

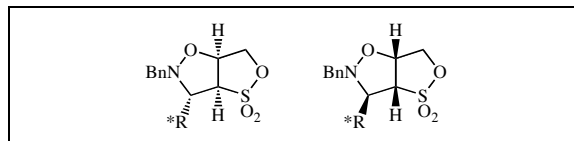
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Asymmetric 1,3-dipolar cycloadditions of chiral nitrones to 1-propene-1,3-sultone (**1**) were investigated. Chiral nitrones **6a-e** reacted with sultone **1** in toluene at 90 °C for 24-36 h to give the corresponding isoxazolidines in moderate yields with high regioselectivities and stereoselectivities. The diastereoselectivity of this reaction varied with the choice of dipolarophile and the steric demands of nitrones. When sultone **1** was allowed to react chiral nitron **6e**, a much better diastereoselectivity of up to 5.1:1 was observed.

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INTRODUCTION

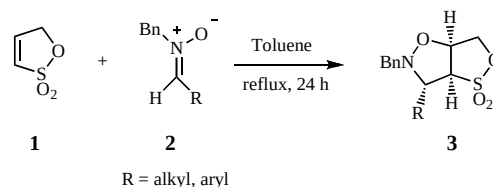
1,3-Dipolar cycloaddition reaction has been extensively used for the syntheses of five-membered heterocyclic compounds [1]. The nitron-olefin 1,3-dipolar cycloaddition, giving isoxazolidine, is a powerful reaction in that it can produce as many as three new contiguous stereogenic centers in a single step [2]. Asymmetric synthesis of isoxazolidine is a main challenge in the field. During the past two decades, great effort has been dedicated to asymmetric 1,3-dipolar cycloaddition reaction, performed variously with chiral nitrones [3], chiral olefins [4] and under catalytic conditions in the presence of Lewis acid complexes [5]. Based on an evaluation of the nitron cycloaddition reaction, it was considered that the new chiral centers could be influenced if the reaction system was properly designed, and the regio- and stereoselectivity could also be controlled.

Isoxazolidines obtained by 1,3-dipolar cycloaddition of nitron with olefin could be converted into 1,3-amino alcohols *via* reductive cleavage of N-O bond of the compound, which are versatile intermediates for the synthesis of natural products and biologically interesting compounds [6]. To extend the scope of the 1,3-dipolar cycloaddition reaction, the development of new dipolarophiles has attracted the attention of many scientific investigations [7]. α,β -Unsaturated sultones exemplified by 1-propene-1,3-sultone in which the double bond was activated by the electron -withdrawing group $-\text{SO}_2$ was developed as an effective dienophile in the Diels-Alder reaction [8]. As a part of our program exploring the chemistry of unsaturated sultone [9], we report herein the asymmetric 1,3-dipolar cycloaddition reaction of chiral nitrones to 1-propene-1,3-sultone.

RESULTS AND DISCUSSION

We have previously reported the synthesis of racemic isoxazolidines by 1,3-dipolar cycloaddition reaction of 1-propene-1,3-sultone (**1**) with nitrones (**2**) in an earlier paper [9a]. When the cycloaddition reactions were performed in refluxing toluene for 24 h, good yields (70% - 86%) of isoxazolidines (**3**) with high regioselectivities and *endo/exo* stereoselectivities were obtained (Scheme 1).

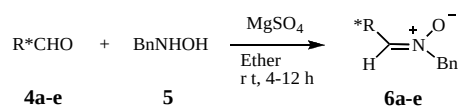
Scheme 1



Based on the successful synthesis of racemic isoxazolidine, we were hopeful to extend the methodology to the asymmetric 1,3-dipolar cycloaddition by using chiral nitrones as starting materials. Adopting the synthetic protocol previously established in our laboratory, we prepared the optically active isoxazolidines by asymmetric cycloadditions.

Chiral nitrones could be prepared from the corresponding aldehyde [10]. To set the stage for our study, five chiral aldehydes (**4a-e**) were chosen, among which aldehydes **4b**, **4c** and **4d** were prepared by modified literature procedures [11]. These chiral aldehydes were allowed to react with benzyl hydroxylamine in dichloromethane or ether at ambient temperature to afford chiral nitrones **6a-e** in 60-73 % isolated yield (Scheme 2).

