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Use of enantiomerically pure methylsulfinylmethylisoxazolines in the stereoselective synthesis of 1,5,6,7-tetrahydroxy-3-heptanone derivatives

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Abstract—Aldol-type reactions of enantiomerically pure 4,5-diphenyl-3-(methylsulfinyl)methylisoxazolines and 2,3-*O*-isopropylidene-D-glyceraldehyde were examined in order to establish the stereochemical preferences. Catalytic hydrogenation of the resulting trihydroxyisoxazoline derivatives using a Raney-Ni/H_3BO_3 system provides an access to diastereomerically pure 1,5,6,7-tetrahydroxy-3-heptanones. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Diastereoselective addition reactions of five-membered heterocycles, such as 2-substituted-furans, pyrroles, thiophenes[1] and thiazoles[2] as well as 4-substituted isoxazoles,[3] to enantiopure aldehydo or imino sugars have shown to be a key step for the construction of complex molecules bearing multiple contiguous stereogenic centres. For this purpose, isoxazolines are an important class of heterocycle since, in contrast to other heterocycles, they can bear two stereogenic centres (at C(4) and C(5)) and, moreover, they are useful intermediates in organic synthesis.[4] One of their most useful transformations is reductive ring cleavage to give either γ-amino alcohols[5] or β-hydroxy ketones[6] because these units are present in the backbone of a variety of biologically active compounds. Additionally, isoxazolines can be used as valuable synthetic building blocks capable of being inserted into other molecules. In this sense, reactions between carbonyl compounds and isoxazoline *exo*-azaenolates[7] are very attractive since these processes are equivalent to a regioselective double-aldol reaction of a ketone with two different aldehydes, where one of the two ketol functionalities can be kept in a latent form, available for subsequent modification. This strategy, applied to asymmetric synthesis allows the stereoselective preparation of polyol chains but requires an access to isoxazolines, carbonyl compounds (or both) in enantiomerically pure form.[8] In this field we have recently reported the four carbon homologation of 2,3-*O*-isopropylidene-D-glyceraldehyde, **1**, using an enantiomerically pure 3-sulfinylmethylisoxazoline as a chiral nucleophile.[9] In order to evaluate the feasibility of this strategy in the stereoselective synthesis of polyols,[10] and in connection with our research devoted to develop new applications of the sulfinyl group,[11] we have studied the aldol-type reactions of two pairs of enantiomers of 4,5-diphenyl-3-(methylsulfinyl)methyl isoxazolines **2** and **3**, with aldehyde **1**, and the subsequent reductive ring cleavage of the resulting aldol adducts. These processes have allowed us to synthesise four stereoisomers of 1,2-diphenyl-1,5-dihydroxy-6,7-isopropylidenedioxy-3-heptanone, compounds **18**–**21**, in diastereomerically pure form.

2. Results and discussion

The starting enantiomerically pure 4,5-diphenyl-3-(methylsulfinyl)methylisoxazolines, **2** and **3**, were prepared by regioselective metallation of racemic 3-methylisoxazolines and subsequent Andersen reaction with (R_S)- and (S_S)-methanesulfinates of diacetone-D-glucose as previously described.[9,12] We selected these four stereoisomers as chiral nucleophile reagents with the aim of evaluating the relative influence of the configuration at sulfur and at the two stereogenic cen-

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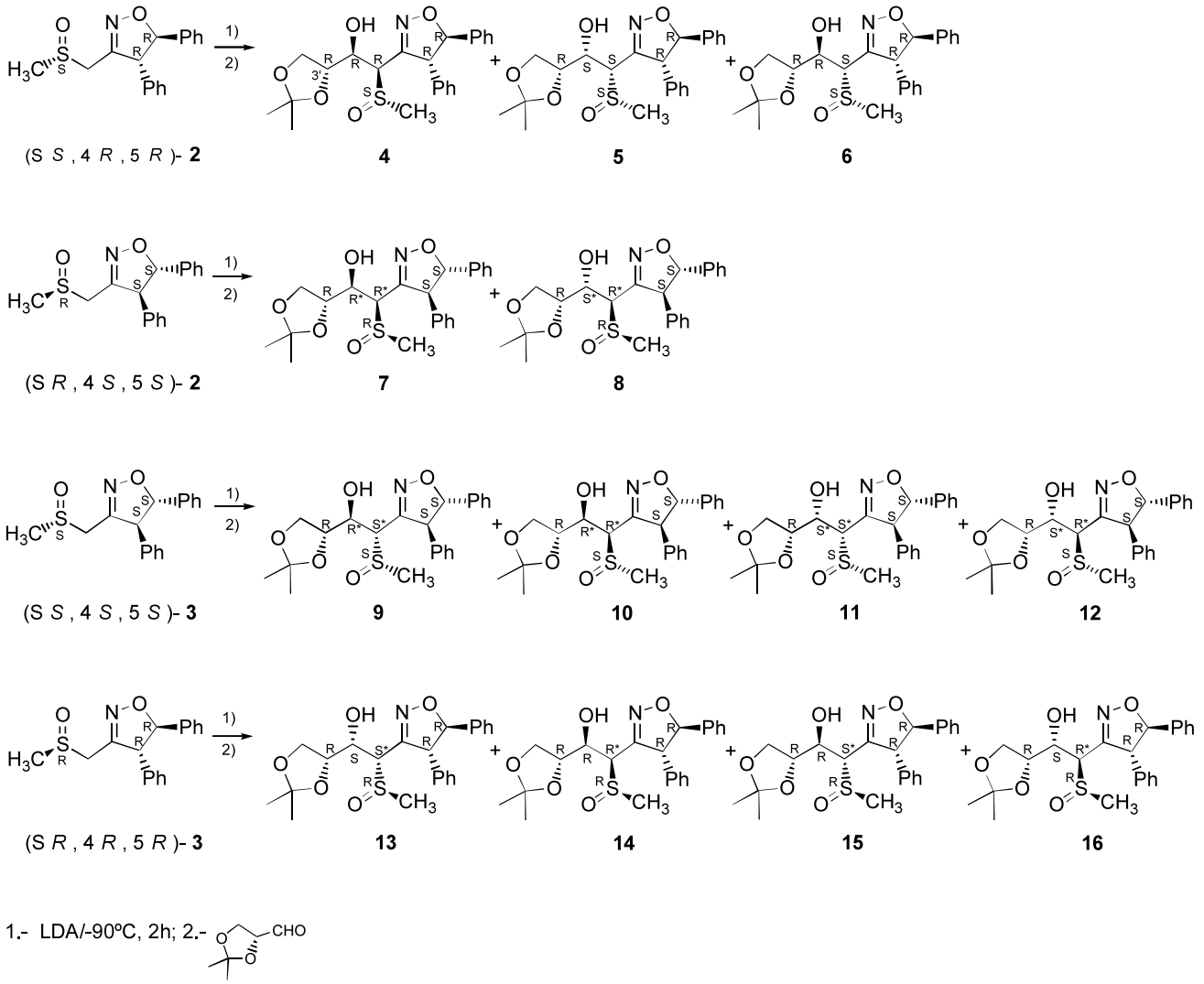
tres of the isoxazoline ring in the stereoselectivity of the addition reactions to aldehyde **1**.

Metallation of diastereomerically pure 3-sulfinylmethylisoxazolines **2** and **3** with LDA, under very mild conditions (–90°C), gave rise exclusively to the corresponding *exo*-azaenolates. The subsequent aldol-type reaction of the *exo*-azaenolates derived from (S_S,4*R*,5*R*)-**2**, (R_S,4*S*,5*S*)-**2**, (S_S,4*S*,5*S*)-**3** (R_S,4*R*,5*R*)-**3** and aldehyde **1** (–90°C, 1 h) afforded mixtures of the corresponding trihydroxyisoxazoline derivatives **4**–**16**. The results are summarised in Scheme 1 and Table 1 where the reaction of isoxazoline (S_S,4*R*,5*R*)-**2** and aldehyde **1** has been included for comparative purposes.[9] The best level of diastereoselectivity was obtained in the reaction of isoxazoline (R_S,4*S*,5*S*)-**2**, which affords two diastereoisomers, **7** and **8**, in a ratio of 80:20, respectively. Both products could be easily isolated and purified, obtaining the major isomer, **7**, in a 60% isolated yield. In the reaction of its enantiomer (S_S,4*R*,5*R*)-**2** a high diastereoselectivity was also observed (**4**:**5**:**6**, 12:4:84) obtaining the major compound **6** in a 48% isolated yield. However the reactions of isoxazolines (S_S,4*S*,5*S*)-**3** and (R_S,4*R*,5*R*)-**3** were less stereoselective affording all four possible aldol products in a moderate diastereoisomer ratio (compounds **9**–**12** and **13**–**16**, respectively; Scheme 1, Table 1). Nevertheless all stereoisomers could be obtained in pure form by column chromatography.



