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# Intramolecular Cycloaddition of Nitrones and Nitrile Oxides with Sulfur-Substituted Dienes and Its Synthetic Applications

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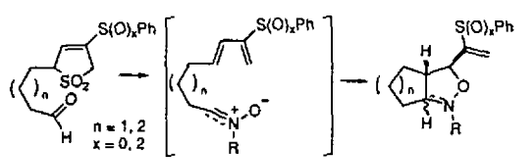
A series of sulfur-substituted dienyl nitrones and oximes were conveniently prepared from the 3-sulfolene precursors. Regiospecific intramolecular 1,3-dipolar cycloadditions of nitrones and nitrile oxides with sulfur-substituted dienes have been efficiently carried out from the suitable 3-sulfolene precursors. The stereochemistry of the cycloaddition of nitrones depends on the structure of the substituent (sulfide or sulfone) on the diene as well as on the chain length connecting the diene and nitrone. The fused bicyclic products obtained from these reactions have been converted to some interesting heterocyclic compounds which have the useful structure of vinyl sulfide or sulfone.

## INTRODUCTION

The 1,3-dipolar cycloaddition reaction of nitrones and nitrile oxides with alkenes is a powerful synthetic tool for the preparation of 1,3-amino alcohols,[1] and has attracted considerable attention as a convenient method for the rapid construction of widely varied classes of natural products.[2] In recent years, both intramolecular nitrone-olefin and nitrile oxide-olefin cycloaddition have been of considerable synthetic interest because the resulting fused bicyclic isoxazolidine and isoxazoline moieties could undergo many interesting transformations.[3] A significant body of information regarding the regiochemistry of intermolecular cycloaddition has been collected since the pioneering work of Huisgen.[4] Most of this data has been interpreted by considering frontier molecular orbital properties of the nitrone or nitrile oxide and the alkene reaction partners.[5] The regio- and stereochemistry of the intramolecular version of this reaction, however, is complicated by a complex interplay of factors such as alkene polarity, ring strain, and other nonbonded interactions.[6]

Although the intramolecular cycloaddition of nitrones and nitrile oxides with alkenes has been extensively studied, the corresponding reaction of nitrones and nitrile oxides with conjugated dienes has not been reported.[7] As an extension of our interest in the synthesis and reactions of sulfur-substituted dienes via 3-sulfolenes,[8] we herein report the first synthesis of sulfur-substituted dienes bearing the nitrone or nitrile oxide group from the corresponding 3-sulfolenes (eq. 1). The regio- and stereochemistry of the intramolecular 1,3-dipolar cycloaddition as well as some of the synthetic applications are studied.[9]




(1)

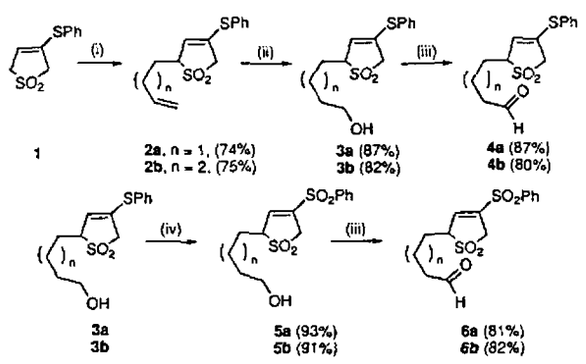
## RESULTS AND DISCUSSION

The sulfolene aldehydes **4** and **6** required for the conversion to the nitrone or nitrile oxide moiety were prepared by the reaction sequence as outlined in Scheme I. Treatment of 3-phenylthio-3-sulfolene (**1**)[10] with BuLi (1 equiv) in THF at -105 °C in the presence of hexamethylphosphoric amide (HMPA, 4 equiv) followed by the addition of 4-iodo-1-butene or 5-iodo-1-pentene (2 equiv) gave the alkylated products **2** in good yield. The alkylation occurred regiospecifically at the C-5 position of the sulfolene as expected.[8a] Hydroboration of **2** with 9-BBN in THF, followed by the oxidation with alkaline aqueous hydrogen peroxide, produced the terminal alcohols **3**, which were further oxidized to the corresponding aldehydes **4**. The sulfonyl aldehydes **6** were also obtained in excellent yield by treatment of **3** with MCPBA (2.5 equiv) to give the sulfonyl alcohols **5**, which were then oxidized with PCC (2 equiv). Attempted oxidation of **4** with MCPBA to **6** gave complex results.

Once the sulfolene aldehydes were in hand, the targeted nitrones were readily prepared by condensation of the aldehyde group with an alkyl (methyl, *t*-butyl or benzyl) hydroxylamine hydrochloride salt (1.1 equiv) and NaOMe (1.1 equiv) in toluene. After the mixture was stirred at room temperature for 10 min, the nitrones formed were then heated to first undergo the cheletropic removal of $SO_2$, and

Dedicated to Professor Hsien-Ju Tien on the occasion of his 65th birthday.

**Scheme I**




**Reagents :** (i) BuLi, HMPA, THF, -105 °C; $CH_2$=$CH(CH_2)_nCH_2I$, -90 °C to -50 °C; *(ii)* 9-BBN, THF, 0 °C; NaOH, $H_2O_2$, 0 °C; (iii) PCC, $CH_2Cl_2$, rt; (iv) MCPBA, $CH_2Cl_2$, 0 °C.

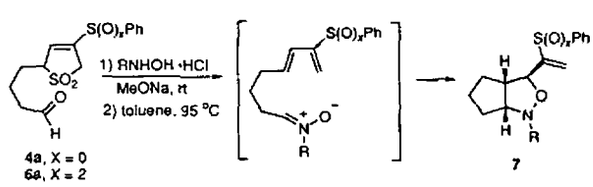
then the intramolecular 1,3-dipolar cycloaddition to give the isoxazolidine products (Tables 1 and 2).

Whether the substituent on the diene was the phenylthio or sulfonyl group, the 3-sulfolenes **4a** and **6a** proceeded through the 5-dienyl nitrones to give only the *cis*-fused bicyclic isoxazolidines **7** (Table 1). The formation of only the *cis*-fused products is expected as from the studies by LeBel.[6a] Apparently, the more strained *trans* isomer would proceed through a transition state of much higher activation energy.[5] However, in the case of 6-dienyl nitrones, the phenylthio-substituted 3-sulfolene **4b** gave a mixture of *cis*- and *trans*-fused products **8** and **9**, with the *cis* isomer slightly dominating. It is very interesting to note that the sulfone-substituted analog **6b** gave only the *cis*-fused products **8** (Table 2). It should also be mentioned that neither the adducts derived from the reaction of the nitrone group with the terminal olefin nor the bridged cyclization products were detected in any of the above cases.

Since the 2,4-disubstituted 3-sulfolenes open exclusively to give the dienes with *E*-configuration,[8a,8q] and the 1,3-dipolar cycloaddition reactions retain the stereochemistry of the alkene,[6b] the H-3/H-3a *anti* products were expected. The stereochemistry of the cycloadducts **7-9** was established by $^1$H NMR decoupling experiments and NOE studies. Analysis of the $^1$H NMR signals for the proton (H-3) adjacent to the isoxazolidine ring oxygen of compounds **7-9** allows us to assign their stereochemistry. In **9** this proton exhibits a large vicinal coupling constant (≥ 7 Hz) with the bridgehead proton (H-3a). In **8** the relatively small value of this coupling constant (≤ 5 Hz) as compared with that of **9** suggests that compounds **8** have the *cis* ring fusion and **9** the *trans* ring fusion.[6a,c] In **7** the coupling constant (6.6-8.4 Hz) for proton H-3 with the bridgehead proton (H-3a) corresponds to an *anti* relationship. In addition, the NOE studies reconfirm these assignments (Fig. 1).