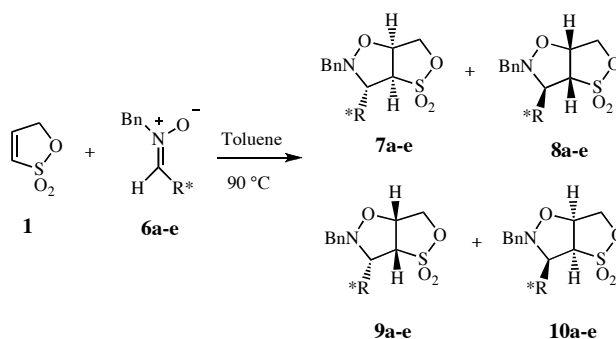
Scheme 2



Then, chiral nitrones **6a-e** were subjected to 1,3-dipolar cycloaddition with 1-propene-1,3-sultone (Scheme 3) to examine the stereoselectivity effect on the nitron moiety in the cycloadditions. In principle, a (*Z*)-nitron reacted with an unsymmetric dipolarophile might produced eight possible cycloadducts, *cis*- and *trans*-isomers for each pair of regioisomers from *anti* and *syn* attack. The cycloaddition of the chiral nitrones to 1-propene-1,3-sultone were performed in toluene at 90 °C for 24-36 h. ^1H NMR analysis of the mixtures showed four diastereometric isoxazolidines (**7-10**) were obtained. The major products **7** and **8** (72% - 78%) could be isolated by flash column chromatography on silica gel. The ratios of the diastereoisomers were determined from either ^1H NMR spectra of crude product or from isolated yields. The results were summarized in Table 1.

Quoting the structural analysis of racemic isoxazolidine from the literature [9a], the stereochemical and regiochemical assignment for the product of asymmetric cycloaddition could be pitched based on the ^1H NMR spectra. X-ray crystal structure analysis further confirmed the structure of the cycloadduct (Figure 1). The analysis of product configuration indicated that C₈-*R*, C₉-*R* and

Scheme 3



C₁₀-*R* were formed for **7**, while C₈-*S*, C₉-*S*, and C₁₀-*S* were produced for **8**. Selected bond lengths and angles for the adduct **8** indicated that torsion angle (plane H₁₀-C₁₀-C₁₁-H₁₁) and the dihedral angle between the protons are approximately 143° and 37°, respectively. From inspection of molecular model it is clear that a dihedral angle of 37° could be achieved when the protons have a *trans* relationship. It was reported that the conformation adopted by the five-membered ring is envelope and the ring is non-planar [12], in accord with what has been made in the present X-ray crystalline diffraction.

The stereoselectivity of cycloaddition between nitron and unsymmetric olefin would appear to depend on the structural changes in both reactants. 1,3-Dipolar cycloaddition of α -substituted nitrones has been shown to occur preferentially