Scheme 1.

Table 1. Aldol-type reactions of 4,5-diphenyl-3-(methylsulfinyl)methyl isoxazolines, **2** and **3**, and aldehyde **1**

3-Sulfinylmethyl isoxazoline	Trihydroxyisoxazolines (d.r.)				Ratio (*R*)-C(2′):(*S*)-C(2′)
(S_S,4*R*,5*R*)-**2**	**4** (12)	**5** (4)	**6** (84)		96:4
(R_S,4*S*,5*S*)-**2**	**7** (80)	**8** (20)			80:20
(S_S,4*S*,5*S*)-**3**	**9** (57)	**10** (25)	**11** (14)	**12** (4)	82:18
(R_S,4*R*,5*R*)-**3**	**13** (10)	**14** (53)	**15** (34)	**16** (3)	87:13

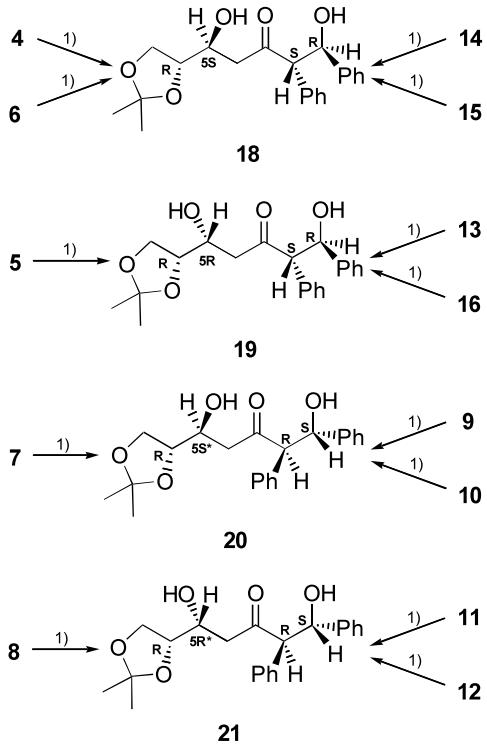
As a second stage of this research we investigated the reductive ring cleavage of the trihydroxyisoxazoline derivatives **4**–**16**. For this purpose, we chose hydrogenation catalysed by Raney-Ni/H_3BO_3 system[6a] since it allows ring opening and desulfurisation in a one-pot procedure.[8b]

With the aim of establishing the optimum reaction conditions, we first carried out hydrogenation of 3-sulfinylmethylisoxazoline (R_S,4*S*,5*S*)-**2**. Thus, we observed that reaction performed at room temperature afforded the desired compound (3*R*,4*S*)-3,4-diphenyl-4-hydroxy-2-butanone, **17**, in only 18% yield together with the products resulting from retroaldol reaction (benzaldehyde and benzylmethyl ketone). Fortunately, when the reaction was carried out at 0°C, the β-hydroxyketone **17** was exclusively formed in almost quantitative yield (see Section 4).[13]

The same procedure was then applied to each of the 13 diastereoisomers isolated (compounds **4**–**16**). Only one tetrahydroxyheptanone was detected in each of the reductions, with total consumption of the starting material in all cases. These results show that the reduction takes place without epimerisation at the stereogenic centres of the isoxazoline ring and, therefore, the tetrahydroxyheptanone derivatives obtained are enantiomerically pure. The results of these experiments are summarised in Scheme 2. As expected, only the four heptanones **18**–**21**, were obtained from all of the 13 reactions performed, because the diastereoisomers with the same absolute configuration at the hydroxyl-bearing carbon, C(2′), and the two stereogenic centres of the isoxazoline, C(4) and C(5), gave rise to the same heptanone (Scheme 2).

In order to establish the absolute configuration of all stereogenic centres of trihydroxyisoxazolines **4**–**16** and heptanones **18**–**21** we have take into account the results obtained in the reduction processes and the known structural assignment of compound **6**[9] (previously established by X-ray crystallographic analysis as 4*R*,5*R*,1′*S*,2′*R*). Thus, we can assign the same absolute configuration, (*R*) at C(2′), for compounds **4**, **14** and **15**, because they all gave rise to the same heptanone **18**, which has (5*S*)-absolute configuration (Scheme 2). Analogously, we can establish a (2′*S*)-absolute configuration for isoxazolines **5**, **13** and **16** and (5*R*) for heptanone **19** (Scheme 2).

On the other hand, the ^{1}H NMR data of the isoxazolines **4**–**16** allowed us to establish a correlation between vicinal coupling constants, J_{vic}, and the absolute configuration for each compound.[14] Thus, as we can see in Table 2 the $J_{2',3'}$ value is larger for compounds with (2′*R*)-absolute configuration ($\geq$7.4 Hz for compounds **6**, **14** and **15**; Table 2, entries 3, 11 and 12) than for compounds with (2′*S*)-absolute configuration ($\leq$3 Hz for **5** and **16**; Table 2, entries 2 and 13). Bearing in mind the dependence existing between J_{vic} value and the dihedral angle formed by the implied hydrogen atoms, a preferential *anti* or *syn* arrangement between C(2′)H and C(3′)H hydrogens, respectively, may be inferred for



Scheme 2.

these compounds. In the same way a *syn*-relationship can also be established for compounds **8**, **11** and **12** ($J \leq 1.6$ Hz; Table 2, entries 5, 8 and 9) and another *anti* arrangement for compound **10** ($J = 7.9$ Hz; Table 2, entry 7). From all these data we have assigned (*S**)-configuration at C(2′) for compounds **8**, **11** and **12** and (*R**)-configuration at C(5) for heptanone **21**.

For the same reasons, we have assigned (*R**)-configuration at C(2′) for compounds **7**, **9** and **10**, and (*S**)-configuration at C(5) for heptanone **20**.

A similar correlation was also observed for the vicinal coupling constant between C(1′) and C(2′), so an *anti* relationship can also be inferred for those compounds with $J_{1',2'}$ value larger than 6.4 Hz (compounds **5**, **7**, **10**, **11** and **13**; Table 2, entries 2, 4, 7, 8 and 10) and another *syn* arrangement for those compounds with $J_{1',2'}$ value smaller than 2.4 Hz (compounds **6**, **8**, **9**, **12**, **15** and **16**; Table 2, entries 3, 5, 6, 9, 12 and 13). As compound **6** has a (1′*S*,2′*R*)-absolute configuration and a *syn* arrangement between both hydrogens ($J_{1',2'} = 2.3$ Hz) we can assume that the spatial arrangement of the sulfinyl group in this compound is that depicted in Fig. 1, which would be favoured by the hydrogen bonding formed between the hydroxyl proton and the sulfinyl oxygen.[15] Analogously similar conformations can be assumed for all stereoisomers. Thus, as shown in Fig. 1, for compounds with (2′*R*)-absolute configuration and a *syn*-relationship between C(1′)H/C(2′)H (compounds **9** and **15**; Fig. 1 and Table 2) (*S*)-configuration at C(1′) can be proposed, whereas (1′*R*)-configuration can be

Table 2. ^{1}H NMR vicinal coupling constants (J_{vic} in Hz) for compounds **4**–**16**

Entry	Compound	$J_{2',3'}$ (r.a.[a])	$J_{1',2'}$ (r.a.[b])	Absolute configuration C(1′),C(2′)
1	**4**	–[c]	–[c]	*R*,*R*
2	**5**	2.9 (*syn*)	8.4 (*anti*)	*S**,*S*
3	**6**	8.8 (*anti*)	2.3 (*syn*)	*S*,*R*[d]
4	**7**	–[c]	8.4 (*anti*)	*R**,*R**
5	**8**	1.3 (*syn*)	2.2 (*syn*)	*R**,*S**
6	**9**	–[c]	1.3 (*syn*)	*S**,*R**
7	**10**	7.9 (*anti*)	6.4 (*anti*)	*R**,*R**
8	**11**	1.6 (*syn*)	10 (*anti*)	*S**,*S**
9	**12**	0.9 (*syn*)	2.3 (*syn*)	*R**,*S**
10	**13**	–[c]	8.3 (*anti*)	*S**,*S*
11	**14**	7.4 (*anti*)	4.7	*R**,*R*
12	**15**	9.7 (*anti*)	2.4 (*syn*)	*S**,*R*
13	**16**	3.0 (*syn*)	2.3 (*syn*)	*R**,*S*

[a] Relative arrangement between C(2′)H–C(3′)H.
[b] Relative arrangement between C(1′)H–C(2′)H.
[c] Although J_{vic} cannot be measured, the absolute configurations were established from their conversions to tetrahydroxy heptanones.
[d] The absolute configuration was established by X-ray analysis (Ref. 9).