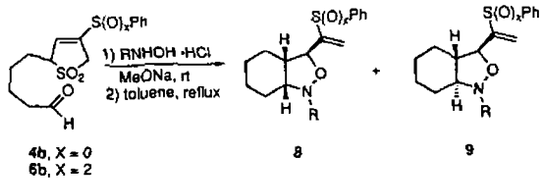
The stereoselectivity of the cycloaddition can be explained by comparing the possible transition states (Fig. 2). Two transition states are most favorable for the cyclization.[6a] The transition state **A** leading to the *cis* ring fusion products **8** requires the six-membered carbocyclic ring to adopt a twist conformation. The other transition state **B** leading to the *trans* products **9** involves only a slightly deformed chair arrangement. However, there are steric interactions between the C-1 hydrogen atom and the C-5

Table 1. Intramolecular Cycloaddition of 5-Dienyl Nitrones




| Compound | R | Product (Yield, %) |
|---|---|---|
| **4a** | $CH_3$ | **7a** (73) |
| **4a** | $CH_2Ph$ | **7b** (61) |
| **4a** | $C(CH_3)_3$ | **7c** (54) |
| **6a** | $CH_3$ | **7d** (65) |
| **6a** | $CH_2Ph$ | **7e** (60) |

Table 2. Intramolecular Cycloaddition of 6-Dienyl Nitrones




| Compound | R | Product (Yield, %) |
|---|---|---|
| **4b** | $CH_3$ | **8a** (38) + **9a** (27) |
| **4b** | $CH_2Ph$ | **8b** (36) + **9b** (18) |
| **6b** | $CH_3$ | **8c** (56) |
| **6b** | $CH_2Ph$ | **8d** (45) |

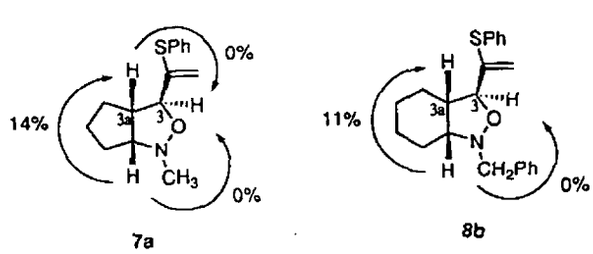
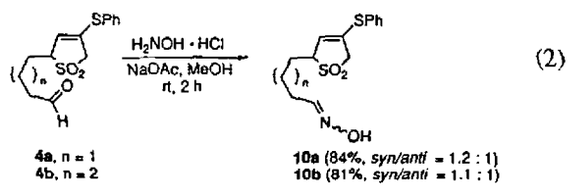



Fig. 1. NOE experiments for **7a** and **8b**.

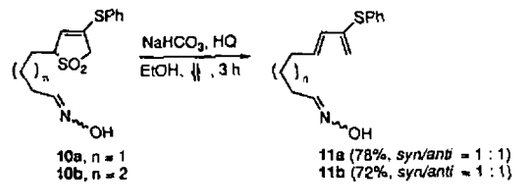
methylene group, as well as between the $R^1$ and $R^2$ groups in the transition state **B**. Thus, the transition state **A** competes more favorably. The isomer ratio for **8a:9a** was *ca.* 1.4:1, which increased to *ca.* 2:1 for **8b:9b** where the substituent $R^1$ is larger. When the phenylthio substituent on the diene is replaced by the larger phenylsulfonyl group, the transition state **B** for the formation of the *trans* product **9** involves greater steric repulsion between the phenylsulfonyl group and the substituent on the nitrogen. Thus only the *cis* products **8c** and **8d** were obtained.

For the intramolecular nitrile oxide-diene cycloaddition, the nitrile oxide moiety will be generated from the aldoxime by oxidation.[11] The aldehydes **4** were treated with hydroxylamine hydrochloride (1.5 equiv) in the presence of sodium acetate (1.5 equiv) to produce the aldoximes **10** in good yield (eq. 2). A mixture of *syn/anti* isomers was obtained, and these products were characterized by their $^1$H NMR spectra featuring the aldoxime =CH signal at $\delta$ 7.21-7.45 (*syn* to -OH) and 6.16-6.72 (*anti* to -OH).[12]



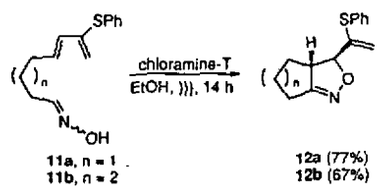
(2)

Since the attempted tandem cycloaddition of the *in-situ* generated nitrile oxide from the oxime with the diene moiety generated by thermal desulfonylation from compounds **10** failed, we then isolated the dienyl oximes **11** first. When aldoximes **10** were refluxed in EtOH in the presence of $NaHCO_3$,[13] the desired dienyl oximes **11** could be obtained (eq. 3). $^1$H NMR decoupling experiments for **11** showed that the coupling constant between the two internal vinyl protons of the diene is 15.4 Hz, which indicates that dienes **11** have the *E*-configuration.



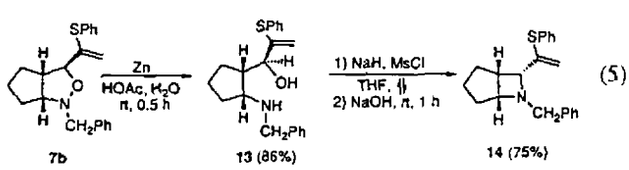
(3)

Attempted *in situ* generation of nitrile oxides from oximes **11** and subsequent cycloaddition gave only complex results when NCS or NaOCl was used as the oxidant. However, when Chloramine-T was used,[14] the cycloaddition products **12** could be obtained in low yield. The yield, however, was improved by carrying out the reaction in an ultrasound cleaning bath (eq. 4).[15] The cycloaddition reaction retains the stereochemistry of the alkene,[6e,16] thus the H-3/H-3a *anti* products **12** were obtained from the (*E*)-dienyl oximes **11**.



(4)

We have also studied some synthetic applications of these products. Reductive cleavage of the N-O bond in **7b** with Zn (10 equiv) in 50% aqueous HOAc[17] produced the amino alcohol **13**, not affecting the configuration of the stereocenters (eq. 5). After treatment of **13** with NaH (1.1 equiv) and MsCl (1.1 equiv) followed by the reaction with aqueous NaOH (3 equiv), the bicyclic azetidine product **14** was obtained in good yield. The stereochemistry of the product **14** was assigned by the NOE studies (Fig. 3).



(5)

On the other hand, the reaction of **7e** with Zn (3 equiv) in 50% aqueous HOAc produced directly the bicyclic piperidine product **15** as a diastereomeric mixture (1.3:1). This indicates that the vinyl sulfone is a good Michael acceptor, which could react with the free amine generated from cleavage of the N-O bond. After heating in 50% aque-

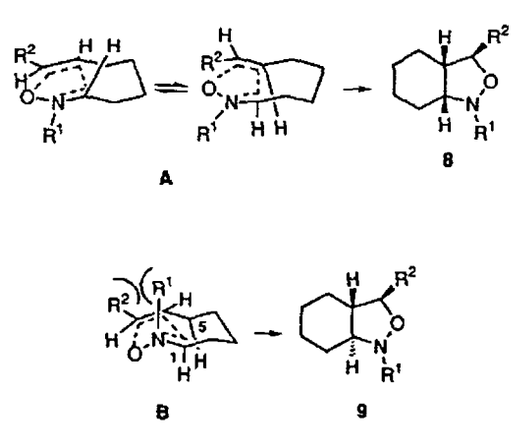
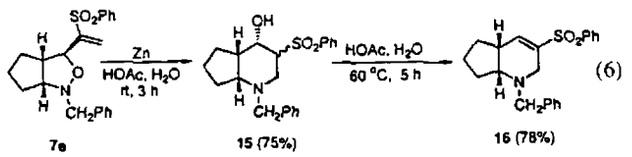



Fig. 2. Transition states for intramolecular cycloaddition of **4b** and **6b**.

ous HOAc at 60 °C for 5 h, the dehydration product **16** was obtained in good yield (eq. 6).