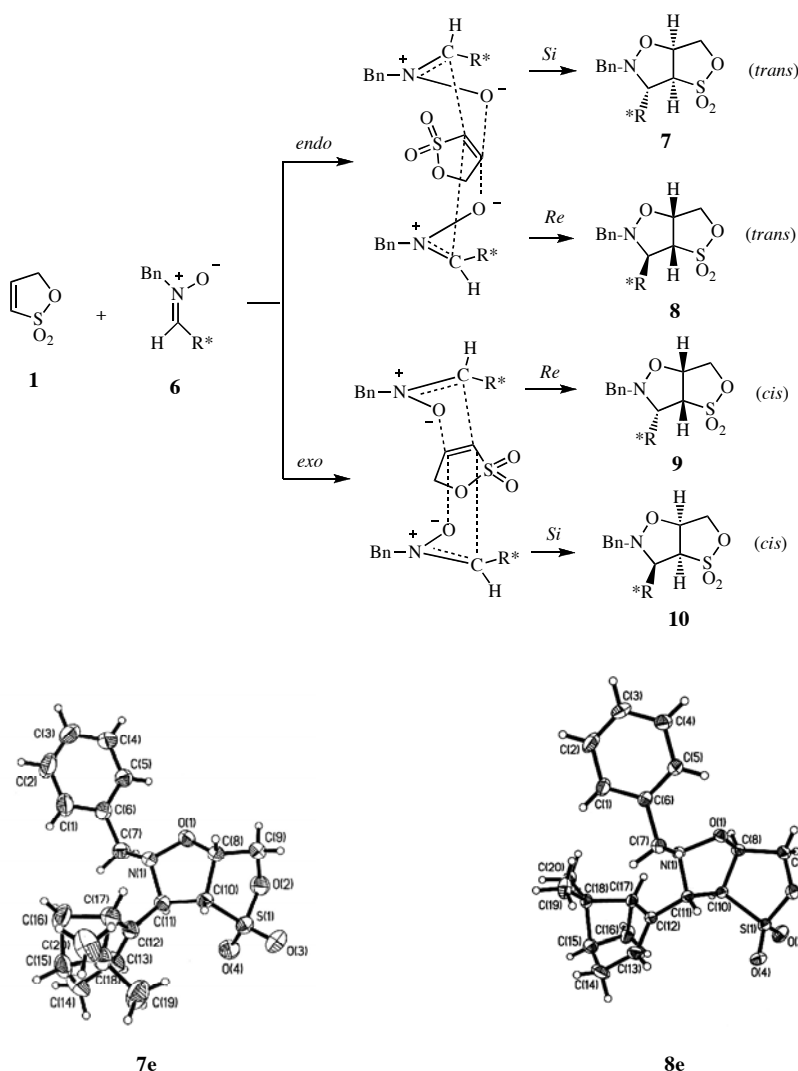
Table 1

Asymmetric cycloaddition of nitrones with 1-propene-1,3-sultone^a

Entry	Nitron	R*	Reaction time (h)	endo:exo	7/8 ^b	Yield ^c (%)
1	6a		24	>96 : <4	2.6 : 1	87
2	6b		36	>96 : <4	3.1 : 1	68
3	6c		24	>96 : <4	2.3 : 1	77
4	6d		24	>96 : <4	2.8 : 1	72
5	6e		36	>96 : <4	5.1 : 1	73

a. Propene sultone (1.0 mmol) and chiral nitron (3.0 mmol) in toluene at 90 °C. b. Entry **2** and **3** were determined by ^1H NMR. Other entries were determined by isolate yield. c. **7** and **8**, isolated yield.

Scheme 4

Figure 1 X-ray structure of cycloadducts **7e** and **8e**

via transition states in which the developing C-C bond avoids steric interaction with the more bulky group [13]. Obviously, steric hindrance played an important role for the formation of cycloadduct in the cycloaddition. For the present reaction, excellent *endo:exo* >96:<4 are observed in all the cases. The *endo* approach of the dipole, referred as to *anti-facial* preference [14], accounts for the formation of the isoxazolidines. However, the experimental results showed that the diastereoselectivities for the cycloaddition reactions are moderate to good (dr=2.3-5.1). The best one in this series was observed with chiral nitron **6e** to give **7e** and **8e** in 73% yield and the diastereoselectivity was high as an *endo:exo* ratio of >96:<4 with dr up to 5.1:1 (Table 1, entry 5).

The analysis of adduct configurations suggested that the major product arises from a manner which has occurred

on the less sterically accessible face of nitron, via an *endo* transition state with antiperiplanar relationship of the double bond of sultone and α -alkyl (aryl) group of nitron (Scheme 4). As shown in Scheme 4, the major *trans* adducts **7** and **8** could be formed by *endo* attack on the (*Z*)-nitron. Similarly, the minor *cis* adducts **9** and **10** could be formed by *exo* attack. Dipolarophiles capable of secondary orbital interactions [15], proceed via *endo* transition states referring to the literature [16]. The preferential diastereofacial *Si* selectivity induced by the chiral moiety of nitron showed that *Si* face attack of nitron is favors in the cycloaddition. The formation of the predominant adduct **7** came from *Si* attack by (*Z*)-*endo* manner. It is reasonable that steric hindrance present in the approach lead to higher diastereoselectivity (for instance, see Table 1, entry 5).

It is interesting to note that isoxazolidine like **3** could be transferred to the corresponding sultam by the strategy of ring opening-closure [9c]. The particularly valuable feature for this transformation lies in the fact that a racemic isoxazolidine could be converted into the optically active sultam. The latter could be further transferred to the corresponding N-H compound by debenzilation with formic acid [17], and the N-H compound is a precursor used for synthesizing chiral auxiliary [9c,18].

In summary, a regio- and stereoselective synthesis of isoxazolidine by asymmetric 1,3-dipolar cycloaddition reaction of nitron with 1-propene-1,3-sultone was investigated. A series of isoxazolidines with sultone moiety was prepared. The resulting cycloadducts are useful intermediates in organic synthesis. Study on the application in synthetic chemistry is in progress.

EXPERIMENTAL

Unless otherwise noted, solvents and starting materials were obtained from commercial suppliers without further purification. Melting points were taken on a MEL-TEMP2 (unchecked). ¹H NMR and ¹³C NMR spectra were recorded on a Varian INOVA Unity (400 MHz) or on a JOEL JNM-EX 270 (270 MHz) in CDCl₃. Chemical shifts were recorded in ppm (δ) relative to TMS. Optical rotations were taken on a JASCO DIP-1000 digital polarimeter. Elemental analysis was performed on a Perkin Elmer 240B microanalyzer. IR was recorded on a Nicolet Magna 550 spectrometer. EI (70 eV) or FAB mass spectra were measured with a Finnigan MAT SSQ-710 spectrometer. HRMS were recorded on a QSTAR Pulsar/LC/MS/MS system. All glass equipments were dried in an oven at 120 °C prior to use.

General Procedure for the preparation of isoxazolidines 7a-e and 8a-e. Benzyl hydroxylamine [19] and nitrones **6a-6e** were prepared by modified literature methods [10].