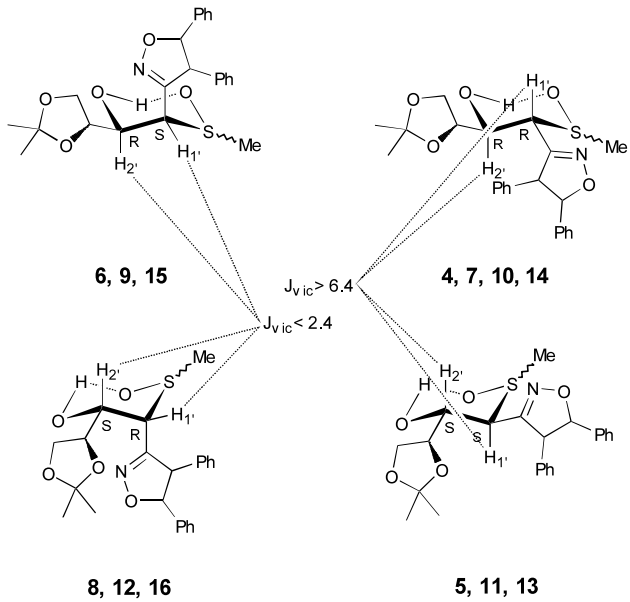
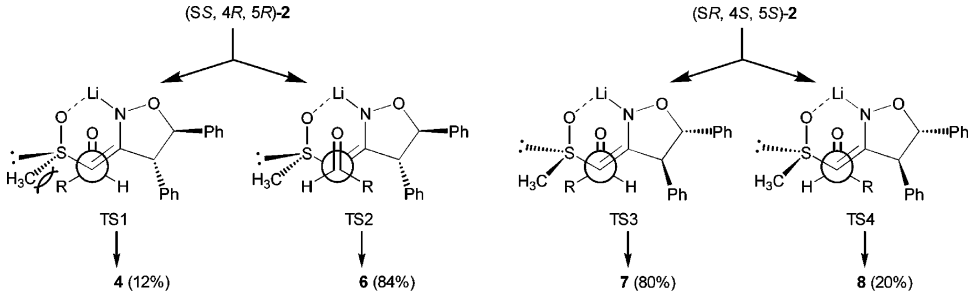


Figure 1.

established if both hydrogens have an *anti* arrangement (compounds **4**, **7**, **10** and **14**; Fig. 1 and Table 2). Following the same logic we propose (1′*S*)-absolute configuration for compounds **5**, **11** and **13** (*anti* arrangement between C(1′)H and C(2′)H, Table 2 and Fig. 1) and (1′*R*)-absolute configuration for compounds **8**, **12** and **16** (*syn* arrangement between C(1′)H and C(2′)H).

From the data reported in Scheme 1 and Table 1 a trend is evident: a high predominance of the adducts with (*R*)-configuration at C(2′) is observed, which indicates that the directing effect of the aldehyde is greater than that of the sulfinyl group and the isoxazoline ring according to a non-chelation controlled addition (Felkin–Anh–Houk model).[16] These last cases exert their effect only on the extent of the stereoselectivity. The minimal influence of the sulfinyl group on the stereochemical control at the hydroxyl-bearing stereogenic centre could be expected, since the addition of α-sulfinylcarbanions to carbonyl compounds usually takes place with poor 1,3-induction.[17] The highest diastereofacial selection with respect to the aldehyde (94%) was obtained using the 3-sulfinylmethylisoxazoline (S_S,4*R*,5*R*)-**2** (Table 1, entry 1). In contrast, the lowest diastereofacial selection (60%) occurred when the enantiomeric (R_S,4*S*,5*S*)-**2**, was used. Nevertheless, complete diastereofacial selection with respect to the azaenolate was achieved, affording only two diastereoisomers with the same configuration at C(1′) (Scheme 1 and Table 2). These results show the influence of the sulfinyl group and the isoxazoline ring on the stereochemical control at the newly formed C(1′) stereogenic centre.

The stereochemical course of these processes can be explained by assuming that the *exo*-azaenolate must be stabilised by chelation of the lithium cation with the sulfinyl oxygen (Scheme 3).[18] This assumption causes chiral azaenolates derived from (S_S,4*R*,5*R*)-**2** and (R_S,4*S*,5*S*)-**2** to have a distinct facial bias, with one of the faces shielded by the phenyl group at C(4) and the methyl group at sulfur. So, from a steric point of view, the aldehyde approaches the azaenolate from the less hindered face, i.e. the *Re* face for (S_S,4*R*,5*R*)-**2** (TS2, Scheme 3) and the *Si* face for its enantiomer (R_S,4*S*,5*S*)-**2** (TS3 and TS4, Scheme 3). This model is in accord with the absolute configuration established for the major product (1′*S*,2′*R*)-**6**, which must result from the most favourable transition state TS2, and the model also justifies the low d.r. for compound (1′*R*,2′*R*)-**4** which come from TS1, where aldehyde approaches the azaenolate from the most hindered face. Analogously, the proposed configuration of the major compound **7** (1′*R**,2′*R**), formed in reaction of isoxazoline (R_S,4*S*,5*S*)-**2**), must be a consequence of the attack of the aldehyde, from its *Si* face, to the *Si* face of the azaenolate through TS3. On the other side the *Re* approach of the aldehyde from the less hindered face of



Scheme 3.

the azaenolate derived of (R_S,4*S*,5*S*)-**2** would give compound **8** with (1′*R**,2′*S**) configuration, which is formed in 20% yield (TS4).

On the contrary, for azaenolates derived from (S_S,4*S*,5*S*)-**3** and (R_S,4*R*,5*R*)-**3** one of the faces is shielded by the phenyl group and the opposite by the methyl group, so approach of the aldehyde from both faces can occur, which is in accord with the low diastereoselectivity obtained with these enolates.

3. Conclusion

In summary, the aldol-type reactions of enantiomerically pure 3-sulfinylmethylisoxazolines and 2,3-*O*-isopropylidene-D-glyceraldehyde take place under very mild conditions to afford trihydroxyisoxazoline derivatives in high yield, which serves to confirm the potential and versatility of 3-sulfinylmethylisoxazolines as functional and chiral non-racemic elongation reagents. Catalytic hydrogenation of the products of the aldol reaction provides an easy access to diastereomerically pure 1,5,6,7-tetrahydroxy-3-heptanones. In this paper we have applied this sequence to prepare compounds **18**–**21**. The described sequence could be applied to other 3-sulfinylmethylisoxazolines, as well as to different aldehydo or imino sugars in order to obtain a variety of open-chain oxygen compounds, which incorporate the complete carbon skeleton chirality of the respective precursors.

4. Experimental

Dry solvents and liquid reagents were distilled under argon just prior to use: THF was distilled from sodium and benzophenone ketyl, CH_2Cl_2 was dried over P_2O_5 and diisopropylamine over KOH. Boric acid and methanol were commercially available from Aldrich Chemical Co. and used without further purification. All reaction vessels, after being flame-dried, were kept under argon. Organic solutions were dried over anhydrous sodium or magnesium sulfates, and the solvent was evaporated at reduced pressure below 40°C. Column chromatography was performed by using Silica Gel Merck 60 (230–400 mesh). Optical rotations were measured with a 141 Perkin–Elmer polarimeter. ^{1}H NMR spectra (300 MHz, $CDCl_3$) and ^{13}C NMR (80 MHz, $CDCl_3$) were performed with a Bruker AC-300 spectrometer. Chemical shifts (δ) are given in ppm, relative to TMS, coupling constants (J) in Hz. IR spectra were measured on a Nicolet FTIR-20-SX spectrometer. Mass spectra were recorded by the direct insertion technique by electronic impact (EI) or chemical ionisation (CI), using a HP-588-A spectrometer at 230 eV with a temperature source of 200°C. Elemental analyses were performed in a Carlo Erba elemental analyser 1106. 2,3-*O*-Isopropylidene-D-glyceraldehyde,[19] **1**, and 4,5-diphenyl-3-(methylsulfinyl)methyl-4,5-dihydroisoxazoles[9] were prepared as previously described.

