Enantioselective Preparation of Alkyl Alkylsulfanylmethyl Sulfoxides and 4,5-Dihydroisoxazoles from Alkanesulfinates of 1,2:5,6-Di-*O*-isopropylidene-D-glucose

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Reaction of (*R*)- and (*S*)-alkanesulfinates of 1,2:5,6-di-*O*-isopropylidene-D-glucose (DAG) with methylsulfanylmethyllithium produces their corresponding dithioacetal mono-*S*-oxides with enantiomeric excesses ranging from 95 to 100%. On the other hand, exo-metallation of 3-methyl-4,5-dihydroisoxazoles and their subsequent reaction with (*R*)- and (*S*)-alkanesulfinates of DAG produces optically active 3-ethylsulfinylmethyl-4,5-dihydroisoxazoles.

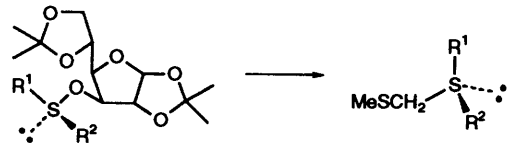
Optically active sulfoxides are considered to be among the most important organic sulfur compounds because they are used in asymmetric synthesis.[1] In order to prepare chiral sulfoxides with high enantiomeric excess (e.e.), many different approaches have been undertaken. Two of them, the asymmetric oxidation of prochiral sulfoxides[2,3] and the Andersen method from chiral sulfinates,[4] should be emphasized. The utility of these methods to prepare dialkyl sulfoxides with high optical yields is, unfortunately, very limited. Hence, Kagan[5] has prepared this kind of sulfoxide starting from the (*S*)-ethyl lactate, and Llera,[6] more recently, has developed a new and efficient procedure for the preparation of optically active methyl sulfoxides by stereoselective conversion of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (DAG) into their (*S*)- or (*R*)-methanesulfinates and subsequent reaction using an appropriate Grignard reagent. Taking into consideration the aforementioned antecedents, we were concerned with evaluating the effectiveness of Llera's method in the synthesis of optically active alkylsulfanylmethylsulfoxides and diastereoisomerically pure 3-alkylsulfinylmethyl-4,5-dihydroisoxazoles, compounds which have not yet been obtained as pure isomers. The utility of the former compounds is due to their being chiral equivalents to an acyl anion; thus they have many synthetic applications[7,8] in alkylation reactions, Michael additions, hydroxyalkylations, aminoalkylations and acylations.[9] The latter compounds are interesting because they are predecessors of some types of very functionalized molecules, such as β,β-dihydroxy ketones,[10] γ-alkylamines,[11] sugars, aminosugars and complex heterocycles.[12]

Results and Discussion

In this paper, we describe the preparation of (*R*)- and (*S*)-glucose diacetonide ethanesulfinates, **1** by the Llera[6] method for the elaboration of methanesulfinates of DAG. Compound (*R*)-**1**, with an 84% diastereoisomeric excess (d.e.), was obtained in a 94% chemical yield (c.y.) by treatment of a solution of DAG in toluene with ethanesulfinyl chloride in the presence of pyridine, whereas the utilization of Pr^i_2EtN brought about the preparation of isomer (*S*)-**1** with d.e. ≥ 98% and c.y. 96%. With methylene dichloride or THF as solvent, the same reaction products with similar d.e.s but with lower c.y.s (50–70%) were obtained.

After purification the sulfinic esters (*R*)-**1** and (*S*)-**1** were transformed into the corresponding enantiomerically pure ethyl methylsulfanylmethyl sulfoxides (*R*)-**3** and (*S*)-**3** by reaction with methylsulfanylmethyllithium, $MeSCH_2Li$ [prepared *in situ* from dimethyl sulfide, BuLi and tetramethylethane-1,2-diamine (TMEDA)[13]] as a displacement reagent of the DAG group.

By using the same procedure the two methyl methylsulfanylmethyl sulfoxide enantiomers (*R*)-**4** and (*S*)-**4** were obtained from the corresponding (*R*)- and (*S*)-methanesulfinates of DAG, (*R*)-**2** and (*S*)-**2** respectively, with 97% and 95% e.e. respectively [eqn. (1)].