(Z)-N-(1-Deoxy-2,3-O-isopropylidene-D-glycero-1-yliden-*e*)benzylamine N-oxide (6a). Yield: 70 %; thick oil; [α]_D²¹ +90.2° (c 0.85, CHCl₃); ¹H nmr (400 MHz, CDCl₃) δ 1.36 (s, 3 H), 1.40 (s, 3 H), 3.86 (dd, *J* = 6.0, 8.8 Hz, 1 H), 4.37 (dd, *J* = 7.6, 8.8 Hz, 1 H), 4.85 (s, 2 H), 5.14 (ddd, *J* = 4.0, 6.2, 7.8 Hz, 1 H), 6.87 (d, *J* = 4.4 Hz, 1 H), 7.46 (s, 5 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 24.7, 26.0, 67.6, 68.7, 71.8, 109.7, 128.9, 129.0, 129.2, 131.9, 139.2; ir (KBr): 1590 cm⁻¹; ms (FAB): *m/z* 236 (M+H)⁺; C₁₃H₁₇NO₃ requires 235; *Anal.* Calcd. for C₁₃H₁₇NO₃: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.30; H, 7.21; N, 6.01.

(Z)-N-1-Deoxy-2,3,4,5-di-O-isopropylidene-D-mannito-1-yliden)benzylamine N-oxide (6b). Yield: 60 %; thick oil; [α]_D²¹ +17.2° (c 1.35, CHCl₃); ¹H nmr (400 MHz, CDCl₃) δ 1.28 (s, 3 H), 1.32 (s, 3 H), 1.33 (s, 3 H), 1.42 (s, 3 H), 3.92 (dd, *J* = 5.6, 8.4 Hz, 1 H), 3.98 (dd, *J* = 5.2, 7.6 Hz, 1 H), 4.08 (dd, *J* = 6.4, 8.6 Hz, 1 H), 4.31 (ddd, *J* = 5.2, 6.4, 6.8 Hz, 1 H), 4.86 (s, 2 H), 4.95 (dd, *J* = 5.8, 7.2 Hz, 1 H), 6.74 (d, *J* = 6.4 Hz, 1 H), 7.36 (s, 5 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 25.1, 26.2, 26.6, 26.7, 65.6, 69.8, 73.1, 75.9, 79.7, 109.4, 110.8, 128.9, 129.1, 129.4, 132.2, 135.8; ir (KBr): 1582 cm⁻¹; ms (FAB): *m/z* 336 (M+H)⁺; C₁₈H₂₃NO₅ requires 335; hrms (ESI): *m/z* C₁₈H₂₆NO₅ (M+H)⁺. Calcd: 336.1811. Found: 336.1817.

(Z)-N-[(S)-Benoxypopylidene]benzylamine N-oxide (6c). Yield: 73 %; thick oil; [α]_D²¹ -13.8° (c 1.10, CHCl₃); ¹H nmr (400 MHz, CDCl₃) δ 1.36 (d, *J* = 6.0 Hz, 3 H), 4.45 (d, *J* = 11.6 Hz, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.81 (m, 1 H), 4.83 (s, 2 H), 6.67 (d, *J* = 6.4 Hz, 1 H), 7.24-7.44 (m, 10 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 17.1, 69.5, 70.4, 72.0, 127.8, 128.4, 129.0, 129.3, 132.1, 137.6, 137.7, 141.9; ir (KBr): 1585 cm⁻¹; ms (FAB): *m/z* 270 (M+H)⁺; C₁₇H₁₆NO₂ requires 269; *Anal.* Calcd. for C₁₇H₁₆NO₂: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.73; H, 7.04; N, 5.28.

(Z)-N-[(S)-Benzoxypopylidene]benzylamine N-oxide (6d). Yield: 72 %; thick oil; [α]_D²¹ -29.7° (c 1.05, CHCl₃); ¹H nmr (400 MHz, CDCl₃) δ 4.99 (q, *J* = 11.2 Hz, 1 H), 4.82 (s, 2 H), 5.74 (d, *J* = 6.4 Hz, 1 H), 6.90 (d, *J* = 6.4 Hz, 1 H), 7.28-7.50 (m, 10 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 69.5, 71.2, 75.4, 127.1, 127.8, 127.9, 128.3, 128.4, 128.6, 128.9, 129.0, 129.3, 132.3, 137.6, 137.7, 139.0; ir (KBr): 1582 cm⁻¹; ms (FAB): *m/z* 332 (M+H)⁺; C₂₂H₂₁NO₂ requires 331; *Anal.* Calcd. for C₂₂H₂₁NO₂: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.62; H, 6.31; N, 4.30.