4.1. Addition of 4,5-diphenyl-3-(methylsulfinyl)methylisoxazolines, 2 and 3, to 2,3-*O*-isopropylidene-D-glyceraldehyde, 1. General procedure

To a stirred solution of the corresponding isoxazoline **2** or **3** (1 g, 3.34 mmol) in THF (70 mL) cooled at −90°C, LDA (5 mmol) as a solution in THF was added dropwise. After 2 h at −90°C, freshly distilled aldehyde **1** (1.3 g, 10.03 mmol) was added at once and the reaction mixture was stirred for an additional hour, then quenched by addition of a saturated aqueous ammonium chloride solution and warmed to rt. The organic layer was separated and the aqueous phase extracted twice with dichloromethane; the combined organic layers were dried and concentrated under reduced pressure.

4.1.1. From isoxazoline (R_S,4*S*,5*S*)-2. Reaction of (R_S,4*S*,5*S*)-**2** (1 g, 3.34 mmol) with **1** (1.3 g, 10.0 mmol) following the general procedure, and work-up as described, gave rise to a crude containing compounds **7** and **8** in a 80:20 ratio (estimated by integration of the signals corresponding to H-C1′ in the ^{1}H NMR spectrum of the crude reaction). Column chromatography using diethyl ether:hexane (1:1) as the eluent afforded pure **7** (860 mg, 60% yield) as a clear foamy syrup and pure **8** (258 mg, 18% yield) as a white solid.

4.1.1.1. (R_S,4*S*,5*S*,1′*R,2′*R**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy-3′,4′-isopropylidenedioxy-1′-methylsulfinyl)-butylisoxazoline, 7**. $[\alpha]_D^{20}=+220.1$ (*c* 1.01, $CHCl_3$); ^{1}H NMR: δ 1.19 and 1.30 (2s, each 3H, C(C**H**$_3$)$_2$), 2.78 (s, 3H, C**H**$_3$-SO-), 3.53 (d, 1H, $J_{1',2'}=8.4$, **H**-C1′), 3.87–3.94 (m, 2H, **H**-C2′ and **H**-C3′), 4.03 (dd, 1H, $J_{gem}=8.3$, $J_{4',3'}=3.3$, **H**-C4′), 4.19 (dd, 1H, $J_{gem}=8.3$, $J_{4'',3'}=6.6$, **H**′-C4′), 4.52 (b, 1H, **HO**-C2′, exchanges with D_2O), 4.74 (d, 1H, $J_{4,5}=7.3$, **H**-C4), 5.60 (d, 1H, $J_{5,4}=7.3$, **H**-C5) and 7.27–7.46 (m, 10H, **H**-arom.); ^{13}C

NMR: δ 25.2 and 26.4 (C(**C**H$_3$)$_2$), 35.3 (**C**H$_3$-SO-), 58.1 (**C**2′), 64.5 (**C**4), 66.0 (**C**4′), 72.1 (**C**3′), 77.2 (**C**1′), 91.0 (**C**5), 109.9 (**C**(CH$_3$)$_2$), 125.5, 128.2, 128.4, 128.7 and 129.7 (**C**H-arom.), 137.2 (**C**arom.-C4), 139.5 (**C**arom.-C5) and 153.7 (**C**3); IR (KBr, liquid film): 3300, 1605, 1495, 1460, 1385, 1375, 1150, 1060, 1025, 760 and 705 cm^{-1}; EI-MS m/z (rel. int.): 328 (3, M$^+$–C$_5$H$_9$O$_2^+$), 265 (1, C$_{17}$H$_{15}$NO$_2^+$), 101 (44, C$_5$H$_9$O$_2^+$). Anal. calcd for C$_{23}$H$_{27}$NO$_5$S: C, 64.32; H, 6.34, N, 3.26. Found: C, 64.18; H, 6.35, N, 3.27%.

4.1.1.2. (R_S,4*S*,5*S*,1′*R,2′*S**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 8**. Mp 159–160°C (isopropanol/diethyl ether); $[\alpha]_D^{20}$ = +251.0 (*c* 0.50, CHCl$_3$); ^{1}H NMR: δ 1.24 and 1.28 (2s, each 3H, C(C**H**$_3$)$_2$), 2.79 (d, 1H, $J_{2',OH}$ = 10.9, **HO**-C2′, exchanges with D$_2$O), 2.86 (s, 3H, C**H**$_3$-SO-), 3.41 (d, 1H, $J_{1',2'}$ = 2.2, **H**-C1′), 3.87–4.00 (m, 3H, two **H**-C4′ and **H**-C3′), 4.43 (ddd, 1H, $J_{2',1'}$ = 2.2, $J_{2',3'}$ = 1.3, $J_{2',OH}$ = 10.9, **H**-C2′, collapses to dd on exchange with D$_2$O, $J_{2',1'}$ = 2.2, $J_{2',3'}$ = 1.3), 4.65 (d, 1H, $J_{4,5}$ = 7.9, **H**-C4), 5.55 (d, 1H, $J_{5,4}$ = 7.9, **H**-C5) and 7.20–7.46 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.4 and 25.9 (C(**C**H$_3$)$_2$), 35.8 (**C**H$_3$-SO-), 60.4 (**C**2′), 62.9 (**C**4), 66.0 (**C**3′), 66.1 (**C**4′), 79.0 (**C**1′), 90.5 (**C**5), 110.1 (**C**(CH$_3$)$_2$), 125.5, 128.2, 128.5, 128.8 and 129.7 (**C**H-arom.), 136.8 (**C**arom.-C4), 140.0 (**C**arom.-C5) and 153.7 (**C**3); IR (KBr, liquid film): 3300, 1605, 1495, 1460, 1385, 1375, 1150, 1060, 1025, 760 and 705 cm^{-1}; EI-MS m/z (rel. int.): 429 (2, M$^+$), 414 (2, M$^+$–15), 366 (3, M$^+$–CH$_3$SO), 266 (36, C$_{17}$H$_{16}$NO$_2^+$), 101 (99, C$_5$H$_9$O$_2^+$), 43 (100, C$_2$H$_3$O$^+$). Anal. calcd for C$_{23}$H$_{27}$NO$_5$S: C, 64.32; H, 6.34, N, 3.26. Found C, 64.42; H, 6.33, N, 3.26%.

4.1.2. From isoxazoline (S_S,4*S*,5*S*)-3. Reaction of (S_S,4*S*,5*S*)-**3** (836 mg, 2.80 mmol) with **1** (1.09 g, 8.4 mmol) following the general procedure, and work-up as described, gave rise to a crude containing compounds **9**, **10**, **11** and **12** in a 57:25:14:4 ratio, respectively (estimated by integration of the signals corresponding to CH$_3$SO in the ^{1}H NMR spectrum of the crude reaction). Column chromatography using diethyl ether:hexane (1:1) as the eluent afforded pure **9** (428 mg, 36% yield) as a white solid, a fraction (300 mg, 25% yield) containing a mixture of compounds **10** and **11**, and pure **12** (54 mg, 5% yield) as a white solid. After subsequent chromatography (isopropanol:hexane, 1:40) pure **10** and pure **11** were obtained as white solids.

4.1.2.1. (S_S,4*S*,5*S*,1′*S,2′*R**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 9**. Mp 130–131°C (diethyl ether/hexane); $[\alpha]_D^{20}$ = +251.0 (*c* 0.40, CHCl$_3$); ^{1}H NMR: δ 1.21 (s, 6H, C(C**H**$_3$)$_2$), 2.70 (s, 3H, C**H**$_3$-SO-), 3.90 (d, 1H, $J_{1',2'}$ = 1.3, **H**-C1′), 3.94 (b, 1H, **HO**-C2′, exchanges with D$_2$O), 4.00 (dd, 1H, J_{gem} = 7.8, $J_{4',3'}$ = 3.7, **H**-C4′), 4.02–4.11 (m, 2H, **H**-C2′ and **H**-C3′), 4.15 (dd, 1H, J_{gem} = 7.8, $J_{4',3'}$ = 5.5, **H**′-C4′), 4.52 (d, 1H, $J_{4,5}$ = 7.7, **H**-C4), 5.53 (d, 1H, $J_{5,4}$ = 7.7, **H**-C5) and 7.23–7.43 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.1 and 26.7 (C(**C**H$_3$)$_2$), 36.8 (**C**H$_3$-SO-), 60.1 (**C**2′), 65.5 (**C**4), 67.9 (**C**4′), 70.1 (**C**3′), 75.5 (**C**1′), 90.4 (**C**5), 109.8 (**C**(CH$_3$)$_2$), 125.7, 128.4, 128.5, 128.8, 129.0 and 129.5 (**C**H-arom.), 136.3 (**C**arom.-C4), 139.1 (**C**arom.-C5) and 156.4 (**C**3); IR (KBr, liquid film): 3300, 1605, 1495, 1460, 1415, 1385, 1375, 1160, 1075, 1025 and 705 cm^{-1}; EI-MS m/z (rel. int.): 429 (2, M$^+$), 366 (2, M$^+$–CH$_3$SO), 299 (10, C$_{17}$H$_{17}$NO$_2$S$^+$), 266 (34, C$_{17}$H$_{16}$NO$_2^+$), 101 (100, C$_5$H$_9$O$_2^+$), 43 (74, C$_2$H$_3$O$^+$). Anal. calcd for C$_{23}$H$_{27}$NO$_5$S: C, 64.32; H, 6.34, N, 3.26. Found C, 64.28; H, 6.32; N, 3.31%.