(1)

(*R*)-**1** R^1 = Et, R^2 = O — (*R*)-**3** R^1 = Et, R^2 = O, $[\alpha]_D$ +153.2 (*c* 1.28), 46% (100% e.e.)

(*S*)-**1** R^1 = O, R^2 = Et — (*S*)-**3** R^1 = O, R^2 = Et, $[\alpha]_D$ −151.7 (*c* 3.08), 56% (100% e.e.)

(*R*)-**2** R^1 = Me, R^2 = O — (*R*)-**4** R^1 = Me, R^2 = O, $[\alpha]_D$ +92.2 (*c* 1.08), 48% (95% e.e.)

(*S*)-**2** R^1 = O, R^2 = Me — (*S*)-**4** R^1 = O, R^2 = Me, $[\alpha]_D$ −97.0 (*c* 1.44), 58% (97% e.e.)

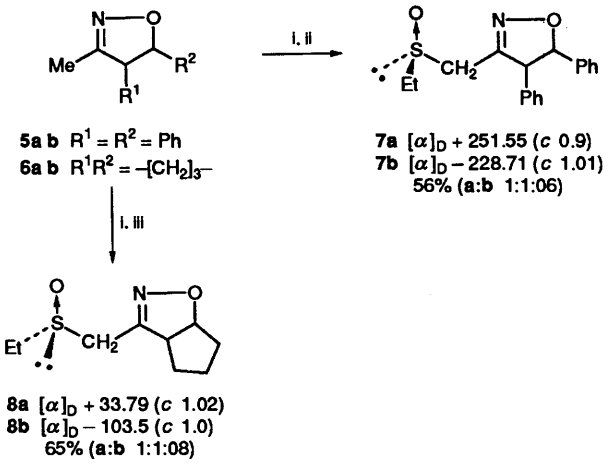
Reagent: $MeSCH_2Li$

Since the known mechanism of the Andersen[4] reaction predicts that the substitution process takes place with inversion of configuration at the sulfur atom, the configuration *R* was assigned to the sulfur atom of the dithioacetal mono-*S*-oxides coming from the substrates (*R*)-**1** and (*R*)-**2**, whereas the configuration *S* was assigned to the compounds obtained from the sulfinates (*S*)-**1** and (*S*)-**2**. The optical-rotation values are positive when measuring the isomers with *R* configuration and negative when measuring the isomers with *S* configuration. These results agree [and coincide in (*R*)-**4** and (*S*)-**4**] with the values already proposed for this type of compound, which have been previously synthesized by asymmetric oxidation[3a] of the corresponding dithioacetals, based on the reaction mechanism proposed by Kagan.[2a]

Taking into consideration the high stereoselectivities obtained (95–100% e.e.) and the acceptable chemical yields obtained (45–56%), we think that this method should be used in order to synthesize high-optical-purity alkylsulfanylmethyl sulfoxides since the results obtained have advantages over

either asymmetric oxidation methods or the Andersen synthesis which allows us to access only those sulfoxides having an aryl moiety as one of the groups R in RS(O)R'.

From the sulfinates (*R*)-**1** and (*S*)-**1**, diastereoisomerically pure (R_S) and (S_S)-3-ethylsulfinylmethyl-4,5-dihydroisoxazoles have been also synthesized as intermediates in the subsequent preparation of hydroxyisoxazolines.[14] By treatment of the racemic 3-methyl-4,5-dihydroisoxazoles **5a**, **b** and **6a**, **b** with lithium diisopropylamide (LDA) and subsequent reaction with (*R*)- or (*S*)-ethanesulfinates of DAG, ethylsulfinylmethyl-4,5-dihydroisoxazoles **7a**, **b** and **8a**, **b** were obtained in good yields as diastereoisomeric mixtures which were later separated by column chromatography (Scheme 1).