(Z)-N-(1R)-Myrtenylidenebenzylamine N-oxide (6e). Yield: 68 %; thick oil; [α]_D²¹ -4° (c 1.50, CHCl₃); ¹H nmr (400 MHz, CDCl₃) δ 0.83 (s, 3 H), 1.21 (d, *J* = 6.2 Hz, 1 H), 1.28 (s, 3 H), 2.11 (m, 1 H), 2.19 (m, 1 H), 2.38-2.48 (m, 3 H), 4.89 (s, 2 H), 6.65 (s, 1 H), 7.36-7.41 (m, 5 H), 7.75 (s, 1 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 21.1, 26.1, 31.5, 32.7, 37.8, 40.3, 46.3, 70.3, 128.6, 128.7, 128.9, 131.7, 133.3, 133.4, 137.2; ir (KBr): 1546 cm⁻¹; ms (FAB): *m/z* 256 (M+H)⁺; C₁₇H₂₁NO requires 255; *Anal.* Calcd. for C₁₇H₂₁NO: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.89; H, 8.32; N, 5.58.

Asymmetric Cycloaddition Reactions. A mixture of chiral nitrones **6a-6e** (3.0 mmol) and 1-propene-1,3-sultone (1.0 mmol) in 15 mL of dry toluene was heated under nitrogen at 90 °C with stirring for the required time (see Table 1). Saturated ammonium chloride solution (15 mL) was added. Organic phase was separated, and aqueous phase was extracted with ether. The combined organic phase was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The residue was subjected to flash column chromatography on silica gel with ethyl acetate/petroleum ether to afford the pure cycloadducts.

(3R,3aR,6aR)-2-Benzyl-3-[(4S)-(2,2-dimethyl-1,3-dioxolan-4-yl)]-4,5-oxthiain-4,4-dioxide[3,4-d]isoxazolidine (7a). White solid; mp 136-138 °C; [α]_D²¹ -20.2° (c 1.3, CHCl₃); ¹H nmr (400 MHz, CDCl₃): δ 1.32 (s, 3 H), 1.44 (s, 3 H), 3.57 (m, 1 H), 3.69 (dd, *J* = 4.0, 4.8 Hz, 1 H), 4.04 (m, 2 H), 4.14 (dd, *J* = 12.8, 19.2 Hz, 2 H), 4.33 (dd, *J* = 4.0, 7.2 Hz, 1 H), 4.33 (dd, *J* = 3.4, 7.2 Hz, 1 H), 4.53 (d, *J* = 10.8 Hz, 1 H), 5.10 (dd, *J* = 3.4, 7.2 Hz, 1 H), 7.31-7.40 (m, 5 H); ¹³C nmr (100.6 MHz, CDCl₃): δ 25.0, 26.5, 61.2, 64.4, 67.1, 70.5, 70.6, 73.6, 81.0, 110.2, 128.0, 128.6, 129.2, 135.7; ir (KBr): 3073, 2986, 1499, 1457, 1361, 1267, 1225, 1154, 1051, 830, 782 cm⁻¹; hrms (ESI): *m/z* C₁₆H₂₂NO₆S (M+H)⁺. Calcd: 356.1167. Found: 356.1169. *Anal.* Calcd. for C₁₆H₂₁NO₆S: C, 54.07; H, 5.96; N, 3.94. Found: C, 53.96; H, 6.06; N, 3.86.

(3S,3aS,6aS)-2-Benzyl-3-[(4S)-(2,2-dimethyl-1,3-dioxolan-4-yl)]-4,5-oxathiaain-4,4-dioxide[3,4-d]isoxazolidine (8a). White solid; mp 120-122 °C; [α]_D²¹ +13.2° (c 1.6, CHCl₃); ¹H nmr (270 MHz, CDCl₃): δ 1.33 (s, 3 H), 1.50 (s, 3 H), 3.65 (dd, *J* = 2.7, 10.8 Hz, 1 H), 3.98 (dd, *J* = 5.4, 18.9 Hz, 2 H), 4.02 (dd, *J* = 5.4, 16.2 Hz, 1 H), 4.04 (d, *J* = 8.1 Hz, 1 H), 4.17 (ddd, *J* = 2.7, 5.4, 8.1 Hz, 1H), 4.29 (dd, *J* = 5.4, 10.8 Hz, 1 H), 4.33 (dd,

$J = 5.4, 10.8$ Hz, 1 H), 4.44 (d, $J = 10.8$ Hz, 1 H), 4.95 (dd, $J = 2.7, 5.4$ Hz, 1 H), 7.32-7.36 (m, 5 H); ^{13}C nmr (67.8 MHz, CDCl_3): δ 24.6, 26.2, 61.3, 64.9, 65.7, 68.8, 70.9, 74.2, 79.9, 110.3, 127.6, 128.4, 128.6, 136.0; ir (KBr): 3074, 2981, 1492, 1454, 1225, 1150, 1048, 821, 731 cm^{-1} ; ms (FAB): m/z 356 ($\text{M}+\text{H}^+$); hrms (ESI): m/z $\text{C}_{16}\text{H}_{22}\text{NO}_6\text{S}$ ($\text{M}+\text{H}^+$). Calcd: 356.1167. Found: 356.1164.