4.1.2.2. (S_S,4*S*,5*S*,1′*R,2′*R**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 10**. Mp 153–154°C (diethyl ether/hexane); $[\alpha]_D^{20}$ = +214.0 (*c* 1.00, CHCl$_3$); ^{1}H NMR: δ 1.12 and 1.28 (2s, each 3H, C(C**H**$_3$)$_2$), 2.45 (s, 3H, C**H**$_3$-SO-), 3.36 (d, 1H, $J_{1',2'}$ = 6.4, **H**-C1′), 3.95 (dd, 1H, J_{gem} = 8.4, $J_{4',3'}$ = 4.9, **H**-C4′), 4.00–4.15 (m, 1H, $J_{2',3'}$ = 7.9, $J_{3',4'}$ = 4.9, $J_{3',4''}$ = 13.1, **H**-C3′), 4.09 (dd, 1H, J_{gem} = 8.4, $J_{4'',3'}$ = 13.1, **H**′-C4′), 4.21 (ddd, 1H, $J_{2',1'}$ = 6.4, $J_{2'OH}$ = 3.4, $J_{2',3'}$ = 7.9, **H**-C2′, collapses to dd on exchanges with D$_2$O, $J_{2',1'}$ = 6.4, $J_{2',3'}$ = 7.9), 4.50 (d, 1H, $J_{2',OH}$ = 3.4, **HO**-C2′, exchanges with D$_2$O), 4.59 (d, 1H, $J_{4,5}$ = 7.7, **H**-C4), 5.69 (d, 1H, $J_{5,4}$ = 7.7, **H**-C5) and 7.24–7.49 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.1 and 26.4 (C(**C**H$_3$)$_2$), 38.6 (**C**H$_3$-SO-), 62.5 (**C**2′), 65.2 (**C**4), 67.2 (**C**4′), 73.9 (**C**3′), 77.2 (**C**1′), 89.8 (**C**5), 110.1 (**C**(CH$_3$)$_2$), 125.3, 128.2, 128.4, 128.8 and 129.8 (**C**H-arom.), 136.7 (**C**arom.-C4), 140.0 (**C**arom.-C5) and 155.0 (**C**3); IR (KBr, liquid film): 3250, 1605, 1495, 1460, 1385, 1375, 1070, 1045, 1035, 1025, 915 and 705 cm^{-1}; EI-MS m/z (rel. int.): 414 (0.6, M$^+$–15), 366 (4, M$^+$–CH$_3$SO), 299 (9, C$_{17}$H$_{17}$NO$_2$S$^+$), 266 (58, C$_{17}$H$_{16}$NO$_2^+$), 101 (100, C$_5$H$_9$O$_2^+$), 43 (75, C$_2$H$_3$O$^+$). Anal. calcd for C$_{23}$H$_{27}$NO$_5$S: C, 64.32; H, 6.34, N, 3.26. Found C, 64.19; H, 6.36; N, 3.25%.

4.1.2.3. (S_S,4*S*,5*S*,1′*S,2′*S**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 11**. Mp 157–159°C (carbon tetrachloride); $[\alpha]_D^{20}$ = +251.7 (*c* 0.90, CHCl$_3$); ^{1}H NMR: δ 1.24 and 1.31 (2s, each 3H, C(C**H**$_3$)$_2$), 2.78 (s, 3H, C**H**$_3$-SO-), 3.09 (d, 1H, $J_{2',OH}$ = 7.6, **HO**-C2′, exchanges with D$_2$O), 3.77 (d, 1H, $J_{1',2'}$ = 10.2, **H**-C1′), 3.95 (dd, 1H, J_{gem} = 8.1, $J_{4',3'}$ = 6.7, **H**-C4′), 4.04 (dd, 1H, J_{gem} = 8.1, $J_{4'',3'}$ = 6.8, **H**′-C4′), 4.26 (ddd, 1H, $J_{2',3'}$ = 1.6, $J_{3',4'}$ = 6.7, $J_{3',4''}$ = 6.8, **H**-C3′), 4.50 (d, 1H, $J_{4,5}$ = 7.9, **H**-C4), 4.61 (ddd, 1H, $J_{2',1'}$ = 10.2, $J_{2'OH}$ = 7.6, $J_{2',3'}$ = 1.6, **H**-C2′, collapses to dd on exchanges with D$_2$O, $J_{2',1'}$ = 10.2, $J_{2',3'}$ = 1.6), 5.53 (d, 1H, $J_{5,4}$ = 7.9, **H**-C5) and 7.23–7.44 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.0 and 26.0 (C(**C**H$_3$)$_2$), 38.4 (**C**H$_3$-SO-), 61.2 (**C**2′), 65.9 (**C**4), 65.4 (**C**4′), 68.7 (**C**3′), 75.0 (**C**1′), 91.3 (**C**5), 109.5 (**C**(CH$_3$)$_2$), 126.1, 128.4, 128.6, 128.9 and 129.5 (**C**H-arom.), 136.6 (**C**arom.-C4), 139.3 (**C**arom.-C5) and 154.2 (**C**3); IR (KBr, liquid film): 3300, 1615, 1605, 1495, 1460, 1415, 1405, 1385, 1375, 1065, 1035, 915 and 705 cm^{-1}; EI-MS m/z (rel. int.): 430 (1, M$^+$+1), 429 (5, M$^+$), 366 (4, M$^+$–CH$_3$SO), 299 (13, C$_{17}$H$_{17}$NO$_2$S$^+$), 266 (82, C$_{17}$H$_{16}$NO$_2^+$), 101 (95, C$_5$H$_9$O$_2^+$), 43 (100, C$_2$H$_3$O$^+$). Anal. calcd for C$_{23}$H$_{27}$NO$_5$S: C, 64.32; H, 6.34, N, 3.26. Found C, 64.25; H, 6.35; N, 3.23%.

4.1.2.4. (S_S,4*S*,5*S*,1′*R,2′*S**,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 12**. Mp 174–175°C (isopropanol/diethyl ether); $[\alpha]_D^{20}=-265.0$ (*c* 0.20, $CHCl_3$); ^{1}H NMR: δ 1.14 and 1.21 (2s, each 3H, C(C**H**$_3$)$_2$), 2.26 (s, 3H, C**H**$_3$-SO-), 2.76 (d, 1H, $J_{2',OH}=11.0$, **H**O-C2′, exchanges with D_2O), 3.15 (d, 1H, $J_{1',2'}=2.3$, **H**-C1′), 3.92 (dd, 1H, $J_{gem}=6.0$, $J_{4',3'}=9.5$, **H**-C4′), 3.99–4.03 (m, 1H, **H**-C3′), 4.06 (dd, 1H, $J_{gem}=6.0$, $J_{4'',3'}=0.8$, **H**′-C4′), 4.33 (ddd, 1H, $J_{2',1'}=2.3$, $J_{2'OH}=11.0$, $J_{2',3'}=0.9$, **H**-C2′, collapses to dd on exchange with D_2O, $J_{2',1'}=2.3$, $J_{2',3'}=0.9$), 4.71 (d, 1H, $J_{4,5}=7.6$, **H**-C4), 5.78 (d, 1H, $J_{5,4}=7.6$, **H**-C5) and 7.23-7.49 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.6 ad 25.7 (C(**C**H$_3$)$_2$), 37.0 (**C**H$_3$-SO-), 65.2 (**C**2′), 65.4 (**C**4), 66.5 (**C**4′), 66.1 (**C**3′), 77.2 (**C**1′), 89.1 (**C**5), 110.5 (**C**(CH$_3$)$_2$), 125.3, 128.2, 128.4, 128.9, 129.0 and 129.8 (**C**H-arom.), 136.2 (**C**arom.-C4), 140.3 (**C**arom.-C5) and 153.9 (**C**3); IR (KBr, liquid film): 3150, 3050, 3010, 2950, 2900, 1605, 1495, 1460, 1385, 1370, 1295, 1215, 1060, 1025, 915, 860 and 705 cm^{-1}; EI-MS *m*/*z* (rel. int.): 414 (0.15, M$^+$−15), 366 (1, M$^+$−CH$_3$SO), 299 (4, $C_{17}H_{17}NO_2S^+$), 266 (26, $C_{17}H_{16}NO_2^+$), 101 (100, $C_5H_9O_2^+$), 43 (84, $C_2H_3O^+$). Anal. calcd for $C_{23}H_{27}NO_5S$: C, 64.32; H, 6.34, N, 3.26. Found C, 64.31; H, 6.31; N, 3.29%.

