$PhMe_2PS$, 1707-00-2; Ph_2PMe, 1486-28-8; Ph_2MePS, 13639-74-2; $PhC{\equiv}CH$, 536-74-3; 4-isopropyl-2-nitrophenol, 1576-10-9; 2-nitro-4-methylphenol, 119-33-5; *p*-cresol, 106-44-5; acetone, 67-64-1; thioanisole, 100-68-5; 2-nitro-*p*-cresol, 119-33-5; 1,3-dithiane, 505-23-7; 2,6-dichloro-4-methylphenol, 2432-12-4; 2,6-dibromo-4-methylphenol, 2432-14-6; 5,6,7,8-tetrahydro-2-naphthyl acetate, 89228-44-4; 1-nitro-5,6,7,8-tetrahydro-2-naphthyl acetate, 109928-87-2; 3-nitro-5,6,7,8-tetrahydro-2-naphthyl acetate, 100192-99-2; 3-nitro-5,6,7,8-tetrahydro-2-naphthol, 6240-79-5.

Supplementary Material Available: Additional experimental details including preparative and characterization data for all new compounds prepared (27 pages). Ordering information is given on any current masthead page.

Regio- and Stereoselective Synthesis of Substituted 2-(Phenylthio)-1,3-butadienes

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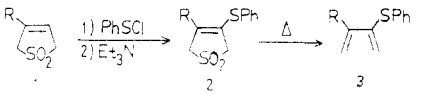
Sulfur-substituted 1,3-butadienes are useful reagents in organic synthesis. We now report two general methods for the regio- and stereoselective synthesis of substituted 2-(phenylthio)-1,3-butadienes **4** and **5**. 3-(Phenylthio)-3-sulfolenes **2** can be specifically alkylated at C5 under basic conditions. Extrusion of sulfur dioxide by lithium aluminum hydride then gives the dienes **4**. On the other hand 2-substituted 3-sulfolenes **11** can be converted to the 3-phenylthio derivatives **9**, which upon heating give the dienes **5**.

Sulfur-substituted dienes have widely been used in the Diels–Alder reaction.[1] The sulfur atom not only increases the reactivity of the diene but also adds control to the regioselectivity of this reaction. Since the sulfur is more directive than an alkyl group, after removing the sulfur group reductively, a reversed Diels–Alder regioselectivity is then achieved. With this strategy Hopkins et al. have recently synthesized 1,5-disubstituted cyclohexenes.[2]

It is now well established that 3-sulfolenes are useful precursors for substituted 1,3-butadienes.[3] Thus, the most convenient method for the synthesis of 2-(phenylthio)-1,3-butadienes **3** is by extrusion of sulfur dioxide from 3-(phenylthio)-3-sulfolenes **2**, which in turn are readily prepared from 3-sulfolenes **1** by chlorosulfenylation–dehydrochlorination.[2,4] So far, however, only two compounds of the structure **3** are known (R = H, Me).



1 2 3

(1) (a) Petrzilka, M.; Grayson, J. L. *Synthesis* **1981**, 753. (b) Overman, L. E.; Petty, C. B.; Ban, T.; Huang, G. T. *J. Am. Chem. Soc.* **1983**, *105*, 6335. (c) Cohen, T.; Kosarych, Z. *J. Org. Chem.* **1982**, *47*, 4005. (d) Kozikowski, A. P.; Huie, E. M. *J. Am. Chem. Soc.* **1982**, *104*, 2923. (e) Bridges, A. J.; Fischer, J. W. *Tetrahedron Lett.* **1983**, *24*, 445, 447. (f) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3548, 3554. (g) Cohen, T.; Mura, A. J., Jr.; Shull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218. (h) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075.

(2) Proteau, P. J.; Hopkins, P. B. *J. Org. Chem.* **1985**, *50*, 141.