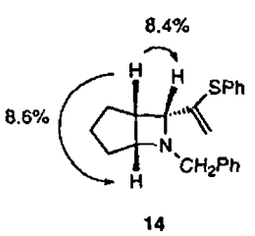



(6)

In summary, regiospecific intramolecular cycloadditions of nitrones and nitrile oxides with sulfur-substituted dienes have been efficiently carried out from the suitable 3-sulfolene precursors. The cycloaddition of nitrile oxides gave only one diastereomer. The stereochemical outcome of the cycloaddition of nitrones is influenced by the structure of the substituent (sulfide or sulfone) on the diene as well as on the chain length connecting the diene and nitrone. The fused bicyclic products obtained from these reactions have been converted to some interesting heterocyclic compounds, and the functional group of vinyl sulfide or sulfone should be useful for further transformations.[18]

## EXPERIMENTAL SECTION

Infrared spectra were recorded with a FT-IR spectrometer Analect RFX-65. $^1$H and $^{13}$C NMR spectra were measured for samples in $CDCl_3$ with a FT-NMR spectrometer Bruker AC-300 at 300 and 75 MHz, respectively, with tetramethylsilane as the internal standard. Mass spectra were recorded with a spectrometer JEOL JMS-D-100. High resolution mass spectra were measured with a mass spectrometer JEOL TMS-HX 110. Melting points were measured with an apparatus Mel-Temp and are uncorrected. The silica gel used for flash column chromatography was made by Merck (60 H). The sealed tube used for thermolysis was made by Ace Glass (catalog no. 8648-23). Compound **2b** was prepared by a procedure in the literature.[6a] Zn powder (325 mesh) was activated before the reaction.[19] All reagents were of reagent grade and were purified prior to use.[20]




14

Fig. 3. NOE experiments for **14**.

**2-(3-Butenyl)-4-phenylthio-3-sulfolene (2a)**

To a solution of 3-(phenylthio)-3-sulfolene (**1**) (5.20 g, 23 mmol) in THF (90 mL) and HMPA (17.4 mL, 92 mmol) at -105 °C was added dropwise a solution of BuLi in hexane (19.1 mL, 1.2 M, 23 mmol). The solution was slowly warmed to -90 °C, and 4-iodo-1-butene (16.7 g, 92 mmol) was then added in one portion. The reaction mixture was poured into a saturated ammonium chloride solution (80 mL) at -50 °C. The solvent was removed under vacuum, and the residue was extracted with $CH_2Cl_2$ (50 mL × 3). The organic solution was dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:6) as eluent to give **2a** (4.8 g, 74% yield); IR (neat) 3074, 2976, 2927, 2852, 1440, 1313 ($SO_2$), 1219, 1128 ($SO_2$), 916, 749, 692 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.63-1.78 (1H, m), 2.01-2.13 (1H, m), 2.20-2.28 (2H, m), 3.64-3.78 (2H, m), 3.82-3.87 (1H, m), 5.02-5.11 (2H, m), 5.69-5.83 (2H, m), 7.36-7.47 (5H, m); $^{13}$C NMR ($CDCl_3$) δ 27.9, 30.7, 57.3, 66.1, 116.4, 125.3, 129.0, 129.6, 131.4, 133.1 (×2), 136.2; MS (rel intensity) *m/z* 280 ($M^+$, 2), 216 (100), 109 (66), 91 (80); exact mass calcd for $C_{14}H_{16}O_2S_2$ *m/z* 280.0593, found 280.0597.

**2-(4-Hydroxybutyl)-4-phenylthio-3-sulfolene (3a)**

To a solution of **2a** (3.60 g, 12.9 mmol) in dried THF (5 mL) at 0 °C was added 9-BBN (27 mL, 13.5 mmol; 0.5 M in THF). The solution was then stirred at room temperature for 3 h. Residual hydride was decomposed by adding water (5 mL) followed by adding 3 N NaOH (4.7 mL) and 30% $H_2O_2$ (4.7 mL) at 0 °C. The mixture was warmed to room temperature, and stirred for 1 h. The solvent was removed under vacuum, and the residue was extracted with $CH_2Cl_2$ (20 mL × 3). The organic solution was dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:1) as eluent to give **3a** (3.14 g, 87% yield); IR (neat) 3450 (OH), 3080, 2950, 2880, 1440, 1311, 1218, 1130, 750, 701 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 1.51-1.71 (5H, m), 1.91-1.99 (2H, m), 3.61-3.81 (5H, m), 5.72-5.74 (1H, m), 7.36-7.43 (5H, m); $^{13}$C NMR ($CDCl_3$) δ 23.2, 28.6, 32.1, 57.5, 62.1, 67.2, 125.5, 129.1, 129.6, 129.7, 131.5, 133.2; MS (rel intensity) *m/z* 298 ($M^+$, 1), 234 (11), 110 (100), 109 (32), 64 (39); exact mass calcd for $C_{14}H_{18}O_3S_2$ *m/z* 298.0698, found 298.0693.

**2-(5-Hydroxypentyl)-4-phenylthio-3-sulfolene (3b)**

To a solution of **2b** (4.50 g, 15.31 mmol) in dried THF (5 mL) at 0 °C was added 9-BBN (46 mL, 22.96 mmol; 0.5 M in THF). The mixture was then stirred at room temperature for 3 h. Residual hydride was decomposed by adding water (5 mL) followed by adding 3 N NaOH (5.2 mL) and

30% $H_2O_2$ (5.2 mL) at 0 °C. The workup procedure was the same as that for **3a** to give **3b** (3.92 g, 82% yield); IR (neat) 3416 (OH), 2934, 2860, 1476, 1440, 1309, 1220, 1127, 749, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.33-1.63 (7H, m), 1.87-1.92 (1H, m), 2.44 (1H, br s, OH), 3.54-3.80 (5H, m), 5.71-5.73 (1H, m), 7.31-7.40 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 25.3, 26.4, 28.5, 32.0, 57.3, 62.2, 67.0, 125.7, 128.8, 129.5 (×2), 131.1, 132.9; MS (rel intensity) *m/z* 312 ($M^+$, 3), 248 (21), 110 (100), 109 (36), 77 (25), 64 (44); exact mass calcd for $C_{15}H_{20}O_3S_2$ *m/z* 312.0855, found 312.0862.

**2-(4-Oxobutyl)-4-phenylthio-3-sulfolene (4a)**

To a stirred solution of PCC (1.20 g, 5.4 mmol) in dried $CH_2Cl_2$ (50 mL) was added a solution of **3a** (806 mg, 2.71 mmol) in $CH_2Cl_2$ (10 mL) at room temperature under nitrogen. After stirring for 2 h, the reaction mixture was diluted with dried ether (70 mL). The ether layer was filtered through Celite, dried ($MgSO_4$), and concentrated by a rotary evaporator. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:3) as eluent to give **4a** (694 mg, 87% yield); IR (neat) 3070, 2950, 1715 (C=O), 1440, 1310, 1220, 1130, 750, 698 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.68-1.94 (4H, m), 2.50-2.55 (2H, t, $J$ = 6.6 Hz), 3.65-3.81 (3H, m), 5.69-5.70 (1H, m), 7.37-7.45 (5H, m), 9.76 (1H, br s, CHO); $^{13}C$ NMR ($CDCl_3$) δ 19.4, 28.4, 43.2, 57.6, 66.9, 124.6, 129.2, 129.4, 129.8, 132.1, 133.4, 201.1; MS (rel intensity) *m/z* 296 ($M^+$, 2), 232 (14), 218 (51), 110 (100), 109 (70), 77 (49), 64 (48); exact mass calcd for $C_{14}H_{16}O_3S_2$ *m/z* 296.0542, found 296.0542.

**2-(5-Oxopentyl)-4-phenylthio-3-sulfolene (4b)**

To a stirred solution of PCC (2.15 g, 9.76 mmol) in dried $CH_2Cl_2$ (25 mL) was added a solution of **3b** (1.52 g, 4.88 mmol) in $CH_2Cl_2$ (5 mL) at room temperature under nitrogen. After stirring for 2 h, the same workup procedure as that for **4a** gave **4b** (1.21 g, 80% yield); IR (neat) 3070, 2934, 1720 (C=O), 1440, 1309, 1221, 1126, 749, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.47-1.73 (5H, m), 1.94-1.97 (1H, m), 2.45-2.50 (2H, m), 3.64-3.81 (3H, m), 5.70-5.72 (1H, m), 7.38-7.45 (5H, m), 9.76 (1H, t, $J$ = 1.4 Hz, CHO); $^{13}C$ NMR ($CDCl_3$) δ 21.7, 26.4, 28.7, 43.4, 57.5, 66.9, 125.1, 125.2, 129.1, 129.7, 131.7, 133.3, 201.7; MS (rel intensity) *m/z* 310 ($M^+$, 1), 246 (68), 228 (64), 137 (47), 110 (59), 109 (55), 91 (60), 77 (59), 64 (100); exact mass calcd for $C_{15}H_{18}O_3S_2$ *m/z* 310.0698, found 310.0705.