(3R,3aR,6aR)-2-Benzyl-3-(1-deoxy-2,3:4,5-di-O-isopropylidene-D-mannito-1-yl)-4,5-oxathiaian-4,4-dioxide[3,4-d]-isoxazolidine (7b). Thick oil; $[\alpha]_{\text{D}}^{21} +14.7^\circ$ (c 1.0, CHCl_3); ^1H nmr (270 MHz, CDCl_3): δ 1.35 (s, 6 H), 1.44 (s, 6 H), 3.76 (t, $J = 7.6$ Hz, 1 H), 3.87 (dd, $J = 2.2, 5.7$ Hz, 1 H), 3.92-4.08 (m, 4 H), 4.16 (q, $J = 5.7$ Hz, 1 H), 4.26 (d, $J = 13.8$ Hz, 1 H), 4.37 (dd, $J = 3.3, 11.1$ Hz, 1 H), 4.43 (d, $J = 4.3$ Hz, 1 H), 4.45 (d, $J = 10.8$ Hz, 1 H), 4.98 (dd, $J = 3.0, 6.8$ Hz, 1 H), 7.31-7.38 (m, 5 H); ^{13}C nmr (67.8 MHz, CDCl_3): δ 25.3, 26.4, 26.9, 27.0, 61.3, 63.5, 67.9, 69.5, 69.7, 77.1, 78.1, 78.8, 80.3, 110.0, 110.3, 127.7, 128.3, 129.0, 135.9; ir (KBr): 2928, 2860, 2363, 1462, 1379, 1213, 1167, 1084, 851, 711 cm^{-1} ; ms (FAB): m/z 456 ($\text{M}+\text{H}^+$); hrms (ESI): m/z $\text{C}_{21}\text{H}_{29}\text{NO}_8\text{NaS}$ ($\text{M}+\text{Na}^+$). Calcd: 478.1512. Found: 478.1516.

(3S,3aS,6aS)-2-Benzyl-3-(1-deoxy-2,3:4,5-di-O-isopropylidene-D-mannito-1-yl)-4,5-oxathiaian-4,4-dioxide[3,4-d]-isoxazolidine (8b). Thick oil; $[\alpha]_{\text{D}}^{21} -38.7^\circ$ (c 1.0, CHCl_3); ^1H nmr (270 MHz, CDCl_3): δ 1.26 (s, 3 H), 1.38 (s, 3 H), 1.40 (s, 3 H), 1.44 (s, 3 H), 3.58 (dd, $J = 5.9, 7.8$ Hz, 1 H), 3.83-3.93 (m, 2 H), 3.98-4.11 (m, 2 H), 4.18-4.31 (m, 2 H), 4.28 (dd, $J = 2.4, 8.4$ Hz, 1 H), 4.39 (d, $J = 4.9$ Hz, 1 H), 4.41 (d, $J = 6.5$ Hz, 1 H), 4.65 (d, $J = 14.3$ Hz, 1 H), 4.94 (dd, $J = 3.0, 6.8$ Hz, 1 H), 7.27-7.37 (m, 5 H); ^{13}C nmr (67.8 MHz, CDCl_3): δ 25.6, 26.0, 26.7, 27.1, 61.5, 64.8, 68.3, 68.9, 71.4, 77.2, 79.7, 79.8, 81.8, 110.4, 110.5, 127.2, 128.1, 128.5, 137.2; ir (KBr): 2933, 2860, 2368, 1742, 1457, 1384, 1224, 1167, 1073, 856, 700 cm^{-1} ; hrms (ESI): m/z $\text{C}_{21}\text{H}_{29}\text{NO}_8\text{NaS}$ ($\text{M}+\text{Na}^+$). Calcd: 478.1511. Found: 478.1508; Anal. Calcd. for $\text{C}_{21}\text{H}_{29}\text{NO}_8\text{S}$: C, 55.37; H, 6.42; N, 3.07. Found: C, 55.29; H, 6.37; N, 3.12.