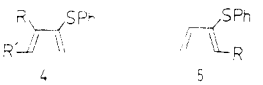
(3) (a) Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *Chem. Lett.* **1983**, 1003. (b) Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *J. Org. Chem.* **1986**, *51*, 4934. (c) Nomoto, T.; Takayama, H. *Heterocycles* **1985**, *23*, 2913. (d) Chou, T. S.; Tso, H.-H.; Chang, L.-J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 515. (e) Chou, T. S.; Tso, H.-H.; Chang, L.-J. *J. Chem. Soc., Chem. Commun.* **1984**, 1323. (f) Chou, T. S.; Tso, H.-H.; Chang, L.-J. *J. Chem. Soc., Chem. Commun.* **1985**, 236. (g) Tso, H.-H.; Chang, L.-J.; Lin, L. C.; Chou, T. S. *J. Chin. Chem. Soc.* **1985**, *32*, 333. (h) Chou, T. S.; Chang, L.-J.; Tso, H-H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1039. (i) Chou, T. S.; Tso, H.-H.; Lin, L. C. *J. Org. Chem.* **1986**, *51*, 1000. (j) Chou, T. S.; You, M.-L. *Bull. Inst. Chem., Acad. Sin.* **1986**, *33*, 13. (k) Chou, T. S.; Hung, S. C. *Heterocycles* **1986**, *24*, 2303. (l) Chou, T. S.; Tso, H.-H., Tao, Y.-T.; Lin, L. C. *J. Org. Chem.* **1987**, *52*, 244.

(4) (a) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208. (b) Gundermann, K. D.; Holtman, P. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 678.

Table I. Preparation of Dienes 4

		6		4	
2, R	R′X		% yield		% yield
2a, H	MeI	**6a**	92	**4a**	99
	EtI	**6b**	75	**4b**	71
	$CH_2{=}CHCH_2Br$	**6c**	65	**4c**	92
	$PhCH_2Br$	**6d**	85	**4d**	99
2b, Me	MeI	**6e**	71	**4e**	99
	EtI	**6f**	67	**4f**	82
	$CH_2{=}CHCH_2Br$	**6g**	64	**4g**	99
	$PhCH_2Br$	**6h**	55	**4h**	99

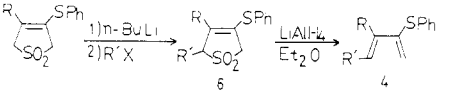
We now report two general methods for the regio- and stereoselective synthesis of substituted 2-(phenylthio)-1,3-butadienes **4** and **5**.



4 5

Results and Discussion

3-(Phenylthio)-3-sulfolenes **2** can be deprotonated[5] by *n*-butyllithium in THF/HMPA at low temperatures (−105 °C for **2a**; −78 °C for **2b**) to give immediately a dark green solution. Addition of an alkyl halide then gives the 5-alkylated product **6**. Treatment of **6** with lithium aluminum hydride then gives the desired dienes **4** in good yield (Table I).



6 4

2a, R = H
2b, R = Me

The structures of **6** are based on spectral and chemical methods. The ^1H NMR spectrum of **2a** has two sets of methylene protons at δ 3.65 and 3.8. The more downfield signals correspond to the C5 hydrogens because these are more split by the vinyl proton. After alkylation the ^1H

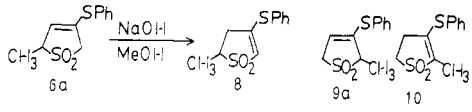
(5) For part of our preliminary results, see: Tao, Y.-T.; Liu, C.-L.; Lee, S.-J.; Chou, S.-S. P. *J. Org. Chem.* **1986**, *51*, 4718.

0022-3263/87/1952-4468$01.50/0

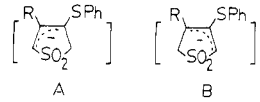
Table II. Preparation of Dienes 5

11, R	9	% yield	5	% yield (Z/E)
11a, Me	**9a**	80	**5a**	99 (86:14)
11b, Et	**9b**	85	**5b**	85 (90:10)
11c, *i*-Pr	**9c**	60	**5c**	99 (100:0)
11d, $PhCH_2$	**9d**	67	**5d**	99 (96:4)

NMR spectrum of the product **6** clearly shows that one of the C5 hydrogens has disappeared. Simple chemical transformations also confirm this assignment. For example, treatment of **6a** with NaOH/MeOH gives a mixture of **8** and **6a** in a ratio of 7:3. The methyl group in **8** is clearly a doublet. Had the product of methylation been **9a**, this treatment with NaOH would have yielded **10**, which should have neither this doublet nor the vinyl proton.

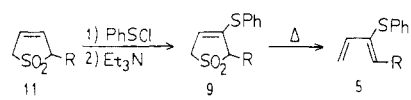


The regioselective alkylation of **2** at C5 can be explained by comparing the stability of the two carbanion intermediates A and B. Due to the electron-withdrawing ability of the sulfur group it is expected that A is more stable than B, and thus should be formed preferentially.