**2-(4-Hydroxybutyl)-4-(phenylsulfonyl)-3-sulfolene (5a)**

To a solution of **4a** (3.14 g, 10.54 mmol) in dried $CH_2Cl_2$ (30 mL) in an ice bath was added dropwise a solution of MCPBA (11.37 g, 26.35 mmol) in $CH_2Cl_2$ (10 mL). The mixture was stirred for 1 h, and then washed with 5% $Na_2S_2O_3$, 5% $NaHCO_3$, dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (2:1) as eluent to give **5a** (3.24 g, 93% yield); IR (neat) 3551 (OH), 3063, 2934, 2867, 1447, 1406, 1221, 1156, 1087, 732, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.57-1.61 (4H, m), 1.73-1.80 (1H, m), 1.99-2.07 (2H, m), 3.59-3.63 (2H, m), 3.83-3.84 (2H, m), 3.96-4.01 (1H, m), 6.99-7.01 (1H, m), 7.56-7.61 (2H, m), 7.67-7.73 (1H, m), 7.83-7.86 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 23.2, 27.5, 31.8, 53.6, 61.8, 67.3, 128.1, 129.8, 134.7, 137.1, 137.1, 137.4; MS (rel intensity) *m/z* 330 ($M^+$, 1), 266 (6), 234 (11), 110 (100), 109 (32), 64 (39); exact mass calcd for $C_{14}H_{18}O_3S$ ($M^+$-64) *m/z* 266.0977, found 266.0978.

**2-(5-Hydroxypentyl)-4-(phenylsulfonyl)-3-sulfolene (5b)**

To a solution of **4b** (3.84 g, 12.32 mmol) in dried $CH_2Cl_2$ (60 mL) in an ice bath was added dropwise a solution of MCPBA (13.29 g, 30.79 mmol) in $CH_2Cl_2$ (10 mL). The mixture was stirred for 1 h, and the same workup procedure as that for **5a** gave **5b** (4.17 g, 91% yield); IR (neat) 3552 (OH), 3063, 2934, 2862, 1447, 1320, 1222, 1155, 1030, 735, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.38-1.56 (6H, m), 1.69-1.76 (1H, m), 1.91-2.01 (2H, m), 3.59 (2H, t, $J$ = 6.4 Hz), 3.82-3.83 (2H, m), 3.94-3.98 (1H, m), 6.97-7.00 (1H, m), 7.56-7.61 (2H, m), 7.66-7.72 (1H, m), 7.83-7.86 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 25.3, 26.5, 27.6, 32.0, 53.6, 62.2, 67.2, 128.1, 129.8, 134.6, 137.1, 137.2, 137.5; MS (rel intensity) *m/z* 280 ($M^+$-64, 10), 143 (54), 79 (100), 77 (97), 64 (59); exact mass calcd for $C_{15}H_{20}O_3S$ ($M^+$-64) *m/z* 280.1132, found 280.1129.

**2-(4-Oxobutyl)-4-(phenylsulfonyl)-3-sulfolene (6a)**

To a stirred solution of PCC (4.31 g, 19.61 mmol) in dried $CH_2Cl_2$ (25 mL) was added a solution of **5a** (3.24 g, 9.80 mmol) in $CH_2Cl_2$ (5 mL) at room temperature under nitrogen. After stirring for 2 h, the same workup procedure as that for **4a** gave **6a** (2.61 g, 81% yield); IR (neat) 3064, 2934, 1719 (C=O), 1447, 1320, 1220, 1155, 736, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.74-2.00 (4H, m), 2.51 (2H, t, $J$ = 6.3 Hz), 3.82 (2H, br s), 3.97-4.00 (1H, m), 6.97-6.99 (1H, m), 7.54-7.59 (2H, m), 7.65-7.69 (1H, m), 7.81-7.84 (2H, m), 9.70 (1H, br s, CHO); $^{13}C$ NMR ($CDCl_3$) δ 19.1, 27.0, 42.8, 53.5, 66.9, 128.0, 129.7, 134.6, 136.7, 137.0, 137.5, 200.9; MS (rel intensity) *m/z* 328 ($M^+$, 1), 264 (11), 187 (28), 123 (59), 77 (100); exact mass calcd for $C_{14}H_{16}O_3S$ ($M^+$-64) *m/z* 264.0819, found 264.0815.

**2-(5-Oxopentyl)-4-(phenylsulfonyl)-3-sulfolene (6b)**

To a stirred solution of PCC (0.795 g, 3.58 mmol) in

dried $CH_2Cl_2$ (15 mL) was added a solution of **5b** (0.615 g, 1.788 mmol) in $CH_2Cl_2$ (10 mL) at room temperature under nitrogen. After stirring for 2 h, the same workup procedure as that for **4a** gave **6b** (0.501 g, 82% yield); IR (neat) 3063, 2934, 2865, 1720 (C=O), 1447, 1320, 1155, 1130, 735, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.53-1.80 (5H, m), 1.97-2.04 (1H, m), 2.45-2.50 (2H, m), 3.83-3.84 (2H, m), 3.94-3.99 (1H, m), 6.96-6.98 (1H, m), 7.57-7.62 (2H, m), 7.68-7.73 (1H, m), 7.84-7.88 (2H, m), 9.75 (1H, t, *J* = 1.2 Hz, CHO); $^{13}C$ NMR ($CDCl_3$) δ 21.4, 26.3, 27.6, 43.2, 53.7, 67.1, 128.2, 129.8, 134.7, 136.8, 137.3, 137.8, 201.5; MS (rel intensity) *m/z* 342 ($M^+$, 1), 278 (25), 246 (68), 228 (64), 137 (47), 110 (59), 109 (55), 91 (60), 77 (59), 64 (100); exact mass calcd for $C_{15}H_{18}O_3S$ ($M^+$-64) *m/z* 278.0977, found 278.0980.

**(3*S**,3a*S**,6a*R**)-1-Methyl-3-[1-(phenylthio)ethenyl]-hexahydro-1*H*-cyclopent[*c*]isoxazole (7a)**

A mixture of **4a** (0.14 g, 0.47 mmol), *N*-methylhydroxylamine hydrochloride (45 mg, 0.52 mmol) and NaOMe (28 mg, 0.52 mmol) in toluene (30 mL) was stirred at rt for 10 min and was then heated at 95 °C for 5 h. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography using ethyl acetate/hexane (1:10) as eluent to give **7a** (90 mg, 73% yield); IR (neat) 3056, 2965, 2870, 1477, 1068, 1024, 877, 751, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.43-1.53 (1H, m), 1.58-1.83 (5H, m), 2.74 (3H, s, $CH_3$), 2.97-3.05 (1H, m, H-3a), 3.11-3.15 (1H, m, H-6a), 4.12 (1H, d, *J* = 7.1 Hz, H-3), 4.83 (1H, s, C=$CH_2$), 5.48 (1H, d, *J* = 0.5 Hz, C=$CH_2$), 7.27-7.49 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.6, 30.5, 30.9, 44.2, 55.1, 75.6, 86.3, 113.3, 128.0, 129.2, 132.5, 133.4, 144.6; MS (rel intensity) *m/z* 261 ($M^+$, 34), 152 (100), 124 (50), 110 (57), 91 (70), 73 (98); exact mass calcd for $C_{15}H_{19}NOS$ *m/z* 261.1189, found 261.1189.

