethylsulfinyl)-1-ethylthio-3,4-O-*isopropylidene-*D-erythrose,* **7**. White solid (680 mg, 8%): mp 97.2-97.7 °C (from hexane-carbon tetrachloride); $[\alpha]_D$ -176.8° (*c* 0.63, chloroform); ^1H NMR ($CDCl_3$) δ 1.25-1.50 (12H, m, $SCH2C\underline{H}_3$, $SOCH_2-C\underline{H}_3$, $C(Me)_2$), 2.62-2.90 (2H, c, J=7.5 Hz, $SC\underline{H}_2-CH_3$), 2.90-3.20 (3H, c, J=8 Hz,$SOC\underline{H}_2CH_3$, OH), 4.05-4.20 (3H, m, H-1, H-4, H-4'), 4.25-4.52 (2H, m, H-2, H-3); IR (KBr): 3243, 2979, 2935, 2897, 1434, 1384, 1374, 1257, 1221, 1152, 1120, 1974, 1937, 967, 845 and 638 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_4S$: C, 46.78; H, 7.85. Found: C, 46.67; H, 7.91.

(1S)-1-(R-ethylsulfinyl)-1-ethylthio-3,4-O-isopropylidene-D-erythrose, **8**. White solid (540 mg, 6%): mp 101-101.6 °C (from hexane-carbon tetrachloride), $[\alpha]_D$ +170.6° (*c* 0.98, chloroform); ^1H NMR ($CDCl_3$) δ 1.15-1.42 (12H, m,$SCH2C\underline{H}_3$, $SOCH_2-C\underline{H}_3$, $C(Me)_2$), 2.50 (1H, s broad, OH, disappears on deuteration), 2.55-2.83 (2H, c, J= 8 Hz,

$SC\underline{H}_2CH_3$), 2.77-3.07 (2H, c, J= 8 Hz, $SOC\underline{H}_2CH_3$, 3.55 (1H, d, $J_{1,2}$= 2 Hz, H-1), 3.80-4.05 (2H, m, H-4, H-4'), 4.10-4.40 (2H, m, H-2, H-3); IR (KBr): 3414, 2987, 2929, 1454, 1378, 1261, 1213, 1162, 1073, 1041, 1017, 974, and 866 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_4S_2$: C, 46.78; H, 7.85. Found: C, 46.80; H, 7.54.

*(1R)-1-(*R*-ethylsulfinyl)-1-ethylthio-3,4-O-isopropylidene-***D***-erythrose,* **9**. Colorless syrup (1.26 g, 20%): $[\alpha]_D$ +14.7°(*c* 0.82, chloroform); ^1H NMR ($CDCl_3$) δ 1.17-1.55 (12H, m, SCH2$C\underline{H}_3$, $SOCH_2C\underline{H}_3$, $C(Me)_2$), 2.62-3.25 (5H, 2 c, J=8 Hz, $SC\underline{H}_2CH_3$, $SO\underline{H}_2CH_3$, OH), 3.70-3.87 (1H, dd, $J_{4,3}$=5 Hz, $J_{4,4'}$=9 Hz, H-4), 4.00-4.17 (2H, m, H-1, H-4'), 4.20- 4.50 (2H, m, H-2, H-3); IR (KCl) 3250, 2990, 2925, 1455,1380, 1370, 1255, 1210, 1150, 1970, 1010, 970 and 850 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_4S_2$: C, 46.78; H, 7.85. Found: C, 46.98; H, 7.82.

Reaction of 2,3-*O*-Isopropylidene-D-glyceraldehyde, 1, with (+)-(R)-Ethyl Ethylthiomethyl Sulfoxide, (+)-R-2. A solution of the sulfoxide (+)-(*R*)-**2** (1.5 g, 9.87 mmol) in THF (6.3 mL) was treated with *n*-BuLi (7.3 mL, 15% in hexane) and a solution of **1** (1.28 g, 9.87 mmol) in THF (3 mL), as described above. After processing, the syrupy residue (2.14 g, 77%) was chromatographed, using a gradient of diethyl ether-chloroform. The products obtained were: **5**, (195 mg, 7%); **6**, (600 mg, 22%); **8**, (336 mg, 12%); and **9** (1.91 g, 36%), identified as described above.