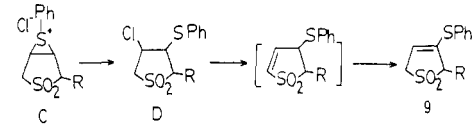


The usual method for removing sulfur dioxide thermally from 3-sulfolenes[6] does not work well for 3-(phenylthio)-3-sulfolenes **6** because complicated product mixtures are obtained. A much more satisfactory method is the use of lithium aluminum hydride in ether.[7] However, it is important that this reaction be done at room temperature for a short period of time; otherwise, overreduction would occur. The dienes **4** obtained as such have exclusively the *E* configuration. The stereochemistry of **4** is determined by an NOE study of the ^1H NMR spectra. For example in **4h**, irradiation of the methyl group increases the intensity of the benzylic protons, but not the internal vinyl proton.

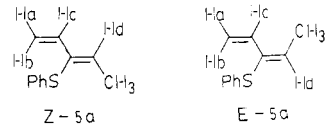
Having established the method for the regio- and stereospecific synthesis of 4-substituted 2-(phenylthio)-1,3-butadienes **4**, we proceeded to synthesize the 1-substituted isomers **5**. Treatment of the readily available[3d] 2-alkyl-3-sulfolenes **11** with phenylsulfenyl chloride in methylene chloride at room temperature, followed by stirring with triethylamine[4] gives the 3-(phenylthio)-3-sulfolenes **9**. Thermal extrusion of sulfur dioxide from **9** by refluxing in toluene then gives the desired dienes **5** in good yield (Table II).



The structure of **9** is determined by comparing the spectra with those of the regioisomer **6a–d**. The exclusive formation of **9** from **11** mandates that the episulfonium intermediate C be attacked by the chloride ion to give only D, presumably due to the steric effect of the alkyl group.



In contrast to the sulfolenes **6**, attempted removal of sulfur dioxide from **9** by lithium aluminum hydride gives rather complicated products. An excellent yield of dienes **5** can be obtained from **9** by the thermal process. Unfortunately, small amounts of the *E* isomer are present in most cases. Although the *Z*/*E* isomers cannot be separated by HPLC, their 400-MHz ^1H NMR signals are well resolved so that the stereochemistry of **5** can be determined by the NOE study. For example in **5a**, irradiation of the methyl groups at δ 1.98 and 1.90 clearly indicates that both H_c (δ 6.71) and H_d (δ 6.26) of the minor isomer show an NOE enhancement, whereas only H_d (δ 6.36) of the major isomer has such an effect. Thus, the major isomer is assigned (*Z*)-**5a** and the minor isomer (*E*)-**5a**.



In summary, substituted 2-(phenylthio)-1,3-butadienes **4** and **5** can be regio- and stereoselectively synthesized from readily available starting materials. The Diels–Alder reaction and some other transformations of **4** and **5** are being studied.

Experimental Section

Infrared spectra were recorded with a Beckman Acculab TM1 infrared spectrometer. ^1H and ^{13}C NMR spectra were taken with a Varian-360L spectrometer or a JEOL FX-100FT or a Bruker AM 400 FT-NMR spectrometer, with tetramethylsilane as the internal standard. Mass spectra were recorded with a JEOL JMS-D-100 spectrometer. High-resolution mass spectra (HRMS) were taken with a JEOL JMS-D-300 mass spectrometer. Elemental analyses were taken with a Perkin-Elmer 240C analyzer. The gas chromatograms were obtained with a Varian 3700 chromatograph on a 5% SE-30 column. All reagents were of reagent grade and were purified prior to use. All reactions were run under a positive pressure of dry nitrogen.

General Procedure for the Alkylation of 2. To a solution of **2** (0.89 mmol) and HMPA (3.54 mmol) in THF (10 mL) at −105 °C was added a solution of *n*-butyllithium (0.89 mmol). The reaction mixture was allowed to warm to −92 °C, and then the alkyl halide (5.31 mmol) was added. After being stirred at −78 °C for 15 min to 2 h, the reaction mixture was poured into saturated ammonium chloride. The THF was evaporated and ethyl acetate was used to extract the solution. The organic solution was washed with water and brine and was dried ($MgSO_4$). After the solvent was removed in vacuum the residue was chromatographed on silica gel (hexane/ethyl acetate, 2:1).