5a b $R^1 = R^2 = Ph$
6a b $R^1R^2 = -[CH_2]_3-$

7a $[\alpha]_D + 251.55$ (*c* 0.9)
7b $[\alpha]_D - 228.71$ (*c* 1.01)
56% (**a**:**b** 1:1:06)

8a $[\alpha]_D + 33.79$ (*c* 1.02)
8b $[\alpha]_D - 103.5$ (*c* 1.0)
65% (**a**:**b** 1:1:08)

Scheme 1 *Reagents:* i, LDA; ii, (*R*)-**1**; iii, (*S*)-**1**

The small or null influence exercised by the position of the groups in the heterocycle (C-4 and C-5) over the reactivity of the exo-metallated isoxazoline gives rise to a diastereoisomeric ratio near to unity, forming two isomers **a** and **b** with the same configuration at the sulfur atom, as a result of the total inversion in the sulfinate **1**, and opposite configurations in positions 4 and 5 of the heterocycle because of working with racemic mixtures **5a**, **b** or **6a**, **b**. The relative stereochemistry at the centres C-4 and C-5 of the isoxazoline ring is determined by the olefinic configuration (*E*-stilbene and cyclopentene) used in the 1,3-dipolar cycloaddition reaction, because this reaction is stereospecific and, besides, the configuration of the carbon atom is not modified during metallation.

Against the classical Andersen method starting from (*S*)-(−)-methyl toluene-*p*-sulfinate, the use of ethanesulfinates of DAG in the preparation of sulfinylmethylisoxazolines has the advantage of their easy accessibility to ethanesulfinates of both *R* and *S* configuration since it has been shown that ethyl sulfoxides, when compared with aryl sulfoxides, are superior substrates in hydroxy alkylation, both in the stereoselectivity of the process and in its chemical yield.[9]

Experimental

Tetrahydrofuran (THF) and toluene were distilled over sodium and benzophenone under argon immediately before use. Extracts were dried over anhydrous sodium or magnesium sulfate, and evaporated under reduced pressure at a temperature below 40 °C. TLC was performed on glass plates coated with Silica Gel G (Merck), spots being detected with iodine vapours or by charring with sulfuric acid in ethanol (10%). Column chromatography was performed using Silica Gel Merck 60 (70–230 mesh). M.p.s 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. $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR spectra for solutions in $CDCl_3$ were measured using a Bruker AM-300 spectrometer at 300 MHz. Chemical-shift values are expressed in ppm (δ), relative to $SiMe_4$ as internal reference; *J*-values are given in Hz. 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]. The ^{13}C NMR spectra were recorded with a Bruker AM-300 spectrometer. IR spectra were measured using a Nicolet FTIR-20-SX spectrometer. Mass spectra were recorded by the direct-insertion technique, using an HP-588-A spectrometer at 230 eV with a temperature source of 200 °C. Elemental analyses were determined with a Carlo Erba Elemental Analyzer 1106.

Synthesis of (S)-*Ethanesulfinate of DAG*, (S)-**1**.—A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (10 g, 38.5 mmol) in toluene (700 cm^3) was cooled to −78 °C, then diisopropylethylamine (8.56 cm^3, 1.3 mol equiv.) and freshly distilled ethanesulfinyl chloride (5.63 g, 50 mmol, 1.3 mol. equiv.) were added in turn. The resulting mixture was stirred at −78 °C, and the reaction was monitored by TLC [hexane–propan-2-ol 1:12 (×2)] until the starting product disappeared (*ca.* 30 min). Then the mixture was washed successively with 1 mol dm^{-3} hydrochloric acid, and saturated aq. sodium hydrogen carbonate. The organic layer was dried with sodium sulfate, the solvent was evaporated off and the residue was chromatographed (hexane–propan-2-ol, 40:1). Compound (*S*)-**1** (12.5 g, 96%) was obtained as a syrup (Found: C, 49.8; H, 7.2. Calc. for $C_{14}H_{24}O_7S$: C, 49.99; H, 7.19%); R_f 0.47 (hexane–propan-2-ol 10:1); $[\alpha]_D$ −76.21 (*c* 0.95, $CHCl_3$) {lit.,[18] $[\alpha]_D$ −63 (*c* 4.3, Me_2CO)}; ν_{max}(neat)/cm^{-1} 3000, 2950, 1460, 1385, 1375, 1260, 1220, 1140, 1075, 1025 and 835; δ_H 1.28 (3 H, t, J_{vic} 7.6, $MeCH_2SO$) 1.32, 1.35, 1.44 and 1.52 (12 H, 4 s, $CHMe_2$), 2.80 (2 H, c, J_{vic} 7.6, $MeCH_2SO$), 4.01 (1 H, dd, $J_{6,6}$ 8.3, $J_{6,5}$ 4.9, 6-H), 4.10 (1 H, dd, $J_{6',6}$ 8.3, $J_{6',5}$ 5.7, 6-H'), 4.29 (2 H, m, 4- and 5-H), 4.62 (1 H, $J_{2,1}$ 3.7, 2-H), 4.74 (1 H, d, $J_{3,4}$ 2.4, 3-H) and 5.92 (1 H, d, $J_{1,2}$ 3.7, 1-H); δ_C 5.33 ($MeCH_2SO$), 25.12, 26.22 and 26.68 ($CHMe_2$), 50.93 ($MeCH_2SO$), 66.65 (C-6), 72.33 (C-5), 79.23 (C-4), 80.34 (C-3), 83.50 (C-2), 104.91 (C-1), 109.18 (CMe_2) and 112.40 (CMe_2); *m*/*z* 321 (10%, $M^+ - 15$), 220 (1, $C_8H_{12}O_5S^+$), 127 (22, $C_6H_7O_3^+$), 101 (100, $C_5H_9O_2^+$), 77 (28, $C_2H_5OS^+$) and 43 (52, $C_2H_3O^+$).