Reaction of 2,3-*O*-Isopropylidene-D-glyceraldehyde, 1, with (-)-(S)-Ethyl Ethylthiomethyl Sulfoxide, (-)-S-2. A solution of the sulfoxide (-)-(*S*)-**2** (370 mg, 3.08 mmol) in THF (2 mL) was treated with *n*-BuLi (2.27 mL, 15% in hexane) and aldehyde **1** (400 mg, 3.08 mmol) in THF (1 mL), as previously described. Compounds **6** to **9** were isolated in the following order of elution: **6** (394 mg, 44%); **7** (83 mg, 10%); **8** (23 mg, 3%) and **9** (96 mg, 11%).

Reaction of 2,3-*O*-Isopropylidene-D-glyceraldehyde, 1, with Methyl Methylthiomethyl Sulfoxide, 3. *n*-BuLi (15% in hexane, 21.65 mL) was slowly added at -30 °C to a stirred solution of sulfoxide **3** (3.9 g, 31.50 mmol) in THF (20 mL). After 30 min the temperature was allowed to rise to 0 °C, and a solution of **1** (4 g, 31.50 mmol) in THF (10 mL) was added. Stirring was continued for 40 min and then water (130 mL) was added. The mixture was extracted several times with ethyl acetate, and the organic extracts were dried and concentrated. The residue was chromatographed (diethyl ether). Two products were isolated and identified as:

(1S)-1-(S)-methylsulfinyl)-1-methylthio-3,4-O-isopropylidene-D-erythrose, **10**. Solid (3.9 g, 49%): mp 145-146 °C (from diethyl ether); $[\alpha]_D$ -64.3° (*c* 0.76, chloroform); ^{1}H NMR (Cl_3CD) δ 1.37-1.42 (6H, two s, $C(Me)_2$), 2.32 (3H, s, $S-CH_3$),2.80 (3H, s, $SOCH_3$), 3.72 (1H s, H-1), 4.05-4.17 (2H, m, H-4, H-4'), 4.25- 4.45 (3H, m, H-2, H-3 and OH); IR (KBr) 3273, 2992, 2949, 2882, 1433, 1385, 1373, 1251, 1218, 1149, 1119, 1097, 1070,1034, 965, 841 and 610 cm^{-1}.

Anal. Calcd for $C_9H_{18}O_4S_2$: C, 42.49; H, 7.13. Found: C, 42.47; H, 7.01.

(1R)-1-(R)-methylsulfinyl)-1-methylthio-3,4-O-isopropylidene-D-erythrose, **11**. Syrup (937 mg, 12%): $[\alpha]_D$ +22.8° (*c* 0.8, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.37-1.47 (6H, 2s, C(Me)2), 2.32 (3H, s, SCH_3), 2.89 (3H, s, $SOCH_3$), 3.77-3.83 (2H, dd, $J_{4,3}$=5 Hz, H-4 and OH), 4.00-4.12 (2H, m, $J_{1,2}$=4 Hz, H-1, H-4'): 4.22-4.55 (2H, m, H-3, H-2); IR (KCl): 3250, 2995, 1420, 1380, 1370, 1255, 1220, 1155, 1020, 950, 850 and 750 cm^{-1}.

Anal. Calcd for $C_9H_{18}O_4S_2$: C, 42.49; H, 7.13. Found: C, 42.30; H, 7.21.