2-Methyl-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6a): IR (neat) 3080, 1320, 1220, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (3 H, d, *J* = 7.0 Hz), 3.62–4.10 (3 H, m), 5.73 (1 H, m), 7.41 (5 H, s); MS, *m*/*z* (relative intensity) 240 (M^+, 17), 176 (100), 110 (53), 99 (33). Anal. Calcd for $C_{11}H_{12}O_2S_2$: C, 54.97; H, 5.03. Found: C, 54.91; H, 5.03.

2-Ethyl-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6b): IR (neat) 3095, 1325, 1232, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (3 H, t, *J* = 7.0 Hz), 1.80 (2 H, m), 3.55–3.90 (3 H, m), 5.73 (1 H, m), 7.39 (5 H, s); MS, *m*/*z* (relative intensity) 254 (M^+, 8), 190 (100), 161 (25), 113 (52), 110 (50). Anal. Calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 56.51; H, 5.67.

2-(2-Propenyl)-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6c): IR (neat) 3118, 1327, 1234, 1142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.50 (2 H, m), 3.58–4.02 (3 H, m), 5.02 (1 H, m), 5.22 (1 H, m), 5.48–6.14 (1 H, m), 7.37 (5 H, s); MS, *m*/*z* (relative intensity) 266 (M^+, 10), 252 (23), 202 (100), 111 (20), 110 (23),

(6) (a) Mock, W. L. *J. Am. Chem. Soc.* **1966**, *88*, 2857. (b) Kellog, S. D.; Lemal, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2858. (c) Kellog, R. M.; Prins, W. L. *J. Org. Chem.* **1974**, *39*, 2366.

(7) Gaoni, Y. *Tetrahedron Lett.* **1977**, *18*, 947.

93 (77). Anal. Calcd for $C_{13}H_{14}O_2S_2$: C, 58.62; H, 5.30. Found: C, 58.81; H, 5.39.

2-(Phenylmethyl)-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6d): IR (neat) 3110, 1330, 1240, 1142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.57–3.50 (2H, m), 3.53–4.17 (3 H, m), 5.73 (1 H, m), 7.31 (10 H, m); MS, m/z (relative intensity) 316 (M^+, 5), 315 (20), 296 (21), 252 (100), 175 (22), 143 (22), 110 (20). Anal. Calcd for $C_{17}H_{16}O_2S_2$: C, 64.53; H, 5.10. Found: C, 64.77; H, 5.17.

2,3-Dimethyl-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6e): IR (KBr) 2960, 1325, 1250, 1142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (3 H, d, J = 7.0 Hz), 2.02 (3 H, m), 3.54–4.30 (3 H, m), 7.34 (5 H, s); MS, m/z (relative intensity) 254 (M^+, 16), 190 (36), 110 (28), 93 (60), 81 (52), 43 (40), 18 (100). Anal. Calcd for $C_{12}H_{14}O_2S_2$: C, 56.69; H, 5.51. Found: C, 56.78; H, 5.68.

2-Ethyl-3-methyl-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6f): IR (KBr) 2985, 1315, 1233, 1134 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (3 H, t, J = 7.0 Hz), 1.82–2.34 (5 H, m), 3.50–3.87 (3 H, m), 7.40 (5 H, s); MS, m/z (relative intensity) 268 (M^+, 29), 204 (79), 127 (100), 94 (74). Anal. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.18; H, 6.10. Found: C, 58.07; H, 6.06.

3-Methyl-4-(phenylthio)-2-(2-propenyl)-2,5-dihydrothiophene 1,1-dioxide (6g): IR (KBr) 3118, 1330, 1243, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02 (3 H, m), 2.65 (2 H, t, J = 6.2 Hz), 3.45–3.90 (3 H, m), 5.10 (1 H, dd, J = 4.0, 2 Hz), 5.33 (1 H, m), 5.58–6.15 (1 H, m), 7.35 (5 H, s); MS, m/z (relative intensity) 280 (M^+, 20), 216 (40), 188 (27), 139 (27), 107 (43), 91 (100). Anal. Calcd for $C_{14}H_{16}O_2S_2$: C, 59.97; H, 5.75. Found: C, 59.99; H, 5.76.