Synthesis of (R)-*Ethanesulfinate of DAG* (R)-**1**.—This experiment was carried out following the aforementioned procedure but using pyridine instead of diisopropylethylamine as base and a reaction time of 3 h. Compound (*R*)-**1** (12.3 g, 94%) was obtained as a syrup (Found: C, 50.0; H, 7.2%); R_f 0.37 (hexane–propan-2-ol 10:1); $[\alpha]_D$ +12.82 (*c* 0.4, $CHCl_3$) {lit.,[18] $[\alpha]_D$ +12 (*c* 1.8, Me_2CO)}; ν_{max}(neat)/cm^{-1} 3000, 2990, 1455, 1385, 1375, 1260, 1220, 1140, 1075, 1025 and 830; δ_H 1.29 (3 H, t, J_{vic} 7.6, $MeCH_2SO$), 1.31, 1.32, 1.42 and 1.50 (12 H, 4 s, $CHMe_2$), 2.79 (1 H, dq, J_{vic} 7.6, J_{gem} 13.5, $MeCH_2SO$), 2.88 (1 H, dq, J_{vic} 7.6, J_{gem} 13.5, $MeCH_2SO$), 3.95–4.01 (1 H, m, 6-H), 4.09–4.11 (1 H, m, 6-H'), 4.13–4.17 (2 H, m, 4- and 5-H), 4.73 (1 H, d, $J_{3,4}$ 1.6, 3-H), 4.79 (1 H, d, $J_{2,1}$ 3.5, 2-H) and 5.92 (1 H, d, $J_{1,2}$ 3.5, 1-H); δ_C 4.94 ($MeCH_2SO$), 25.11, 26.05, 26.60 and 26.72 ($CHMe_2$), 51.30 ($MeCH_2SO_2$), 67.53 (C-6), 71.93 (C-5), 80.76 (C-4), 82.80 (C-3), 83.65 (C-2), 105.19 (C-1), 109.26 (CMe_2) and 112.21 (CMe_2); *m*/*z* 321 (19%, $M^+ - 15$), 220 (3, $C_8H_{12}O_5S^+$), 127 (27, $C_6H_7O_3^+$), 101 (100, $C_5H_9O_2^+$), 77 (29, $C_2H_5OS^+$) and 43 (53, $C_2H_3O^+$).

Synthesis of (R)-*Ethyl Methylsulfanylmethyl Sulfoxide* (R)-**3**.—To a stirred solution of the (*R*)-ethanesulfinate of DAG (3 g,

9 mmol) in dry THF (30 cm^3) cooled to −95 °C were added methyl sulfanylmethyllithium [prepared with TMEDA (1.6 cm^3, 10.8 mmol), BuLi (6.7 cm^3, 4.2 mmol) and dimethyl sulfide (0.8 cm^3, 10.8 mmol) as previously described[13]]. The reaction mixture was stirred for 2 h at −95 °C and then hydrolysed with aq. ammonium chloride and extracted successively with chloroform (2 × 30 cm^3) and ethyl acetate (1 × 30 cm^3). The organic extracts were combined, dried and evaporated, and the residue was column chromatographed (Et_2O). Compound (*R*)-**3** (560 mg, 46%) was obtained as a liquid; R_f 0.22 (EtOAc); $[\alpha]_D$ +153.2 (*c* 1.28, $CHCl_3$). The e.e. was 100% as calculated from the ^1H NMR spectrum with Eu(tfc)$_3$ (δ 3.57 and 3.76 signal); δ_H 1.36 (3 H, t, J_{vic} 7.5, *Me*CH_2SO), 2.33 (3 H, s, SMe), 2.74 and 2.99 (2 H, AB part of an ABX_3 system, J_{vic} 7.5, J_{gem} 13.2, MeCH_2SO) and 3.57 and 3.76 (2 H, AB system, J_{gem} 13.5, $SOCH_2S$).