4.1.3. From isoxazoline (R_S,4*R*,5*R*)-3. Reaction of (R_S,4*R*,5*R*)-**3** (1 g, 3.34 mmol) with **1** (1.3 g, 10.0 mmol) following the general procedure, and work-up as described gave rise to a crude product containing compounds **13**, **14**, **15** and **16** in a 10:53:34:3 ratio, respectively (estimated by integration of the signals corresponding to CH$_3$-SO in the ^{1}H NMR spectrum of the crude reaction). Column chromatography using diethyl ether:hexane (1:1) as the eluent afforded a fraction (582 mg, 41%) containing a mixture of compounds **13** and **14**, pure **15** (341 mg, 24% yield) as a white solid and pure **16** (26 mg, 2%) as a white solid. After subsequent flash chromatography (diethyl ether:hexane, 1:2) pure **13** as a yellow foamy syrup and pure **14** as a white solid were obtained.

4.1.3.1. (R_S,4*R*,5*R*,1′*S,2′*S*,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 13**. $[\alpha]_D^{20}=-177.3$ (*c* 0.64, $CHCl_3$); ^{1}H NMR: δ 1.01 and 1.42 (2s, each 3H, C(C**H**$_3$)$_2$), 2.07 (s, 3H, C**H**$_3$-SO-), 3.52 (d, 1H, $J_{1',2'}=8.3$, **H**-C1′), 3.81–3.85 (m, 2H, **H**-C3′ and **H**′-C4′), 4.03 (dd, 1H, $J_{gem}=9.7$, $J_{4',3'}=5.1$, **H**-C4′), 4.30 (d, 1H, $J_{2',1'}=8.3$, **H**-C2′), 4.54 (d, 1H, $J_{4,5}=4.8$, **H**-C4), 4.63 (s, 1H, **H**O-C2′, exchanges with D_2O), 5.82 (d, 1H, $J_{5,4}=4.8$, **H**-C5) and 7.27–7.49 (m, 10H, **H**-arom.); ^{13}C NMR: δ 24.9 and 26.0 (C(**C**H$_3$)$_2$), 38.1 (**C**H$_3$-SO-), 61.6 (**C**2′), 64.7 (**C**4), 65.0 (**C**4′), 72.5 (**C**3′), 75.3 (**C**1′), 88.4 (**C**5), 109.6 (**C**(CH$_3$)$_2$), 124.6, 127.8, 128.4, 128.9 and 129.7 (**C**H-arom.), 136.7 (**C**arom.-C4), 140.5 (**C**arom.-C5) and 154.7 (**C**3); IR (KBr, liquid film): 3275, 1605, 1495, 1460, 1385, 1375, 1060, 1025, 970, 930 and 705 cm^{-1}; EI-MS *m*/*z* (rel. int.): 430 (0.5, M$^+$+1), 429 (1, M$^+$), 414 (2, M$^+$−15), 366 (6, M$^+$−CH$_3$SO), 266 (100, $C_{17}H_{16}NO_2^+$), 101 (99.5, $C_5H_9O_2^+$), 43 (63, $C_2H_3O^+$). Anal. calcd for $C_{23}H_{27}NO_5S$: C, 64.32; H, 6.34, N, 3.26. Found C, 64.35; H, 6.40, N, 3.25%.

4.1.3.2. (R_S,4*R*,5*R*,1′*R,2′*R*,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 14**. Mp 103–104°C (ether/hexane); $[\alpha]_D^{20}=-232.0$ (*c* 1.00, $CHCl_3$); ^{1}H NMR: δ 1.19 and 1.25 (2s, each 3H, C(C**H**$_3$)$_2$), 2.69 (s, 3H, C**H**$_3$-SO-), 3.63–3.68 (m, 2H, **H**-C4′ and **H**O-C2′, with D_2O integrates like 1H), 3.65 (d, 1H, $J_{1',2'}=4.7$, **H**-C1′), 3.84 (dd, 1H, $J_{gem}=8.7$, $J_{4'',3'}=4.4$, **H**-C4′), 4.02–4.13 (m, 1H, **H**-C3′), 4.38 (ddd, 1H, $J_{2',1'}=4.7$, $J_{2'OH}=2.1$, $J_{2',3'}=7.3$, **H**-C2′; collapses to dd on exchange with D_2O, $J_{2',1'}=4.7$, $J_{2',3'}=7.3$), 4.60 (d, 1H, $J_{4,5}=7.8$, **H**-C4), 5.52 (d, 1H, $J_{5,4}=7.8$, **H**-C5) and 7.30–7.47 (m, 10H, **H**-arom.); ^{13}C NMR: δ 24.9 and 26.5 (C(**C**H$_3$)$_2$), 40.2 (**C**H$_3$-SO-), 60.4 (**C**2′), 65.8 (**C**4′), 66.1 (**C**4), 71.5 (**C**3′), 75.00 (**C**1′), 91.6 (**C**5), 109.5 (**C**(CH$_3$)$_2$), 126.4, 128.1, 128.5, 128.7, 128.8 and 129.7 (**C**H-arom.), 137.1 (**C**arom.-C4), 139.3 (**C**arom.-C5) and 155.5 (**C**3); IR (KBr, liquid film): 3300, 1605, 1495, 1460, 1385, 1375, 1160, 1065, 1025, 915 and 705 cm^{-1}; EI-MS *m*/*z* (rel. int.): 430 (1, M$^+$+1), 429 (5, M$^+$), 366 (3, M$^+$−CH$_3$SO), 266 (47, $C_{17}H_{16}NO_2^+$), 101 (72, $C_5H_9O_2^+$), 43 (100, $C_2H_3O^+$). Anal. calcd for $C_{23}H_{27}NO_5S$: C, 64.32; H, 6.34, N, 3.26. Found C, 64.23; H, 6.36; N, 3.25%.

4.1.3.3. (R_S,4*R*,5*R*,1′*S,2′*R*,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 15**. (Low melting point solid; carbon tetrachloride,); $[\alpha]_D^{20}=-227.2$ (*c* 1.00, $CHCl_3$); ^{1}H NMR: δ 1.08 and 1.35 (2s, each 3H, C(C**H**$_3$)$_2$), 2.05 (s, 3H, C**H**$_3$-SO-), 3.42–3.48 (m, 1H, $J_{3',2'}=9.7$, $J_{3',4'}=5.3$, $J_{3',4''}=6.2$, **H**-C3′), 3.58 (d, 1H, $J_{1',2'}=2.4$, **H**-C1′), 3.85 (dd, 1H, $J_{gem}=8.5$, $J_{4',3'}=5.3$, **H**′-C4′), 3.96 (dd, 1H, $J_{gem}=8.5$, $J_{4'',3'}=6.2$, **H**″-C4′), 4.18 (ddd, 1H, $J_{2',1'}=2.4$, $J_{2'OH}=7.3$, $J_{2',3'}=9.7$, **H**-C2′, collapses to dd on exchange with D_2O, $J_{2',1'}=2.4$, $J_{2',3'}=9.7$), 4.37 (d, 1H, $J_{4,5}=4.1$, **H**-C4), 5.15 (d, 1H, $J_{2',OH}=7.3$, **H**O-C2′, exchanges with D_2O), 5.79 (d, 1H, $J_{5,4}=4.1$, **H**-C5) and 7.27–7.45 (m, 10H, **H**-arom.); ^{13}C NMR: δ 24.9 and 26.8 (C(**C**H$_3$)$_2$), 36.1 (**C**H$_3$-SO-), 63.3 (**C**2′), 65.8 (**C**4), 68.6 (**C**4′), 69.3 (**C**3′), 75.2 (**C**1′), 88.1 (**C**5), 109.9 (**C**(CH$_3$)$_2$), 124.8, 127.7, 128.3, 128.8, 128.9 and 129.6 (**C**H-arom.), 136.76 (**C**arom.-C4), 140.53 (**C**arom.-C5) and 153.96 (**C**3); IR (KBr, liquid film): 3275, 1605, 1495, 1460, 1385, 1375, 1160, 1070, 1025, 915 and 705 cm^{-1}; EI-MS *m*/*z* (rel. int.): 429 (2, M$^+$), 414 (4, M$^+$−15), 366 (12, M$^+$−(CH$_3$-SO)), 266 (95, $C_{17}H_{16}NO_2^+$), 101 (69, $C_5H_9O_2^+$), 43 (100, $C_2H_3O^+$). Anal. calcd for $C_{23}H_{27}NO_5S$: C, 64.32; H, 6.34, N, 3.26. Found C, 64.19; H, 6.40, N, 3.27%.