3-Methyl-2-(phenylmethyl)-4-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (6h): IR (KBr) 3060, 1320, 1250, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.94 (3 H, m), 3.23 (2 H, m), 3.45 (2 H, m), 3.98 (1 H, t, J = 6.4 Hz), 7.35 (10 H, m). MS, m/z (relative intensity) 330 (M^+, 5), 266 (63), 189 (42), 156 (54), 141 (100), 129 (46). Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49. Found: C, 65.56; H, 5.53.

General Procedure for the Preparation of 9. Phenylsulfenyl chloride (9.12 mmol) was first prepared from NCS and PhSH in CH_2Cl_2 (10 mL) according to the literature method,[4a] and then sulfolene **11** (7.6 mmol) in CH_2Cl_2 (5 mL) was added. After being stirred at room temperature for 1–3 days (followed by TLC), the reaction mixture was cooled to 0 °C, and triethylamine was then added. This was stirred at room temperature for 1 day and then at reflux for another day. After washing with 2% HCl, water, and brine, the solvent was evaporated, and the residue was chromatographed on silica gel (hexane/ethyl acetate, 6:1).

2-Methyl-3-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (9a): IR (neat) 3080, 1585, 1480, 1440, 1315, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (3 H, d, J = 7.0 Hz), 3.45–3.85 (3 H, m), 5.75 (1 H, m), 7.50 (5 H, s); MS, m/z (relative intensity) 240 (M^+, 36), 176 (100). Anal. Calcd for $C_{11}H_{12}O_2S_2$: C, 54.97; H, 5.03. Found: C, 54.86; H, 4.94.

2-Ethyl-3-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (9b): IR (neat) 3060, 1725, 1580, 1470, 1435, 1310, 1125 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (3 H, t, J = 7.0 Hz), 1.95 (2 H, m), 3.40–3.75 (3 H, m), 5.65 (1 H, m), 7.45 (5 H, s); MS, m/z (relative intensity) 254 (M^+, 45), 190 (100), 161 (25).

2-(1-Methylethyl)-3-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (9c): mp 54–55 °C; IR (KBr) 3050, 1600, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (3 H, d, J = 7.0 Hz), 1.25 (3 H, d, J = 7.0 Hz), 2.45 (1 H, m), 3.65 (3 H, m), 5.70 (1 H, m), 7.50 (5 H, s); MS, m/z (relative intensity) 268 (M^+, 33), 204 (100), 95 (52). Anal. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.18; H, 6.01. Found: C, 58.15; H, 6.01.

2-(Phenylmethyl)-3-(phenylthio)-2,5-dihydrothiophene 1,1-dioxide (9d): IR (neat) 3100, 1615, 1600, 1510, 1490, 1470, 1455, 1330, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.20 (2 H, d, J = 6.0 Hz), 3.45–4.0 (3 H, m), 5.70 (1 H, m), 7.30 (5 H, s), 7.45 (5 H, s); MS, m/z (relative intensity) 316 (M^+, 25), 252 (100), 143 (100); exact mass calcd for $C_{17}H_{16}O_2S_2$ m/z 316.0593, found m/z 316.0595.

General Procedure for the Preparation of 4. To a mixture of lithium aluminum hydride (1.29 mmol) in anhydrous ether (2.5 mL) at room temperature was added dropwise a solution of sulfolenes **6** (0.16 mmol) in Et_2O (2.5 mL). After being stirred for 20–30 min, the reaction mixture was cooled in an ice bath, and then aqueous sodium sulfate was added dropwise. The mixture was extracted with ether and dried ($MgSO_4$), and the solvent was evaporated to give colorless liquids.

(*E*)-2-(Phenylthio)-1,3-pentadiene (4a): IR (neat) 3100, 1585, 1490, 1450, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (3 H, d, J = 4.4 Hz), 5.05 (1 H, s), 5.36 (1 H, s), 6.16 (2 H, m), 7.30 (5 H, m); MS, m/z (relative intensity) 177 (70), 176 (M^+, 24), 147 (59), 135 (48), 110 (100); exact mass calcd for $C_{11}H_{12}S$ m/z 176.0661, found m/z 176.0665.