Synthesis of (S)-*Ethylmethylsulfanylmethyl Sulfoxide* (S)-**3**.—The (*S*)-ethanesulfinate of DAG (1.2 g, 3.6 mmol) was treated with $MeSCH_2Li$ (7.2 mmol) following the procedure previously described for the synthesis of (*R*)-**3**. After purification by column chromatography (Et_2O), compound (*S*)-**3** (263 mg, 56%) was obtained as a liquid; R_f 0.22 (EtOAc); $[\alpha]_D$ −151.7 (*c* 3.08, $CHCl_3$). The e.e. was 100% as calculated from the ^1H NMR spectrum with Eu(tfc)$_3$. The ^1H NMR data were identical with those of its enantiomer (*R*)-**3**.

Synthesis of (R)-*Methyl Methylsulfanylmethyl Sulfoxide* (R)-**4**.—The (*R*)-methanesulfinate of DAG (4.5 g, 14 mmol) was treated with methylsulfanylmethyllithium (28 mmol) following the procedure previously described for the preparation of (*R*)-**3**, but with a reaction time of 1 h. After purification by column chromatography (Et_2O), compound (*R*)-**4** (833 mg, 48%) was obtained as a liquid; R_f 0.13 (EtOAc); $[\alpha]_D$ +92.2 (*c* 1.08, $CHCl_3$). The e.e. of 95% was calculated from the ^1H NMR spectrum with Eu(tfc)$_3$ (δ 3.69 signal); δ_H 2.33 (3 H, s, Me), 2.69 (3 H, s, MeSO) and 3.69 (2 H, s, $SOCH_2S$).

Synthesis of (S)-*Methyl Methylsulfanylmethyl Sulfoxide* (S)-**4**.—The (*S*)-methanesulfinate of DAG (2 g, 6.2 mmol) was treated with $MeSCH_2Li$ (12.4 mmol) following the procedure previously described for the preparation of (*R*)-**3**. After purification by column chromatography (Et_2O), compound (*S*)-**4** (442 mg, 58%) was obtained as a liquid; R_f 0.13 (EtOAc); $[\alpha]_D$ −97 (*c* 1.44, $CHCl_3$). The e.e. was 97% as calculated from the ^1H NMR with Eu(tfc)$_3$ (δ 3.69 signal). ^1H NMR data were identical with those of its enantiomer (*R*)-**4**.

Synthesis of 3-*Methyl*-4,5-*dihydroisoxazoles*.—Racemic 3-methyl-4,5-dihydroisoxazoles were synthesized using the method described by Mukaiyama.[15] Thus, 3-methyl-4,5-diphenyl-4,5-dihydroisoxazole **5a**, **b** was prepared in 70% yield from (*E*)-stilbene and was purified by column chromatography (hexane–diethyl ether, 10:1). 3-Methyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]isoxazole **6a**, **b** was prepared in 78% yield from cyclopentene and was purified by vacuum distillation (b.p. 50 °C at 1 mmHg; lit.[16] 61 °C at 2 mmHg). Spectroscopic data of both compound mixtures are in agreement with those described in the literature.[16,17]