Reaction of 2,3-*O*-Isopropylidene-D-glyceraldehyde, 1, with Phenyl Phenylthiomethyl Sulfoxide, 4. *n*-BuLi (15% in hexane, 36.9 mL, 50 mmol) was slowly added at -70 °C to a stirred solution of **4** (13.3 g, 53.7 mmol) in dry THF (50

mL). After 30 min, a solution of aldehyde **1** (6.35 g, 48.8 mmol) in dry THF (10 mL) was added. The temperature of the reaction mixture was allowed to rise to 20 °C and an saturated aqueous solution of ammonium chloride (50 mL) was added. The mixture was extracted several times with methylene chloride, the organic extracts were combined, dried, concentrated and the residue was chromatographed using a gradient of hexane-diethyl ether. Four products were isolated and identified, in order of elution, as:

*1-(R)-phenylsulfinyl)-1-phenylthio-3,4-O-isopropylidene-***D***-threose,* **12**. Solid (730 mg, 5%) mp 152.4-153.5 °C (from carbon tetrachloride); $[\alpha]_D$ -190.0° (*c* 1.93, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.33, 1.48 (6H, two s, CH3), 3.75 (1H, s, OH, disappears on deuteration), 3.75-3.90 (1H, dd, $J_{2,1}$= 9.0 Hz, $J_{2,3}$= 2.0 Hz, H-2), 3.93-4.12 (1H, dd, H-4'), 3.98-4.20 (1H, dd, H-4), 4.40-4.51 (1H, dd, $J_{1,2}$= 9.0 Hz, H-1), 4.60-4.85 (1H, m, $J_{3,2}$= 2.0 Hz, $J_{3,4}$= 6.0 Hz, $J_{3,4'}$=8.0 Hz, H-3), 7.06-7.50 (8H, m, aromatic protons), 7.73-7.85 (2H, m, aromatic protons); IR (KBr) 3386, 3064, 2985, 2934, 1575, 1473, 1437, 1380, 1220, 1160, 1115, 1072, 1022, 7309 and 688 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_4S_2$: C, 60.32; H, 5.82. Found: C, 60.34; H, 5.86.

*(1R)-1-(S)-phenylsulfinyl)-1-phenylthio-3,4-O-isopropylidene-***D***-erythrose,* **13**. Solid (2.64 g, 19%): mp 120.7-121.9 °C (from a mixture of carbon tetrachloride-hexane); $[\alpha]_D$ -35.9° (*c* 0.82, chloroform); ^{1}H NMR ($CDCl_3$) δ 0.99, 1.26 (6H, two s, CH3), 4.05-4.09 (1H, dd, $J_{4',3}$= 5.60 Hz, $J_{4',4}$= 8.85 Hz, H-4'), 4.26-4.27 (1H, d, $J_{1,2}$= 1.10 Hz, H-1), 4.27-430 (1H, dd, $J_{2,1}$= 1.10 Hz, $J_{2,3}$= 8.86 Hz, H-2), 4.38-4.44 (1H, m, $J_{3,2}$ = 8.86 Hz, $J_{3,4}$= 3.90 Hz, $J_{3,4'}$= 5.60 Hz, H-3), 7.15-7.29 (3H, m, one *p*-H and two *m*-H C_6H_5-S-), 7.30-7.44 (5H, m, two *o*-H C_6H_5-S-, two *m*-H and one *p*-H C_6H_5-SO-), 7.46-7.60 (2H, m, two *o*-H C_6H_5-SO-); ^{13}C NMR ($CDCl_3$) δ 25.33, 26.67 (CH_3 isopropyl), 66.92 (C-4), 69.79 (C-1), 74.82, 76.75 C-2 and C-3), 109.68 ($C(Me)_2$), 125.34, 127.89, 129.18, 131.52, 132.55, 133.46, 149.82 (aromatic

carbons); IR (KBr) 3293, 3050, 2987, 1581, 1479, 1441, 1371, 1253, 1210, 1160,1068, 1024, 855, 740 and 688 cm^{-1}.

Anal. Calc. for $C_{19}H_{22}O_4S_2$: C, 60.32; H, 5.82. Found: C, 60.42; H, 5.88.