(*E*)-2-(Phenylthio)-1,3-hexadiene (4b): IR (neat) 3090, 2945, 1585, 1465, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (3 H, t, J = 7.0 Hz), 2.06 (2 H, m), 5.09 (1 H, s), 5.43 (1 H, s), 6.23 (2 H, m), 7.44 (5 H, m); MS, m/z (relative intensity) 190 (M^+, 100), 110 (55), 99 (49), 79 (58); exact mass calcd for $C_{12}H_{14}S$ m/z 190.0858, found m/z 190.0851.

(*E*)-2-(Phenylthio)-1,3,6-heptatriene (4c): IR (neat) 3095, 1588, 1482, 1445, 924 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.75 (2 H, m), 4.77 (1 H, dm, J = 7.6 Hz), 5.00 (2 H, s), 5.30 (1 H, s), 5.49–5.62 (1 H, m), 6.04 (2 H, m), 7.22 (5 H, m); MS, m/z (relative intensity) 202 (M^+, 40), 110 (34), 109 (44), 91 (88), 77 (100); exact mass calcd for $C_{13}H_{14}S$ m/z 202.4420, found m/z 202.4428.

(*E*)-5-Phenyl-2-(phenylthio)-1,3-pentadiene (4d): IR (neat) 3070, 1575, 1476, 1439, 965 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.33 (2 H, dm, J = 5.2 Hz), 5.06 (1 H, s), 5.34 (1 H, s), 6.16 (2 H, m), 7.20 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 38.6 (t), 117.9 (t), 126.1 (d), 127.1 (d), 128.4 (d), 128.5 (d), 129.0 (d), 130.3 (d), 131.8 (d), 132.9 (d), 135.7 (s), 139.7 (s), 141.5 (s); MS, m/z (relative intensity) 252 (M^+, 100), 161 (33), 143 (54), 142 (52), 128 (39), 110 (32), 91 (58); exact mass calcd for $C_{17}H_{16}S$ m/z 252.3922, found m/z 252.3927.

(*E*)-3-Methyl-2-(phenylthio)-1,3-pentadiene (4e): IR (neat) 3070, 1572, 1477, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.76 (6 H, m), 5.11 (1 H, s), 5.38 (1 H, s), 6.11 (1 H, br q, J = 7.0 Hz), 7.25 (5 H, m); MS, m/z (relative intensity) 190 (M^+, 100), 110 (63), 43 (41); exact mass calcd for $C_{12}H_{14}S$ m/z 190.0817, found m/z 190.0817.

(*E*)-3-Methyl-2-(phenylthio)-1,3-hexadiene (4f): IR (neat) 3085, 1580, 1485, 1446 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (3 H, t, J = 7.2 Hz), 1.75–2.24 (5 H, m), 5.17 (1 H, s), 5.47 (1 H, s), 6.07 (1 H, br t, J = 7.6 Hz), 7.32 (5 H, m); MS, m/z (relative intensity) 204 (M^+, 100), 127 (96), 94 (55). Anal. Calcd for $C_{13}H_{16}S$: C, 76.42; H, 7.89. Found: C, 76.46; H, 8.03.

(*E*)-3-Methyl-2-(phenylthio)-1,3,6-heptatriene (4g): IR (neat) 3105, 1580, 1483, 1447, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80 (3 H, s), 2.75 (2 H, t, J = 6.4 Hz), 4.7 (1 H, dm, J = 6.6 Hz), 4.95 (1 H, m), 5.15 (1 H, s), 5.40 (1 H, s), 5.53–5.87 (1 H, m), 6.00 (1 H, br t, J = 7.0 Hz), 7.22 (5 H, m); MS, m/z (relative intensity) 216 (M^+, 100), 188 (80), 139 (57), 107 (91), 79 (98). Anal. Calcd for $C_{14}H_{16}S$: C, 77.72; H, 7.45. Found: C, 77.40; H, 7.45.

(*E*)-3-Methyl-5-phenyl-2-(phenylthio)-1,3-pentadiene (4h): IR (neat) 3080, 1582, 1480, 1442, 905 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (3 H, m), 3.35 (2 H, d, J = 7.4 Hz), 5.25 (1 H, s), 5.46 (1 H, s), 6.19 (1 H, br t, J = 7.6 Hz), 6.68–7.40 (10 H, m); ^{13}C NMR ($CDCl_3$) δ 15.2 (q), 34.6 (t), 116.3 (t), 125.9 (d), 126.8 (d), 128.3 (d), 128.4 (d), 128.9 (d), 130.2 (d), 131.2 (d), 133.7 (s), 135.1 (s), 140.4 (s), 146.5 (s); MS, m/z (relative intensity) 266 (M^+, 74), 189 (34), 156 (100), 142 (38), 141 (73), 129 (26). Anal. Calcd for $C_{18}H_{18}S$: C, 81.15; H, 6.81. Found: C, 81.07; H, 6.81.