**(3*S**,3a*S**,6a*R**)-1-(Phenylmethyl)-3-[1-(phenylthio)-ethenyl]-hexahydro-1*H*-cyclopent[*c*]isoxazole (7b)**

A mixture of **4a** (0.6 g, 2.03 mmol), *N*-benzylhydroxylamine hydrochloride (0.37 g, 2.23 mmol) and NaOMe (0.122 g, 2.23 mmol) in toluene (50 mL) was stirred at rt for 10 min and was then heated at 95 °C for 8 h. The same workup procedure as that for **7a** gave **7b** (0.418 g, 61% yield); IR (neat) 3057, 2974, 3053, 2974, 2927, 2876, 1478, 1440, 1230, 1063, 961, 741, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.36-1.86 (6H, m), 3.02-3.07 (1H, m, H-3a), 3.39-3.43 (1H, m, H-6a), 3.98 (1H, d, *J* = 13.4 Hz, $CH_2Ph$), 4.14 (1H, d, *J* = 13.4 Hz, $CH_2Ph$), 4.19 (1H, d, *J* = 7.2 Hz, H-3), 4.92 (1H, s, C=$CH_2$), 5.55 (1H, s, C=$CH_2$), 7.29-7.53 (10H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.6, 30.5, 31.3, 54.8, 61.8, 73.2, 86.1, 113.9, 127.2, 127.8, 128.2, 129.2, 129.3, 132.8, 133.2, 137.4, 144.6; MS (rel intensity) *m/z* 337 ($M^+$, 32), 228 (82), 186 (20), 149 (44), 91 (100), 65 (30); exact mass calcd for $C_{21}H_{23}NOS$ *m/z* 337.1502, found 337.1505.

**(3*S**,3a*S**,6a*R**)-1-*tert*-Butyl-3-[1-(phenylthio)ethenyl]-hexahydro-1*H*-cyclopent[*c*]isoxazole (7c)**

A mixture of **4a** (80 mg, 0.27 mmol), *N*-*t*-butylhydroxylamine hydrochloride (38 mg, 0.30 mmol) and NaOMe (16 mg, 0.30 mmol) in toluene (20 mL) was stirred at rt for 10 min and was then heated at 95 °C for 10 h. The same workup procedure as that for **7a** gave **7c** (44 mg, 54% yield); IR (neat) 3056, 2965, 2870, 1470, 1390, 1365, 1220, 1088, 751, 693 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.15 (9H, s, $C(CH_3)_3$), 1.50-1.82 (6H, m), 2.91-3.00 (1H, m, H-3a), 3.58-3.63 (1H, m, H-6a), 4.09 (1H, d, *J* = 8.4 Hz, H-3), 4.81 (1H, s, C=$CH_2$), 5.46 (1H, s, C=$CH_2$), 7.28-7.49 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.9, 25.8, 29.8, 34.9, 55.3, 58.1, 65.3, 84.6, 113.7, 127.7, 129.1, 133.1, 133.2, 145.0; MS (rel intensity) *m/z* 303 ($M^+$, 51), 288 (100), 135 (14), 91 (21), 57 (31); exact mass calcd for $C_{18}H_{25}NOS$ *m/z* 303.1659, found 303.1662.

**(3*S**,3a*S**,6a*R**)-1-Methyl-3-[1-(phenylsulfonyl)ethenyl]-hexahydro-1*H*-cyclopent[*c*]isoxazole (7d)**

A mixture of **6a** (0.10 g, 0.30 mmol), *N*-methylhydroxylamine hydrochloride (29 mg, 0.34 mmol) and NaOMe (19 mg, 0.34 mmol) in toluene (35 mL) was stirred at rt for 10 min and was then heated at 95 °C for 6 h. The same workup procedure as that for **7a** gave **7d** (58 mg, 65% yield); IR (neat) 3055, 2955, 2868, 1446, 1306 ($SO_2$), 1290, 1140 ($SO_2$), 743, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.48-1.78 (6H, m), 2.62 (3H, s, $CH_3$), 2.86-2.88 (1H, m, H-3a), 3.09-3.12 (1H, m, H-6a), 4.13 (1H, d, *J* = 6.6 Hz), 6.21 (1H, s, C=$CH_2$), 6.51 (1H, s, C=$CH_2$), 7.50-7.55 (2H, m), 7.59-7.64 (1H, m), 7.86-7.89 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.7, 30.5 (× 2), 43.8, 56.4, 75.7, 80.4, 125.0, 128.3, 129.1, 133.5, 139.4, 150.0; MS (rel intensity) *m/z* 293 ($M^+$, 94), 152 (60), 77 (100), 73 (50); exact mass calcd for $C_{15}H_{19}NO_3S$ *m/z* 293.1086, found 293.1092.

**(3*S**,3a*S**,6a*R**)-1-(Phenylmethyl)-3-[1-(phenylsulfonyl)-ethenyl]-hexahydro-1*H*-cyclopent[*c*]isoxazole (7e)**

A mixture of **6a** (0.1 g, 0.31 mmol), *N*-benzylhydroxylamine hydrochloride (55 mg, 0.34 mmol) and NaOMe (19 mg, 0.34 mmol) in toluene (55 mL) was stirred at rt for 10 min and was then heated at 95 °C for 10 h. The same workup procedure as that for **7a** gave **7d** (68 mg, 60% yield); IR (neat) 3062, 3030, 2952, 2868, 1446, 1306 ($SO_2$),

1290, 1141 ($SO_2$), 781, 750, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.41-1.84 (6H, m), 2.91-2.93 (1H, m, H-3a), 3.32-3.37 (1H, m, H-6a), 3.86 (1H, d, $J$ = 13.8 Hz, $CH_2Ph$), 3.93 (1H, d, $J$ = 13.8 Hz, $CH_2Ph$), 4.20 (1H, d, $J$ = 6.7 Hz, H-3), 6.18 (1H, s, $C=CH_2$), 6.49 (1H, s, $C=CH_2$), 7.22-7.32 (5H, m), 7.43-7.48 (2H, m), 7.55-7.60 (1H, m), 7.83-7.86 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.8, 30.5 (× 2), 55.3, 61.2, 73.1, 80.3, 125.2, 127.2, 128.1, 128.3, 128.96, 129.01, 133.4, 137.2, 139.6, 149.8; MS (rel intensity) $m/z$ 369 ($M^+$, 13), 228 (7), 91 (100), 77 (32), 65 (12); exact mass calcd for $C_{21}H_{23}NO_3S$ $m/z$ 369.1399, found 369.1397.

**(3*S**,3a*S**,7a*R**)-1-Methyl-3-[1-(phenylthio)ethenyl]-hexahydro-2,1-benzisoxazoline (8a) and (3*S**,3a*S**,7a*S**)-1-methyl-3-[1-(phenylthio)ethenyl]-hexahydro-2,1-benzisoxazoline (9a)**

A mixture of **4b** (0.213 g, 0.69 mmol), *N*-methylhydroxylamine hydrochloride (65 mg, 0.76 mmol) and NaOMe (41 mg, 0.76 mmol) in toluene (50 mL) was stirred at rt for 10 min and was then heated at reflux for 18 h. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography using ethyl acetate/hexane (1:10) as eluent to give **8a** (72 mg, 38% yield) and **9a** (51 mg, 27% yield). **8a**: IR (neat) 3059, 2965, 2870, 1477, 1450, 1140, 1035, 751, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.25-1.81 (8H, m), 2.57-2.58 (1H, m, H-3a), 2.75 (3H, s, $CH_3$), 2.78-2.80 (1H, m, H-7a), 4.24 (1H, d, $J$ = 3.5 Hz, H-3), 5.00 (1H, s, $C=CH_2$), 5.58 (1H, s, $C=CH_2$), 7.28-7.46 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 21.3, 23.6, 25.9, 27.4, 44.5, 47.8, 65.3, 84.5, 114.5, 127.8, 129.0, 129.2, 132.8, 146.2; MS (rel intensity) $m/z$ 275 ($M^+$, 49), 166 (100), 138 (46), 91 (44), 77 (23); exact mass calcd for $C_{16}H_{21}NOS$ $m/z$ 275.1345, found 275.1342. **9a**: IR (neat) 3060, 2965, 2870, 1450, 1150, 1100, 1020, 752, 693 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.20-1.35 (4H, m), 1.80-1.87 (3H, m), 2.11-2.20 (3H, m), 2.74 (3H, s, $CH_3$), 4.27 (1H, d, $J$ = 8.9 Hz, H-3), 4.87 (1H, s, $C=CH_2$), 5.52 (1H, s, $C=CH_2$), 7.28-7.48 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.0, 25.0, 27.5, 28.3, 44.4, 55.0, 74.0, 82.7, 113.1, 127.7, 129.2, 132.8, 133.2, 145.6; MS (rel intensity) $m/z$ 275 ($M^+$, 100), 229 (44), 166 (44), 119 (17), 91 (55), 77 (25); exact mass calcd for $C_{16}H_{21}NOS$ $m/z$ 275.1345, found 275.1347.