4.1.3.4. (R_S,4*R*,5*R*,1′*R,2′*S*,3′*R*)-4,5-Diphenyl-3-(2′-hydroxy - 3′,4′ - isopropylidenedioxy - 1′ - methylsulfinyl)-butylisoxazoline, 16**. Mp 86–87°C (ether/hexane); $[\alpha]_D^{20}=-218.0$ (*c* 0.50, $CHCl_3$); ^{1}H NMR: δ 1.38 and 1.44 (2s, each 3H, C(C**H**$_3$)$_2$), 2.74 (s, 3H, C**H**$_3$-SO-), 3.46 (d, 1H, $J_{1',2'}=2.3$, **H**-C1′), 3.77 (d, 2H, $J_{4',3'}=J_{4'',3'}=6.8$, **H**-C4′ and **H**-C4′), 3.83 (d, 1H, $J_{2',OH}=10.5$, **H**O-C2′, exchanges with D_2O), 3.92 (dt, 1H, $J_{4',3'}=J_{4'',3'}=6.8$, $J_{3',2'}=3.0$, **H**-C3′), 4.38 (ddd, 1H, $J_{2',1'}=2.3$, $J_{2'OH}=10.5$, $J_{2',3'}=3.0$, **H**-C2′, collapses to dd on exchange with D_2O, $J_{2',1'}=2.3$, $J_{2',3'}=3.0$), 4.40 (d, 1H, $J_{4,5}=7.9$, **H**-C4), 5.55 (d, 1H, $J_{5,4}=7.9$, **H**-C5) and

7.27–7.47 (m, 10H, **H**-arom.); ^{13}C NMR: δ 25.5 and 26.3 (C(**C**H$_3$)$_2$), 35.8 (**C**H$_3$-SO-), 61.1 (**C**2′), 65.6 (**C**4), 66.0 (**C**4′), 65.7 (**C**3′), 78.2 (**C**1′), 90.2 (**C**5), 110.1 (**C**(CH$_3$)$_2$), 125.5, 128.5, 128.7, 129.0 and 129.6 (**C**H-arom.), 136.4 (**C**arom.-C4), 139.2 (**C**arom.-C5) and 154.7 (**C**3); IR (KBr, liquid film): 3300, 1605, 1495, 1460, 1385, 1375, 1160, 1080, 1035, 915 and 700 cm^{-1}; EI-MS m/z (rel. int.): 430 (2, M$^+$+1), 429 (7, M$^+$), 414 (4, M$^+$−15), 366 (8, M$^+$−CH$_3$SO), 299 (12, $C_{17}H_{17}NO_2S^+$), 266 (100, $C_{17}H_{16}NO_2^+$), 101 (82, $C_5H_9O_2^+$), 43 (99, $C_2H_3O^+$). Anal. calcd for $C_{23}H_{27}NO_5S$: C, 64.32; H, 6.34, N, 3.26. Found C, 64.39; H, 6.31; N, 3.20%.

4.2. Reductive ring cleavage

4.2.1. Reductive cleavage of isoxazoline (R_S,4*S*,5*S*)-2. To a solution of isoxazoline (R_S,4*S*,5*S*)-**2** (299 mg, 1 mmol) in 5/1 methanol/water (6 mL) was added boric acid (124 mg, 2 mmol) and a spatula tip (estimated 10–20 mg) of W-2 Raney nickel. The reaction was placed under hydrogen by repeated (ca. five times) evacuation and flushing with H_2 gas. The mixture was stirred vigorously, at rt, until the starting isoxazoline was disappeared and then filtered through Celite into a separatory funnel containing water and CH_2Cl_2. After separation, the aqueous layer was extracted with CH_2Cl_2 three more times and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to yield the crude β-hydroxyketone. Purification was carried out by column chromatography using diethyl ether:hexane, 1:10, as eluent, and 3,4-diphenyl-4-hydroxy-2-butanone **17** (44 mg, 0.18 mmol) was obtained in a 18% yield, and benzyl methyl ketone (87 mg, 0.65 mmol) and benzaldehyde (69 mg, 0.65 mmol) in a 65% yield, as a result of a retroaldol reaction.

When reaction was achieved with the same isoxazoline (R_S,4*S*,5*S*)-**2** (299 mg, 1 mmol) following the general procedure, but at a lower temperature, 0°C, the retro-aldol reaction was prevented. The reaction was quenched after 3 h and the residue purified by column chromatography (diethyl ether:hexane, 1:10). Optically active (3*R*,4*S*)-3,4-diphenyl-4-hydroxy-2-butanone **17** (161 mg, 0.67 mmol) was obtained in a 67% yield.

4.2.1.1. (3*R*,4*S*)-Diphenyl-4-hydroxy-2-butanone, 17. Yellow syrup; $[\alpha]_D$ = +283.0 (c 0.8, CHCl$_3$); ^{1}H NMR: δ 2.13 (3H, s, C**H**$_3$-CO), 3.38 (1H, d, $J_{4,OH}$ = 3.2, **H**O-C4), 3.95 (1H, d, $J_{3,4}$ = 9.3, **H**-C3), 5.20 (1H, dd, $J_{3,4}$ = 9.3, $J_{4,OH}$ = 3.2, **H**-C4) and 6.94–7.26 (10H, m, **C**H-arom.); ^{13}C NMR: δ 30.2 (**C**-1), 67.4 (**C**-3), 75.9 (**C**-4), 126.6, 127.5, 127.6, 127.9, 128.7 and 128.9 (**C**H-arom.), 134.8 (**C**arom.-C3), 140.8 (**C**arom.-C4) and 209.7 (**C**-2); EI-MS m/z (rel. int.): 240 (0.01, M$^+$), 223 (0.18, M$^+$−OH), 197 (0.17, M$^+$−CH$_3$CO), 134 (98, $C_9H_{10}O^+$), 105 (24, $C_7H_5O^+$), 91 (59, $C_7H_7^+$), 77 (54, $C_6H_5^+$), 43 (100, CH$_3$CO$^+$). Anal. calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71%.

4.2.2. Reductive cleavage of isoxazolines 4, 6, 14 and 15. Following the above-described procedure for reductive ring cleavage, starting from β-hydroxyisoxazolines **4**, **6**, **14** and **15**, at 0°C, after 1 h, the reactions were quenched. Only heptanone **18** was detected in the ^{1}H NMR spectra of each one of the crude reactions.

4.2.2.1. (1*R*,2*S*,5*S*,6*R*)-1,2-Diphenyl-1,5-dihydroxy-6,7-isopropylidenedioxy-3-heptanone, 18. White solid, mp 93–94°C (ether/hexane); $[\alpha]_D^{20}$ = −254.4 (c 0.22, CHCl$_3$); ^{1}H NMR: δ 1.26 and 1.29 (2s, each 3H, C(C**H**$_3$)$_2$), 2.64 (dd, 1H, J_{gem} = 16.8, $J_{4,5}$ = 8.3, **H**-C4), 2.75 (dd, 1H, J_{gem} = 16.8, $J_{4',5}$ = 2.9, **H**′-C4), 3.07 (d, 1H, $J_{5,OH}$ = 3.4, **H**O-C5), 3.22 (d, 1H, $J_{1,OH}$ = 3.2, **H**O-C1), 3.83–3.96 (m, 4H, **H**-C5, **H**-C6 and two **H**-C7), 4.04 (d, 1H, $J_{1,2}$ = 9.5, **H**-C2), 5.26 (dd, 1H, $J_{1,2}$ = 9.5, $J_{1,OH}$ = 3.2, **H**-C1), 6.96–7.00 (m, 2H, C4-**C**H-arom.), 7.04–7.07 (m, 2H, C5-**C**H-arom.) and 7.13–7.19 (m, 6H, **C**H-arom.); ^{13}C NMR: δ 25.1 and 26.5 (C(**C**H$_3$)$_2$), 45.9 (**C**-4), 66.3 (**C**-7), 67.6 (**C**-2), 69.4 (**C**-6), 76.2 (**C**-5), 77.4 (**C**-1), 109.4 (**C**(CH$_3$)$_2$), 126.6, 127.7, 127.8, 128.0, 128.8 and 129.0 (**C**H-arom.), 134.0 (C2-**C**-arom.), 140.6 (C1-**C**-arom.) and 212.1 (**C**-3); IR (KBr, liquid film): 3425, 3250, 1710, 1605, 1495, 1460, 1380, 1065, 1045 and 705 cm^{-1}. Anal. calcd for $C_{22}H_{26}O_5$: C, 71.34; H, 7.07. Found C, 71.25; H, 7.05.