General Procedure for the Preparation of 5. A mixture of sulfolene **9** and a catalytic amount of hydroquinone in toluene was refluxed for 40–70 min. The solvent was removed by vacuum, and the residue was chromatographed on silica gel (hexane/ethyl acetate, 6:1).

(*Z*)-3-(Phenylthio)-1,3-pentadiene (5a):[8] IR (neat) 3060, 1615, 1580, 1470, 1430, 970, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (3 H, d, J = 7.0 Hz), 5.02 (1 H, d, J = 10.0 Hz), 5.55 (1 H, d, J = 17.0 Hz), 6.36 (1 H, q, J = 7.0 Hz), 6.43 (1 H, dd, J = 17.0, 10.0 Hz), 7.18 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 16.19 (q), 115.64 (t), 125.01 (d), 127.01 (d), 128.74 (d), 132.72 (s), 136.42 (s), 137.15 (d), 138.97 (d); MS, m/z (relative intensity) 176 (M^+, 100), 161 (23), 143 (19).

(*Z*)-3-(Phenylthio)-1,3-hexadiene (5b): IR (neat) 3100, 1630, 1600, 1490, 1450, 1040, 990, 920, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (3 H, t, J = 8.0 Hz), 2.40 (2 H, m), 5.00 (1 H, dd, J = 10.0, 1.0 Hz), 5.50 (1 H, dd, J = 17.0, 1.0 Hz), 6.25 (1 H, t, J = 7.0 Hz), 6.40 (1 H, dd, J = 17.0, 10.0 Hz), 7.16 (5 H, m); MS, m/z (relative

(8) (*E*)-**5a** has the following spectral data: ^1H NMR ($CDCl_3$) δ 1.90 (3 H, d, J = 7.0 Hz), 5.2 (1 H, d, J = 10.0 Hz), 5.65 (1 H, d, J = 17.0 Hz) 6.26 (1 H, q, J = 7.0 Hz), 6.71 (1 H, dd, J = 17.0, 10.0 Hz), 7.10 (5 H, m).

intensity) 190 (M^+, 100), 161 (34), 81 (28).

(Z)-5-Methyl-3-(phenylthio)-1,3-hexadiene (5c): IR (neat) 3120, 1640, 1600, 1495, 1480, 1460, 1000, 930, 760, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (6 H, d, J = 7.0 Hz), 3.10 (1 H, m), 5.00 (1 H, dd, J = 10.0, 1.5 Hz), 5.50 (1 H, dd, J = 17.0, 1.5 Hz), 6.05 (1 H, d, J = 9.0 Hz), 6.35 (1 H, dd, J = 17.0, 10.0 Hz), 7.16 (5 H, m); MS, m/z 204 (M^+, 100), 95 (49). Anal. Calcd for $C_{13}H_{16}S$: C, 76.42; H, 7.89. Found: C, 76.33; H, 7.85.

(Z)-5-Phenyl-3-(phenylthio)-1,3-pentadiene (5d): IR (neat) 3070, 1620, 1600, 1580, 1490, 1480, 1450, 1430, 975, 910, 740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80 (2 H, d, J = 7.4 Hz), 5.07 (1 H, d, J = 10.5 Hz), 5.61 (1 H, d, J = 16.8 Hz), 6.37-6.43 (2 H, m), 7.05-7.28 (10 H, m); ^{13}C NMR ($CDCl_3$) δ 36.72 (t), 116.89 (t), 125.21 (d), 126.23 (d), 127.25 (d), 128.53 (d), 128.57 (d), 128.79 (d), 132.21 (s), 136.23 (s), 136.81 (d), 139.42 (s), 142.12 (d); MS, m/z (relative intensity) 252 (M^+, 100), 161 (22), 143 (56).