**(3*S**,3a*S**,7a*R**)-1-(Phenylmethyl)-3-[1-(phenylthio)-ethenyl]-hexahydro-2,1-benzisoxazoline (8b) and (3*S**,3a*S**,7a*S**)-1-(phenylmethyl)-3-[1-(phenylthio)-ethenyl]-hexahydro-2,1-benzisoxazoline (9b)**

A mixture of **4b** (0.594 g, 1.92 mmol), *N*-benzylhydroxylamine hydrochloride (0.35 g, 2.11 mmol) and NaOMe (0.12 g, 2.11 mmol) in toluene (100 mL) was stirred at rt for 10 min and was then heated at reflux for 18 h. The same workup procedure as that for **8a** gave **8b** (0.242 g, 36% yield) and **9b** (0.117 g, 18% yield). **8b**: IR (neat) 3060, 3028, 2934, 2855, 1477, 1452, 1440, 1370, 1024, 998, 750, 695 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.28-1.83 (8H, m), 2.70-2.74 (1H, m, H-3a), 3.07-3.08 (1H, m, H-7a), 4.07 (2H, s, $CH_2Ph$), 4.37 (1H, d, $J$ = 5.5 Hz, H-3), 5.03 (1H, s, $C=CH_2$), 5.60 (1H, s, $C=CH_2$), 7.26-7.47 (10H, m); $^{13}C$ NMR ($CDCl_3$) δ 22.0, 23.0, 26.3, 26.7, 46.5, 61.7, 63.0, 84.1, 115.2, 127.1, 127.7, 128.2, 129.0, 129.2, 132.8, 133.1, 138.1, 146.0; MS (rel intensity) $m/z$ 351 ($M^+$, 75), 242 (100), 91 (99); exact mass calcd for $C_{22}H_{25}NOS$ $m/z$ 351.1658, found 351.1652. **9b**: IR (neat) 3060, 3028, 2931, 2857, 1477, 1452, 1440, 1100, 749, 696 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.15-1.39 (4H, m), 1.71-1.81 (3H, m), 2.05-2.36 (3H, m), 3.97 (1H, d, $J$ = 14.1 Hz, $CH_2Ph$), 4.13 (1H, d, $J$ = 14.1 Hz, $CH_2Ph$), 4.23 (1H, d, $J$ = 9.2 Hz, H-3), 4.90 (1H, s, $C=CH_2$), 5.51 (1H, s, $C=CH_2$), 7.22-7.47 (10 H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.1, 25.2, 27.6, 28.9, 54.9, 61.6, 71.7, 82.4, 113.7, 127.0, 127.6, 128.1, 128.9, 129.1, 133.0, 133.1, 137.4, 145.3; MS (rel intensity) $m/z$ 351 ($M^+$, 37), 242 (16), 135 (6), 91 (100); exact mass calcd for $C_{22}H_{25}NOS$ $m/z$ 351.1658, found 351.1655.

**(3*S**,3a*S**,7a*R**)-1-Methyl-3-[1-(phenylsulfonyl)ethenyl]-hexahydro-2,1-benzisoxazoline (8c)**

A mixture of **6b** (90 mg, 0.26 mmol), *N*-methylhydroxylamine hydrochloride (24 mg, 0.29 mmol) and NaOMe (16 mg, 0.29 mmol) in toluene (30 mL) was stirred at rt for 10 min and was then heated at reflux for 18 h. The same workup procedure as that for **8a** gave **8c** (45 mg, 56% yield); IR (neat) 3060, 2932, 2856, 1447, 1316, 1306 ($SO_2$), 1170, 1136 ($SO_2$), 752, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.18-1.30 (1H, m), 1.31-1.43 (2H, m), 1.60-1.66 (4H, m), 1.81-1.88 (1H, m), 2.54-2.67 (2H, m, H-3a, 7a), 2.67 (3H, s, $CH_3$), 4.21 (1H, br s, H-3), 6.18 (1H, d, $J$ = 1.2 Hz, $C=CH_2$), 6.44 (1H, s, $C=CH_2$), 7.49-7.55 (2H, m), 7.59-7.64 (1H, m), 7.83-7.86 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 20.7, 24.2, 25.2, 27.8, 43.8, 49.3, 64.7, 79.0, 124.4, 128.1, 129.2, 133.6, 139.3, 151.9; MS (rel intensity) $m/z$ 307 ($M^+$, 98), 166 (82), 140 (29), 77 (100), 51 (27); exact mass calcd for $C_{16}H_{21}NO_3S$ $m/z$ 307.1243, found 307.1245.

**(3*S**,3a*S**,7a*R**)-1-(Phenylmethyl)-3-[1-(phenylsulfonyl)-ethenyl]-hexahydro-2,1-benzisoxazoline (8d)**

A mixture of **6b** (70 mg, 0.21 mmol), *N*-benzylhydroxylamine hydrochloride (37 mg, 0.23 mmol) and NaOMe (13 mg, 0.23 mmol) in toluene (30 mL) was stirred at rt for 10 min and was then heated at reflux for 19 h. The

same workup procedure as that for **8a** gave **8d** (35 mg, 45% yield); IR (neat) 3062, 3029, 2930, 2856, 1496, 1447, 1316, 1306, 1172, 1139, 750, 688 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.30-1.85 (8H, m), 2.58-2.65 (1H, m, H-3a), 2.83-2.88 (1H, m, H-7a), 3.75 (1H, d, $J$ = 14.1 Hz, $CH_2Ph$), 4.12 (1H, d, $J$ = 14.1 Hz, $CH_2Ph$), 4.24 (1H, br s, H-3), 6.13 (1H, s, C=$CH_2$), 6.44 (1H, s, C=$CH_2$), 7.23-7.35 (5H, m), 7.47-7.52 (2H, m), 7.57-7.62 (1H, m), 7.82-7.84 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 20.9, 24.2, 25.8, 27.5, 48.8, 60.8, 62.0, 78.9, 124.6, 127.3, 128.2, 128.3, 128.7, 129.2, 133.6, 137.5, 139.4, 151.9; MS (rel intensity) *m/z* 383 ($M^+$, 36), 242 (16), 91 (100), 77 (29), 65 (11), 51 (7); exact mass calcd for $C_{22}H_{25}NO_3S$ *m/z* 383.1556, found 383.1557.

**2-(4-Hydroxyiminobutyl)-4-phenylthio-3-sulfolene (10a)**

To a stirred solution of **4a** (0.425 g, 1.44 mmol) in MeOH (10 mL) was added a solution of hydroxylamine hydrochloride (152 mg, 2.16 mmol) and NaOAc (0.18 g, 2.16 mmol) in MeOH (10 mL) at room temperature under nitrogen. The reaction mixture was stirred at rt for 2 h, and then the solvent was removed under vacuum. The residue was extracted with $CH_2Cl_2$ (20 mL × 3). The organic solution was dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:3) as eluent to give a *syn/anti* mixture (1.2:1) of **10a** (0.376 g, 84% yield); IR (neat) 3449 (OH), 3058, 2929, 1655 (C=N), 1440, 1402, 1308, 1219, 1126, 1024, 914, 749, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.64-1.77 (m), 1.90-1.99 (m), 2.21-2.28 (m), 2.39-2.46 (m), 3.64-3.82 (m), 5.70-5.71 (m), 6.71 (br s), 7.36-7.44 (m); $^{13}C$ NMR ($CDCl_3$) δ 23.3, 23.6, 28.2, 28.4, 29.0, 57.4, 66.7, 125.0, 129.1, 129.4, 129.6, 131.6, 133.2, 150.8, 151.2; MS (rel intensity) *m/z* 311 ($M^+$, 1), 218 (18), 138 (58), 110 (84), 109 (56), 77 (58), 64 (100); exact mass calcd for $C_{14}H_{17}NO_3S_2$ *m/z* 311.0651, found 311.0642. These two isomers have distinct $^1H$ NMR absorptions for CH=N-O-: *anti*-form, δ 6.71 (br s); *syn*-form, δ 7.36-7.44 (m).