(3R,3aR,6aR)-3-[(S)-2-(Benzoxy)ethyl]-2-benzyl-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (7c). Thick oil; $[\alpha]_{\text{D}}^{21} -25.6^\circ$ (c 1.3, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 1.19 (d, $J = 6.8$ Hz, 3 H), 3.63 (m, 1 H), 3.74 (dd, $J = 5.2, 6.8$ Hz, 1 H), 3.99 (dd, $J = 6.4, 12.0$ Hz, 1 H), 4.03 (d, $J = 13.6$ Hz, 1 H), 4.21 (d, $J = 14.0$ Hz, 1 H), 4.30 (dd, $J = 3.2, 11.2$ Hz, 1 H), 4.41 (d, $J = 10.8$ Hz, 1 H), 4.55 (q, $J = 12.0$ Hz, 2 H), 4.90 (dd, $J = 3.2, 6.4$ Hz, 1 H), 7.24-7.36 (m, 10 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 15.7, 61.8, 65.2, 69.1, 70.9, 71.6, 73.6, 80.1, 127.6, 127.7, 127.8, 128.3, 128.4, 128.9, 136.4, 137.6; ir (KBr): 3041, 2881, 2358, 1964, 1731, 1612, 1498, 1457, 861 cm^{-1} ; hrms (ESI): m/z $\text{C}_{20}\text{H}_{24}\text{NO}_5\text{S}$ ($\text{M}+\text{H}^+$). Calcd: 390.1374. Found: 390.1389; Anal. Calcd. for $\text{C}_{20}\text{H}_{23}\text{NO}_5\text{S}$: C, 61.68; H, 5.95; N, 3.60. Found: C, 61.58; H, 6.03; N, 3.54.

(3S,3aS,6aS)-3-[(S)-2-(Benzoxy)ethyl]-2-benzyl-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (8c). Thick oil; $[\alpha]_{\text{D}}^{21} +18.4^\circ$ (c 1.35, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 1.27 (d, $J = 6.0$ Hz, 3 H), 3.44 (dd, $J = 2.4, 5.6$ Hz, 1 H), 3.65 (m, 1 H), 3.93 (d, $J = 13.6$ Hz, 1 H), 4.15 (d, $J = 14.0$ Hz, 1 H), 4.27 (dd, $J = 3.2, 11.2$ Hz, 1 H), 4.32 (dd, $J = 5.6, 7.2$ Hz, 1 H), 4.39 (d, $J = 11.6$ Hz, 1 H), 4.65 (d, $J = 2.0$ Hz, 2 H), 4.88 (dd, $J = 3.2, 6.8$ Hz, 1 H), 7.21-7.41 (m, 10 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 18.2, 60.9, 63.7, 69.1, 71.4, 71.8, 74.7, 80.0, 127.5, 127.6, 128.2, 128.4, 128.5, 128.6, 136.5, 137.9; ir (KBr): 3042, 2881, 2368, 1721, 1498, 1457, 13579, 1156, 861 cm^{-1} ; hrms (ESI): m/z $\text{C}_{20}\text{H}_{24}\text{NO}_5\text{S}$ ($\text{M}+\text{H}^+$). Calcd: 390.1374. Found: 390.1385.

(3R,3aR,6aR)-3-[(S)-2-(benzoxy)benzyl]-2-benzyl-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (7d). White solid; mp 146-148 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{21} +9.3^\circ$ (c 1.5, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 3.79 (dd, $J = 5.6, 6.8$ Hz, 1 H), 3.93 (dd, $J = 4.8, 6.8$ Hz, 1 H), 3.99 (d, $J = 14.0, 1$ H), 4.18 (dd, $J = 3.6, 11.2$ Hz, 1 H), 4.32 (q, $J = 11.2$ Hz, 2 H), 4.42 (d, $J = 14.4$ Hz, 1 H), 4.55 (d, $J = 12.0$ Hz, 1 H), 4.57 (d, $J = 6.8$ Hz, 1 H), 4.72 (dd, $J = 2.8, 6.4$ Hz, 1 H), 7.27-7.46 (m, 15 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 62.3, 65.9, 68.6, 70.7, 72.9, 79.7, 81.2, 127.5, 127.9, 128.0, 128.1, 128.3, 128.5, 128.8, 129.0, 129.2, 136.7, 137.1, 137.2; ir (KBr): 3037, 2881, 1457, 1374, 1205, 945, 770 cm^{-1} ; ms (FAB): m/z 452 ($\text{M}+\text{H}^+$); hrms (ESI): m/z $\text{C}_{25}\text{H}_{26}\text{NO}_5\text{S}$ ($\text{M}+\text{H}^+$). Calcd: 452.1531. Found: 452.1547.