3-[(R_S)-*Ethylsulfinylmethyl*]-4,5-*diphenyl*-4,5-*dihydroisoxazole* **7a**, **b**.—To a stirred solution of LDA* (11.5 mmol) in THF (10 cm^3) cooled to −95 °C was added a solution of 3-methyl-4,5-diphenyl-4,5-dihydroisoxazole **5a**, **b** (2.08 g, 15.2 mmol) in THF (30 cm^3) during 10 min. The mixture was stirred for an additional 4 h at −80 °C and then a solution of (*R*)-**1** (2.57 g, 7.6 mmol) in THF (30 cm^3) was slowly added. The reaction mixture was then stirred for 30 min and saturated aq. ammonium chloride was added. The organic layer was separated and the aqueous layer was extracted three times each with methylene dichloride and chloroform; the combined organic layers were dried and concentrated, and the residue was chromatographed (hexane–diethyl ether, 2:1). A mixture of compounds **7a** and **7b** (1.45 g, 56%) was obtained in the ratio 1:1.06 as measured by the 4-H signal (δ 4.61 and 4.44 respectively) in the ^1H NMR spectrum. The mixture of diastereoisomers **a** and **b** was rechromatographed (hexane–diethyl ether, 1:1), to give (i) compound **7a** as a solid; m.p. 105.5–106.5 °C (from diethyl ether–propan-2-ol) (Found: C, 68.8; H, 6.1; N, 4.3. $C_{18}H_{19}NO_2S$ requires C, 68.98; H, 6.11; N, 4.47%); R_f 0.26 (hexane–diethyl ether, 1:20); $[\alpha]_D$ +251.55 (*c* 0.90, $CHCl_3$ $\nu_{max}(CCl_4)/cm^{-1}$ 3010, 3000, 2990, 1605, 1590, 1500, 1460, 1315, 1060, 1025, 920, 760 and 700; δ_H 1.28 (3 H, t, J_{vic} 7.5, *Me*CH_2SO), 2.84–2.72 (2 H, m, MeCH_2SO), 3.47 (1 H, d, J_{gem} 14.0, $SOCH_2CC{=}N$), 3.59 (1 H, d, J_{gem} 14.0, $SOCH_2CC{=}N$), 4.61 (1 H, d, $J_{4,5}$ 7.1, 4-H), 5.58 (1 H, d, $J_{5,4}$ 7.1, 5-H) and 7.24–7.44 (10 H, m, Ph); δ_C 6.79 (*Me*CH_2SO), 44.94 (MeCH_2SO), 45.45 ($SOCH_2CCN$), 64.83 (C-4), 91.07 (C-5), 125.59–129.50 (10 × C, Ph), 137.19 (C-4 arom.), 139.73 (C-5 arom.) and 152.85 (C-3); (ii) and compound **7b** as a yellow syrup (Found: C, 68.9; H, 6.1; N, 4.5%); R_f 0.19 (hexane–diethyl ether, 1:20); $[\alpha]_D$ −228.71 (*c* 1.01, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3010, 2995, 2990, 1605, 1590, 1500, 1460, 1320, 1055, 1030, 920, 760 and 700; δ_H 1.32 (3 H, t, J_{vic} 7.5, *Me*CH_2SO), 2.69 (1 H, dq, J_{vic} 7.5, J_{gem} 13.5, MeCH_2SO), 2.86 (1 H, dq, J_{vic} 7.5, J_{gem} 13.5, MeCH_2SO), 3.40 (1 H, d, J_{gem} 13.4, $SOCH_2CC{=}N$), 3.74 (1 H, d, J_{gem} 13.4, $SOCH_2CC{=}N$), 4.44 (1 H, d, $J_{4,5}$ 7.0, 4-H), 5.57 (1 H, d, $J_{5,4}$ 7.0, 5-H) and 7.22–7.45 (10 H, m, Ph); δ_C 6.07 (*Me*CH_2SO), 46.19 (MeCH_2SO), 48.16 ($SOCH_2CCN$), 64.51 (C-4), 91.04 (C-5), 125.37–129.60 (10 × C, Ph), 136.96 (C-4 arom.), 139.71 (C-5 arom.) and 153.20 (C-3).