**2-(5-Hydroxyiminopentyl)-4-phenylthio-3-sulfolene (10b)**

To a stirred solution of **4b** (1.45 g, 4.52 mmol) in MeOH (10 mL) was added a solution of hydroxylamine hydrochloride (0.484 g, 6.77 mmol) and NaOAc (0.58 g, 6.77 mmol) in MeOH (35 mL) at room temperature under nitrogen. The reaction mixture was stirred at rt for 2 h, and the same workup procedure as that for **10a** gave a *syn/anti* mixture (1.1:1) of **10b** (1.19 g, 81% yield); IR (neat) 3446 (OH), 3058, 2930, 1653 (C=N), 1440, 1402, 1309, 1220, 1126, 1024, 919, 749, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.48-1.69 (m), 1.93-2.02 (m), 2.19-2.25 (m), 2.39-2.41 (m), 3.64-3.80 (m), 5.72-5.74 (m), 6.72 (t, $J$ = 5.5 Hz), 7.36-7.45 (m); $^{13}C$ NMR ($CDCl_3$) δ 24.5, 25.7, 26.1, 26.3, 26.6, 28.5, 29.0, 57.5, 67.0, 125.4, 129.1, 129.6, 129.7, 131.6, 133.2, 151.4, 151.9; Anal. Calcd for $C_{15}H_{19}NO_3S_2$: C, 55.36; H, 5.58. Found: C, 55.18; H, 5.96. These two isomers have distinct $^1H$ NMR absorptions for CH=N-O-: *anti*-form, δ 6.72 (t); *syn*-form, δ 7.36-7.45 (m).

**(*E*)-7-Phenylthio-5,7-octadienaldoxime (11a)**

A mixture of **10a** (0.20 g, 0.64 mmol), hydroquinone (8 mg) and $NaHCO_3$ (54 mg, 0.64 mmol) in EtOH (20 mL) was heated at reflux for 3 h. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography using ethyl acetate/hexane (1:1) as eluent to give a *syn/anti* mixture (1:1) of **11a** (0.124 g, 78% yield); IR (neat) 3260 (OH), 3073, 3008, 2925, 2851, 1650 (C=N), 1478, 1439, 1024, 742, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.51-1.61 (m), 2.09-2.17 (m), 2.30-2.37 (m), 5.11 (s), 5.40 (s), 6.02-6.11 (m), 6.16-6.22 (d, $J$ = 15.4 Hz), 6.69 (t, $J$ = 5.2 Hz), 7.24-7.41 (m), 9.20-9.35 (br s); $^{13}C$ NMR ($CDCl_3$) δ 24.4, 25.4, 25.8, 28.6, 31.6, 31.9, 117.6, 127.0, 128.9, 129.6, 131.6, 133.4, 133.7, 141.2, 151.6, 152.1. These two isomers have distinct $^1H$ NMR absorptions for CH=N-O-: *anti*-form, δ 6.69 (t); *syn*-form, δ 7.24-7.41 (m).

**(*E*)-8-Phenylthio-6,8-nonadienaldoxime (11b)**

A mixture of **10b** (0.289 g, 0.89 mmol), hydroquinone (10 mg) and $NaHCO_3$ (78 mg, 0.89 mmol) in EtOH (45 mL) was heated at reflux for 3 h. The same workup procedure as that for **11a** gave a *syn/anti* mixture (1:1) of **11b** (0.167 g, 72% yield); IR (neat) 3258 (OH), 3073, 3016, 2928, 2857, 1645 (C=N), 1582, 1478, 1439, 1024, 961, 908, 746, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.39-1.42 (m), 2.09-2.19 (m), 2.26-2.35 (m), 5.07 (s), 5.36 (s), 6.02-6.10 (m), 6.16 (d, $J$ = 15.4 Hz), 6.65 (br t, $J$ = 5.3 Hz), 7.21-7.40 (m), 9.20-9.35 (br s); $^{13}C$ NMR ($CDCl_3$) δ 24.6, 25.3, 25.8, 28.4, 28.7, 29.2, 31.9, 32.0, 117.4, 127.0, 128.9, 129.2, 129.6, 131.6, 133.1, 133.9, 134.2, 134.3, 141.4, 151.8, 152.4. These two isomers have distinct $^1H$ NMR absorptions for CH=N-O-: *anti*-form, δ 6.61-6.69 (br t); *syn*-form, δ 7.21-7.40 (m).

**(3*S**,3a*S**)-3-[1-(Phenylthio)ethenyl]-3a,4,5,6-tetrahydro-3*H*-cyclopent[*c*]isoxazole (12a)**

A solution of **11a** (0.1 g, 0.41 mmol) and chloramine-T (0.15 g, 0.53 mmol) in EtOH (40 mL) was reacted in an ultrasound cleaning bath at rt for 14 h. The solvent was removed under vacuum, and the crude product was purified by flash column chromatography using ethyl acetate/hexane (1:10) as eluent to give **12a** (66 mg, 67% yield); IR (neat)

3056, 2965, 2870, 1609, 1582, 1477, 1439, 1247, 1132, 1068, 1024, 936, 908, 877, 750, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.43-1.50 (1H, m), 1.99-2.23 (3H, m), 2.39-2.46 (2H, m), 3.70-3.77 (1H, m, H-3a), 4.76 (1H, d, $J$ = 11.3 Hz, H-3), 5.12 (1H, s, C=$CH_2$), 5.70 (1H, s, C=$CH_2$), 7.27-7.47 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 21.4, 27.8, 28.2, 60.7, 89.1, 116.2, 128.0, 129.3, 132.2, 132.8, 142.4, 172.5; MS (rel intensity) *m/z* 245 ($M^+$, 78), 228 (83), 136 (89), 109 (63), 91 (100), 77 (53); exact mass calcd for $C_{14}H_{15}NOS$ *m/z* 245.0876, found 245.0875.

**(3*S**,3a*S**)-3-[1-(Phenylthio)ethenyl]-3,3a,4,5,6,7-hexahydro-2,1-benzisoxazole (12b)**

A solution of **11b** (86 mg, 0.33 mmol) and chloramine-T (0.118 g, 0.36 mmol) in EtOH (20 mL) was reacted in an ultrasound cleaning bath at rt for 14 h. The same workup procedure as that for **12a** gave **12b** (51 mg, 60 yield); IR (neat) 3057, 2936, 2858, 1634, 1606, 1582, 1477, 1440, 1358, 1321, 1157, 1024, 920, 864, 838, 751, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.29-1.40 (3H, m), 1.80-1.84 (1H, m), 1.95-1.99 (1H, m), 2.07-2.17 (2H, m), 2.70-2.74 (1H, m), 3.09-3.13 (1H, m, H-3a), 4.57 (1H, d, $J$ = 8.6 Hz, H-3), 5.04 (1H, s, C=$CH_2$), 5.60 (1H, s, C=$CH_2$), 7.26-7.45 (5H, m); $^{13}C$ NMR ($CDCl_3$) δ 24.4, 25.2, 26.3, 32.7, 55.0, 86.7, 114.9, 127.9, 129.2, 132.0, 132.7, 143.6, 160.2; MS (rel intensity) *m/z* 259 ($M^+$, 26), 218 (84), 136 (53), 124 (43), 109 (100), 91 (43), 65 (45); exact mass calcd for $C_{15}H_{17}NOS$ *m/z* 259.1032, found 259.1034.