3S,3aS,6aS)-3-[(S)-2-(Benzoxy)benzyl]-2-benzyl-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (8d). White solid; mp 132-134 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{21} +24.2^\circ$ (c 1.5, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 3.60 (d, $J = 14.0$ Hz, 1 H), 3.75 (dd, $J = 5.2, 6.0$ Hz, 1 H), 3.79 (d, $J = 13.6$ Hz, 1 H), 4.29 (d, $J = 12.0$ Hz, 1 H), 4.30 (dd, $J = 5.6, 11.2$ Hz, 1 H), 4.31 (dd, $J = 3.6, 7.6$ Hz, 1 H), 4.33 (d, $J = 6.0$ Hz, 1 H), 4.41 (d, $J = 11.2$ Hz, 1 H), 4.60 (d, $J = 12.0$ Hz, 1 H), 4.88 (dd, $J = 3.2, 6.8$ Hz, 1 H), 7.15-7.44 (m, 10 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 61.6, 65.9, 68.9, 70.5, 74.4, 79.4, 79.7, 127.5, 127.6, 128.0, 128.3, 128.5, 128.8, 129.0, 129.1, 136.5, 137.3, 137.4; ir (KBr): 3037, 2850, 1503, 1349, 1159, 1019, 699 cm^{-1} ; hrms (ESI): m/z $\text{C}_{25}\text{H}_{26}\text{NO}_5\text{S}$ ($\text{M}+\text{H}^+$). Calcd: 452.1531. Found: 452.1546. Anal. Calcd. for $\text{C}_{25}\text{H}_{25}\text{NO}_5\text{S}$: C, 66.50; H, 5.58; N, 3.10. Found: C, 66.40; H, 5.53; N, 3.02.

(3R,3aR,6aR)-2-Benzyl-3-[(1R)-myrtenyl]-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (7e). White solid; mp 213-215 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{21} -80.7^\circ$ (c 1.0, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 0.90 (s, 3 H), 1.12 (d, $J = 8.4$ Hz, 1 H), 1.35 (s, 3 H), 2.19 (m, 1 H), 2.34-2.42 (m, 3 H), 2.49 (m, 1 H), 3.68 (d, $J = 14.4$ Hz, 1 H), 3.71 (d, $J = 10.0$ Hz, 1 H), 3.85 (t, $J = 7.2$ Hz, 1 H), 4.09 (d, $J = 14.4$ Hz, 1 H), 4.72 (dd, $J = 3.6, 11.3$ Hz, 1 H), 4.38 (d, $J = 6.8$ Hz, 1 H), 4.91 (dd, $J = 2.8, 6.8$ Hz, 1 H), 5.88 (m, 1 H), 7.30 (m, 5 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 21.8, 26.0, 31.5, 31.8, 38.0, 40.5, 41.9, 59.6, 65.4, 68.9, 74.6, 79.5, 126.6, 127.5, 128.4, 128.5, 137.0, 140.8; ir (KBr): 2959, 2928, 1742, 1463, 1379, 1163, 954, 866 cm^{-1} ; hrms (ESI): m/z $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{NaS}$ ($\text{M}+\text{Na}^+$). Calcd: 398.1402. Found: 398.1421; Anal. Calcd. for $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{S}$: C, 63.98; H, 6.71; N, 3.73. Found: C, 63.90; H, 6.68; N, 3.68.

(3S,3aS,6aS)-2-Benzyl-3-[(1R)-myrtenyl]-4,5-oxathiaian-4,4-dioxide[3,4-d]isoxazolidine (8e). White solid; mp 153-155 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{21} +12.2^\circ$ (c 1.3, CHCl_3); ^1H nmr (400 MHz, CDCl_3): δ 0.92 (s, 3 H), 1.11 (d, $J = 8.4$ Hz, 1 H), 1.34 (s, 3 H), 2.16 (m, 1 H), 2.33-2.41 (m, 3 H), 2.50 (m, 1 H), 3.70 (d, $J = 2.8$ Hz, 1 H), 3.72 (dd, $J = 2.8, 14.4$ Hz, 1 H), 3.73 (d, $J = 4.8$ Hz, 1 H), 4.05 (d, $J = 14.4$ Hz, 1 H), 4.27 (dd, $J = 3.6, 11.2$ Hz, 1 H), 4.37 (d, $J = 10.8$ Hz, 1 H), 4.92 (dd, $J = 3.6, 6.8$ Hz, 1 H), 5.88 (m, 1 H), 7.27-7.35 (m, 5 H); ^{13}C nmr (100.6 MHz, CDCl_3): δ 21.2, 25.9, 31.6, 37.9, 40.4, 41.4, 59.5, 64.5, 69.0, 75.2, 79.4, 127.3, 127.6, 128.4, 128.6, 237.0, 140.6; ir (KBr): 2954, 2835, 1368, 1213, 1156, 944, 877 cm^{-1} ; ms (FAB): m/z 376 ($\text{M}+\text{H}^+$); hrms (ESI): m/z $\text{C}_{20}\text{H}_{25}\text{NO}_4\text{NaS}$ ($\text{M}+\text{Na}^+$). Calcd: 398.1402. Found: 398.1407.

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