3-[(S_S)-*Ethylsulfinylmethyl*]-4,5,6,6a-*tetrahydro*-3a*H*-*cyclopenta*[d]*isoxazole* **8a**, **b**.—To a stirred solution of LDA (31.64 mmol) in THF (30 cm^3) cooled to −95 °C was added a solution of 3-methyl-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*d*]isoxazole **6a**, **b** (2.82 g, 22.6 mmol) in THF (45 cm^3) over a period of 10 min. The mixture was stirred for an additional 3 h and then a solution of (*S*)-**1** (3.79 g, 11.3 mmol) in THF (45 cm^3) was slowly added. After stirring of the reaction mixture for 30 min at −95 °C, saturated aq. ammonium chloride was added and the mixture was processed as in the preparation of diastereoisomers **7a**, **b**. The residue was chromatographed (hexane–diethyl ether, 2:1). A mixture of compounds **8a** and **8b** (1.46 g, 65%) was obtained in the ratio 1:1.08 as measured by the $SOCH_2CC{=}N$ signals (δ 3.81 and 3.56 respectively) in the ^1H NMR spectrum. The mixture of both diastereoisomers was chromatographed (ethyl acetate–hexane, 1:1) to give isomer **8a** as a yellow syrup (Found: C, 53.7; H, 7.5; N, 7.0. $C_9H_{15}NO_2S$ requires C, 53.7; H, 7.51; N, 6.96%); R_f 0.30 (diethyl ether–propan-2-ol, 5:1); $[\alpha]_D$ +33.79 (*c* 1.02, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2995, 2890, 1455, 1440, 1410, 1350, 1320, 1050, 1025 and 920; δ_H 1.35 (3 H, t, J_{vic} 7.5, *Me*CH_2SO), 1.68–1.78 (4 H, m, 2 × CH_2 of trimethylene), 1.89–1.96 (1 H, m, C*H*H of trimethylene), 2.05–2.15 (1 H, m, C*H*H of trimethylene), 2.85 (2 H, complex, J_{vic} 7.5, MeCH_2SO), 3.52 (1 H, d, J_{gem} 14, $SOCH_2CC{=}N$), 3.81 (1 H, d, J_{gem} 14, $SOCH_2CC{=}N$), 3.83 (1 H, dd, $J_{4,5}$ 8.5, J_{vic} 2.4, 3a-H) and 5.14 (1 H, dd, $J_{5,4}$ 8.5, J_{vic} 4.9, 6a-H); δ_C 6.74 (*Me*CH_2SO), 23.28, 30.23 and 35.75 ($[CH_2]_3$), 44.99

* LDA was prepared by addition of a solution of diisopropylamine (7.14 cm^3, 50.68 mmol) in THF (10 cm^3) to a cooled (−40 °C) solution of BuLi (20 cm^3, 31.64 mmol) in THF. When the addition was complete, the temperature was allowed to slowly rise to 0 °C and the mixture was stirred for 15 min and was then used as such.

(Me*C*H_2SO), 46.52 (SO*C*H_2CC=N), 54.79 (C-3a), 87.32 (C-6a) and 152.13 (C-3).

Compound **8b** was a solid; m.p. 79–80 °C (from hexane–diethyl ether) (Found: C, 53.7; H, 7.5; N, 7.0%); R_f 0.25 (diethyl ether–propan-2-ol, 5:1); $[\alpha]_D$ −103.5 (*c* 1, $CHCl_3$); ν_{max}(CCl_4)/cm^{-1} 2995, 2990, 1455, 1440, 1415, 1345, 1320, 1060, 1025 and 920; δ_H 1.39 (3 H, t, J_{vic} 7.5, *Me*CH_2SO), 1.68–1.83 (4 H, m, 2 × CH_2 of trimethylene), 1.90–1.96 (1 H, m, C*H*H of trimethylene), 2.09–2.13 (1 H, m, CH*H* of trimethylene), 2.77 (1 H, dq, J_{vic} 7.5, J_{gem} 13.4, MeC*H*$_2$SO), 2.95 (1 H, dq, J_{vic} 7.5, J_{gem} 13.4, MeC*H*$_2$SO), 3.56 (1 H, d, J_{gem} 13.3, SOCH_2CC=N), 3.75 (1 H, dd, $J_{4,5}$ 8.8, J_{vic} 8.1, 3a-H), 3.82 (1 H, d, J_{gem} 13.3, SOCH_2CC=N) and 5.13 (1 H, dd, $J_{5,4}$ 8.8, J_{vic} 5.0, 6a-H); δ_C 6.21 (*Me*CH_2SO), 23.20, 30.27 and 35.73 ([CH_2]$_3$), 46.15 (Me*C*H_2SO), 48.89 (SO*C*H_2CC=N), 54.00 (C-3a), 87.36 (C-6a) and 152.62 (C-3).

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