4.2.3. Reductive cleavage of isoxazolines 5, 13 and 16. Following the above-described procedure for reductive ring cleavage, starting from β-hydroxyisoxazolines **5**, **13** and **16**, at 0°C, after 1 h, the reactions were quenched. Only heptanone **19** was detected in the ^{1}H NMR spectra of the crude reactions.

4.2.3.1. (1*R*,2*S*,5*R*,6*R*)-1,2-Diphenyl-1,5-dihydroxy-6,7-isopropylidenedioxy-3-heptanone, 19. White solid, mp 117–118°C (ether:hexane); $[\alpha]_D^{20}$ = −188.0 (c 0.14, CHCl$_3$); ^{1}H NMR: δ 1.34 and 1.41 (2s, each 3H, C(C**H**$_3$)$_2$), 1.58 (b, 1H, **H**O-C5), 2.65 (d, 2H, $J_{4,5}$ = 6.0, two **H**-C4), 3.07 (b, 1H, **H**O-C1), 3.76 (dd, 1H, J_{gem} = 8.2, $J_{7,6}$ = 6.4, **H**-C7), 3.95 (dd, 1H, J_{gem} = 8.2, $J_{7,6}$ = 6.5, **H**-C7), 4.02 (d, 1H, $J_{1,2}$ = 9.3, **H**-C2), 4.03–4.14 (m, 2H, **H**-C5 and **H**-C6), 5.25 (d, 1H, $J_{1,2}$ = 9.3, **H**-C1), 6.97–7.00 (m, 2H, C4-**C**H-arom.), 7.04–7.07 (m, 2H, C5-**C**H-arom.) and 7.13–7.19 (m, 6H, **C**H-arom.); ^{13}C NMR: δ 25.1 and 26.4 (C(**C**H$_3$)$_2$), 46.3 (**C**-4), 65.6 (**C**-7), 66.9 (**C**-2), 67.5 (**C**-6), 76.2 (**C**-5), 77.4 (**C**-1), 109.6 (**C**(CH$_3$)$_2$), 126.6, 127.7, 128.1, 128.8 and 129.0 (**C**H-arom.), 134.0 (C2-**C**-arom.), 140.7 (C1-**C**-arom.) and 210.2 (**C**-3); IR (KBr, liquid film): 3500, 1715, 1495, 1460, 1380, 1160, 1095, 1065, 1045 and 705 cm^{-1}. Anal. calcd for $C_{22}H_{26}O_5$: C, 71.34; H, 7.07. Found C, 71.40; H, 7.03%.

4.2.4. Reductive cleavage of isoxazolines 7, 9 and 10. Following the above-described procedure for reductive ring cleavage, starting from β-hydroxyisoxazolines **7**, **9** and **10** at 0°C, after 2 h, the reactions were quenched. Only heptanone **20** was detected in the ^{1}H NMR spectra of each one of the crude reactions.

4.2.4.1. (1*S*,2*R*,5*S,6*R*)-1,2-Diphenyl-1,5-dihydroxy-6,7-isopropylidenedioxy-3-heptanone, 20**. White solid, mp 92–93°C (hexane); $[\alpha]_D^{20}=+160.3$ (*c* 0.34, $CHCl_3$); ^{1}H NMR: δ 1.30 and 1.37 (2s, each 3H, C(C**H**$_3$)$_2$), 2.57 (dd, 1H, $J_{gem}=17.6$, $J_{4,5}=9.1$, **H**-C4), 2.88 (dd, 1H, $J_{gem}=17.6$, $J_{4,5}=2.8$, **H**-C4), 2.95 (d, 1H, $J_{5,OH}=3.4$, **H**O-C5), 3.03 (1H, a, **H**O-C1), 3.82–3.93 (m, 2H, two **H**-C7), 4.02 (d, 1H, $J_{1,2}=9.7$, **H**-C2), 4.02–4.36 (m, 2H, **H**-C5 and **H**-C6), 5.26 (d, 1H, $J_{1,2}=9.7$, **H**-C1), 6.96–6.99 (m, 2H, C2-**C**H-arom.), 7.04–7.07 (m, 2H, C1-**C**H-arom.) and 7.15–7.19 (m, 6H, **C**H-arom.); ^{13}C NMR: δ 25.1 and 26.6 (C(**C**H$_3$)$_2$), 46.4 (**C**-4), 66.8 (**C**-7), 66.8 (**C**-2), 68.7 (**C**-6), 76.1 (**C**-5), 77.5 (**C**-1), 109.4 (**C**(CH$_3$)$_2$), 126.6, 127.8, 128.1, 128.8 and 129.0 (**C**H-arom.), 134.1 (C2-**C**-arom.), 140.7 (C1-**C**-arom.) and 211.6 (**C**-3); IR (KBr, liquid film): 3450, 1710, 1605, 1495, 1460, 1385, 1375, 1155, 1070, 1045 and 705 cm^{-1}. Anal. calcd for $C_{22}H_{26}O_5$: C, 71.34; H, 7.07. Found C, 71.39; H, 7.09%.

4.2.5. Reductive cleavage of isoxazolines 8, 11 and 12. Following the above-described procedure for reductive ring cleavage, starting from β-hydroxyisoxazolines **8**, **11** and **12**, at 0°C, after 2 h the reactions were quenched. Only heptanone **21** was detected in the ^{1}H NMR spectra of the crude reactions.

4.2.5.1. (1*S*,2*R*,5*R,6*R*)-1,2-Diphenyl-1,5-dihydroxy-6,7-isopropylidenedioxy-3-heptanone, 21**. White solid, mp 65–67°C (hexane:carbon tetrachloride); $[\alpha]_D^{20}=+222.1$ (*c* 0.29, $CHCl_3$); ^{1}H NMR: δ 1.30 and 1.38 (2s, each 3H, C(C**H**$_3$)$_2$), 2.48 (dd, 1H, $J_{gem}=16.6$, $J_{4,5}=3.0$, **H**-C4), 2.74 (dd, 1H, $J_{gem}=16.6$, $J_{4,5}=8.6$, **H**-C4), 2.93 (a, 1H, **H**O-C1), 3.20 (a, 1H, **H**O-C5), 3.78 (dd, 1H, $J_{gem}=6.5$, $J_{7,6}=6.3$, **H**-C7), 3.92 (dd, 1H, $J_{gem}=6.5$, **H**-C7), 3.92–3.98 (m, 1H, **H**-C6), 4.03–4.06 (m, 1H, **H**-C5), 4.04 (d, 1H, $J_{1,2}=9.1$, **H**-C2), 5.25 (d, 1H, $J_{1,2}=9.1$, **H**-C1), 6.97–7.16 (m, 10H, **C**H-arom.); ^{13}C NMR: δ 25.1 and 26.3 (C(**C**H$_3$)$_2$), 46.1 (**C**-4), 65.5 (**C**-7), 67.8 (**C**-2), 68.3 (**C**-6), 76.1 (**C**-5), 77.8 (**C**-1), 109.6 (**C**(CH$_3$)$_2$), 126.6, 127.7, 127.8, 128.0, 128.8 and 129.1 (**C**H-arom.), 134.2 (C2-**C**-arom.), 140.6 (C1-**C**-arom.) and 211.0 (**C**-3); IR (KBr, liquid film): 3500, 1710, 1605, 1495, 1460, 1375, 1160, 1120, 1075, 1045 and 705 cm^{-1}. Anal. calcd for $C_{22}H_{26}O_5$: C, 71.34; H, 7.07. Found C, 71.26; H, 7.06%.

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