**(1*R**,2*S**)-*N*-Benzyl-2-(1*S**-hydroxy-2-phenylthio-2-propenyl)cyclopentamine (13)**

To a solution of **7b** (0.1 g, 0.3 mmol) in 50% aqueous HOAc solution (2 mL) was added Zn powder (0.2 g, 2.97 mmol) at rt. The reaction mixture was stirred for 30 min and was then poured into a 5% aqueous KOH solution (20 mL) in an ice bath. It was then extracted with $CH_2Cl_2$ (20 mL × 3). The organic solution was dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:1) as eluent to give **13** (90 mg, 89% yield); IR (neat) 3285 (OH, NH), 3059, 3026, 2951, 2871, 1605, 1582, 1477, 1439, 1086, 1024, 749, 693 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.60-1.78 (7H, m), 1.88-1.94 (1H, m), 2.37-2.46 (1H, m), 3.29-3.53 (1H, m), 3.80 (2H, s, $CH_2Ph$), 4.37 (1H, d, $J$ = 7.1 Hz), 4.88 (1H, s, C=$CH_2$), 5.48 (1H, s, C=$CH_2$), 7.22-7.43 (8H, m), 7.48-7.52 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 21.6, 26.8, 31.4, 45.0, 52.8, 61.3, 76.2, 112.4, 127.2, 127.7, 128.1, 128.4, 129.0, 132.8, 133.4, 139.2, 149.1; MS (rel intensity) *m/z* 339 ($M^+$, 1), 230 (87), 212 (61), 173 (21), 91 (100), 65 (11); exact mass calcd for $C_{21}H_{25}NOS$ *m/z* 339.1658, found 339.1652.

**(1*S**,5*R**,7*R**)-6-Benzyl-7-[1-(phenylthio)ethenyl]-6-azabicyclo[3.2.0]heptane (14)**

To a solution of **13** (30 mg, 0.089 mmol) in dried THF (3 mL) was added NaH (4 mg, 0.1 mmol) at rt under nitrogen, and then heated at reflux for 5 min. To the mixture was added dropwise a solution of methanesulfonyl chloride (0.008 mL, 0.1 mmol) in THF (1 mL) at reflux. The whole was then stirred at rt for 30 min. The solvent was removed under vacuum and then dissolved in $CH_2Cl_2$ (5 mL). To the reaction mixture was added a 5% aqueous NaOH solution (2 mL). The whole was stirred at rt for 1 h and then extracted with $CH_2Cl_2$ (10 mL × 3). The organic solution was dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography using ethyl acetate/hexane (1:20) and 5 drops of triethylamine as eluent to give **14** (22 mg, 77% yield); IR (neat) 3060, 3027, 2951, 1608, 1583, 1476, 1454, 1439, 1024, 749, 692 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.00-1.04 (1H, m), 1.27-1.39 (2H, m), 1.58-1.66 (1H, m), 1.70-1.91 (2H, m), 2.72-2.79 (1H, m), 3.47 (1H, d, $J$ = 12.8 Hz, $CH_2Ph$), 3.51-3.53 (1H, m, H-5), 3.73 (1H, d, $J$ = 8.1 Hz, H-7), 3.76 (1H, d, $J$ = 12.8 Hz, $CH_2Ph$), 5.18 (1H, s, C=$CH_2$), 5.76 (1H, s, C=$CH_2$), 7.24-7.41 (10H, m); $^{13}C$ NMR ($CDCl_3$) δ 25.8, 26.3, 33.3, 37.9, 61.1, 67.3, 67.8, 114.7, 126.8, 127.5, 128.0, 129.0, 129.1, 132.7, 133.2, 139.1, 142.2; MS (rel intensity) *m/z* 321 ($M^+$, 77), 212 (39), 186 (49), 109 (6), 91 (100), 65 (12); exact mass calcd for $C_{21}H_{23}NS$ *m/z* 321.1553, found 321.1558.

**(4*S**,3*R***S**,4a*S**,7a*R**)-4-Hydroxy-1-(phenylmethyl)-3-(phenylsulfonyl)-2,3,4,4a,5,6,7,7a-octahydro-1*H*-cyclopenta[*b*]pyridine (15)**

To a solution of **7e** (35 mg, 0.1 mmol) in 50% aqueous HOAc solution (1 mL) was added Zn (19 mg, 0.29 mmol) at rt, and the mixture was stirred for 3 h. The same workup procedure as that for **13** gave an inseparable mixture of two diastereomers (1.4:1) **15** (26 mg, 75% yield); IR (neat) 3517 (OH), 3061, 3028, 2954, 2868, 1603, 1585, 1447, 1305 ($SO_2$), 1145 ($SO_2$), 1084, 1027, 738, 690 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.43-2.13 (m), 2.35-2.68 (m), 2.63-2.65 (m), 2.78-2.89 (m), 3.02 (d, $J$ = 13.3 Hz), 3.15 (d, $J$ = 13.3 Hz), 3.24-3.32 (m), 3.41-3.56 (m), 3.89-4.11 (m), 4.11-4.21 (m), 4.22-4.23 (m), 7.12-7.80 (m); $^{13}C$ NMR ($CDCl_3$) δ 21.9, 23.7, 24.2, 26.6, 31.5, 31.7, 42.7, 44.8, 45.2, 49.5, 58.0, 59.3, 64.1, 64.7, 65.5, 67.1, 67.8, 127.1, 127.4, 128.3, 128.5, 128.8, 129.2, 129.3, 133.4, 134.0, 137.3, 137.6, 137.9, 138.0; MS (rel intensity) *m/z* 371 ($M^+$, 22), 342 (40), 229 (38), 109 (100); exact mass calcd for $C_{21}H_{25}NO_3S$ *m/z* 371.1556, found 371.1559. These two isomers have some distinct $^{13}C$ NMR absorptions: the major isomer, δ 21.9, 24.2, 31.5, 44.8, 49.5, 59.3, 64.7, 67.1, 127.1, 129.2, 134.0,

137.6, 137.9; the minor isomer, δ 23.7, 26.0, 31.7, 42.7, 45.2, 58.0, 65.5, 67.8, 127.4, 129.3, 133.4, 137.3, 138.0.

***cis*-1-(Phenylmethyl)-3-(phenylsulfonyl)-2,4a,5,6,7,7a-hexahydro-1*H*-cyclopenta[*b*]pyridine (16)**

A solution of **15** (11 mg, 0.03 mmol) in 50% aqueous HOAc solution (1 mL) was heated at 60 °C for 5 h. The same workup procedure as that for **13** gave **16** (8 mg, 78% yield); IR (neat) 3061, 3028, 2954, 2869, 1652, 1584, 1446, 1304 ($SO_2$), 1148 ($SO_2$), 1087, 742, 689 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.43-1.70 (5H, m), 1.89-1.93 (1H, m), 2.75-2.86 (1H, m, H-4a), 3.01 (1H, d, $J$ = 16.2 Hz, H-2), 3.17-3.22 (1H, m, H-7a), 3.19 (1H, d, $J$ = 16.2 Hz, H-2), 3.37 (1H, d, $J$ = 13.3 Hz, $CH_2Ph$), 3.67 (1H, d, $J$ = 13.3 Hz, $CH_2Ph$), 6.97-7.00 (1H, m, H-4), 7.11-7.12 (2H, m), 7.20-7.26 (3H, m), 7.46-7.51 (2H, m), 7.58-7.63 (1H, m), 7.76-7.79 (2H, m); $^{13}C$ NMR ($CDCl_3$) δ 22.8, 25.0, 29.6, 38.5, 44.3, 59.0, 60.8, 127.1, 127.8, 128.3, 128.6, 129.1 (×2), 133.1 (×2), 140.7 (×2); MS (rel intensity) *m/z* 353 ($M^+$, 24), 212 (64), 91 (100), 77 (13), 65 (9); exact mass calcd for $C_{21}H_{23}NO_2S$ *m/z* 353.1450, found 353.1441.

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