(1S)-1-(S)-phenylsulfinyl)-1-phenylthio-3,4-O-isopropylidene-D-erythrose, **14**. Solid (4.22 g, 30%): mp 118.0-119.0 °C (from hexane-diethyl ether); $[\alpha]_D$ +97.2° (*c* 1.20, chloroform); ^1H NMR ($CDCl_3$) δ 1.38, 1.46 (6H, two s, CH3), 2.57-2.73 (1H, d, OH, disappears on deuteration), 3.77-3.96 (1H, dd, $J_{4',3}$= 7.0 Hz, $J_{4',4}$= 9.0 Hz, H-4'), 4.05-4.08 (1H, d, $J_{1,2}$ = 3.9 Hz, H-1), 4.20-4.30 (1H, dd, $J_{2,1}$= 3.0 Hz, $J_{2,3}$= 5.0 Hz, H-2), 4.43-4.65 (1H, m, $J_{3,2}$= 5.0 Hz, $J_{3,4}$ = 6.0 Hz, $J_{3,4'}$= 7.0 Hz, H-3), 7.05-7.35 (5H, m, aromatic protons for C_6H_5-S-), 7.36-7.60 (3H, m, two *m*-H and one *p*-H C_6H_5-SO-), 7.60-7.90 (2H, m, two *o*-H C_6H_5-SO); IR (KBr): 3381, 3057, 2986, 2934, 2890, 1578, 1476, 1440, 1373, 1258, 1215, 1155, 1067, 1045, 852, 742 and 690 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_4S_2$: C, 60.32; H, 5.82. Found: C, 60.00; H, 5.67.

(1R)-1-(R)-phenylsulfinyl)-1-phenylthio-3-4-O-isopropylidene-D-erythrose, **15**. Solid (1.42 g, 10%) mp 167.0-169.0 °C (from carbon tetrachloride-chloroform); $[\alpha]_D$ +151.4° (*c* 0.96, chloroform); ^1H NMR ($CDCl_3$) δ 1.35, 1.75 (6H, two s, CH3), 3.57-3.80 (1H, d, OH, disappears on deuteration), 3.80-4.04 (1H, dd, $J_{4',3}$= 5.0 Hz $J_{4',4'}$ = 8.0 Hz, H-4'), 3.92-4.13 (1H, dd, $J_{4,3}$= 7.0 Hz, $J_{4,4'}$ = 8.0 Hz, H-4), 4.17-4.35 (2H, m, H-1, H-2), 4.35-4.67 (1H, m, H-3), 7.00-7.33 (5H, m, aromatic protons for C_6H_5-SO), 7.33-7.55 (3H, m, two *m*-H and one *p*-H C_6H_5-SO-), 7.65-7.90 (2H, m, two *o*-H C_6H_5-SO-); IR (KBr) 3290, 3056, 2987, 2929, 1579, 1477, 1441, 1381, 1371, 1257, 1203, 1145, 1105, 1085, 1063, 1026, 1006, 845, 747 and 686 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_4S_2$: C, 60.32; H, 5.82. Found: C, 60.25; H, 5.77.

Hydrolysis of 1-Alkyl(and 1-Phenyl)sulfinyl-1-alkyl (and 1-phenyl)thio-3,4-*O*-isopropylidene-D-tetroses in acidic medium. General procedure: A solution of the

starting compound (0.2 mmol) in THF-water (1:1) (10 mL), and perchloric acid (60 %, 0.5 mL) was heated under reflux during 2 h. After neutralization with Amberlite IRA-93 (HCO_3^-), the solution was extracted with chloroform, the aqueous layer was concentrated and the residue analyzed by paper chromatography. The analysis of the hydrolysate of compounds **5** and **12** showed the presence of only **D**-threose. The material co-chromatographed with an authentic sample of **D**-threose.[14] **D**-threose: R_{ribose} for several eluents are 1.25 (solvent A), 1.41 (solvent B) and 1.50 (solvent C) for products obtained from **5** and **12**. **D**-erythrose was the sole hydrolysis product obtained from compounds **6**, **7**, **8**, **9**, **10**, **11**, **13**, **14** and **15**. The material co-cromatographed with an authentic sample of **D**-erythrose.[14] **D**-erythrose: R_{ribose} values for several eluents are R_r= 1.19 (solvent A), R_r= 1.32 (solvent B) and R_r= 1.26 (solvent C).

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