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Intramolecular Electrophilic Additions to Olefins in Organic Syntheses. Stereoselective Synthesis of 3,4-Substituted β-Lactams by Bromine-Induced Oxidative Cyclization of *O*-Acyl β,γ-Unsaturated Hydroxamic Acid Derivatives

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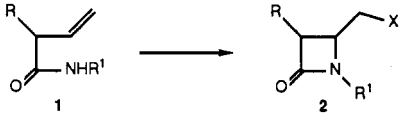
A mild, efficient, and stereoselective preparation of 3,4-disubstituted β-lactams is described. The method involves treatment of *O*-acyl β,γ-unsaturated hydroxamic acids with bromine in mildly basic aqueous acetonitrile at 0 °C. The resulting rapid reaction provides the β-lactams cleanly and stereoselectively in very good yields. The α-substituent has a profound affect on the stereochemical outcome of the reaction. α-Alkyl substituents induce preferential formation of the trans β-lactams, whereas a Cbz-protected α-amino substituent promotes formation of the cis β-lactam as the major product. These results are especially significant since most biologically active α-amino-substituted bicyclic β-lactams are cis substituted and many α-alkylated bicyclic β-lactams are trans substituted. These are also among the first examples to demonstrate the effect of α-substituents on electrophilic cyclizations to four-membered rings. The results are consistent with and help generalize some of the recently proposed theoretical considerations related to other electrophilic addition reactions.

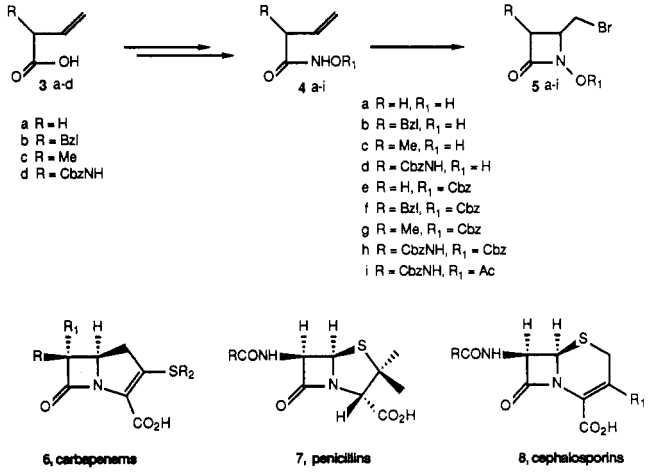
Electrophile-promoted additions to olefins are among the most fundamental and versatile tools in organic synthesis. Recent experimental and theoretical studies have contributed significantly to the understanding of the origin of the stereoselectivity observed during the electrophilic addition to chiral alkenes.[1,2] The stereoselective synthesis of functionalized five- and six-membered heterocyclic ring systems by such oxidative additions has been especially notable.[1,3] However, relatively few examples of oxidative additions to form four-membered rings have been reported.[4-6] The utility of 4-(halomethyl)-2-azetidinones **2** for the synthesis of nuclear analogues of penicillins and cephalosporins,[7a] carbapenems,[7b] and functionalized monocyclic β-lactam antibiotics[7c] made consideration of the oxidative cyclization of the corresponding β,γ-unsaturated amides **1** very attractive (eq 1).



(1)

On the basis of Ganem's precedent,[5a] which indicated that the low pK of the carboxamide group of β,γ-unsaturated *N*-tosylamides **1** (R^1 = Ts) promoted bromine-induced oxidative cyclizations to β-lactams, we recently developed an efficient oxidative cyclization of α-unsubstituted β,γ-unsaturated *O*-acyl hydroxamates to the corresponding α-unsubstituted 4-(bromomethyl) *N*-hydroxy-β-lactams (Scheme I; R = H, R^1 = acyl).[6] However, neither the earlier work on the tosylamide cyclizations nor our preliminary results on the oxidative cyclization of

Scheme I



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(1) (a) Chamberlin, A. R.; Mulholland, Jr., R. L.; Scott, D. K.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672 and references therein. (b) Kahn, S. D.; Rau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650. (c) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 666. (d) Chemberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819. (e) Chamberlin, A. R.; Dezube, M.; Dessault, P. *Tetrahedron Lett.* **1981**, *22*, 4611.

(2) (a) Houk, K. N.; Paddon-Row, M. N.; Gordon, N. G.; Wu, Y. D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science (Washington, D.C.)* **1986**, *231*, 1108 and references therein. (b) Houk, K. N.; Wu, Y. D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754. (c) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondon, N. G.; Jager, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880 and references therein. (d) Houk, K. N.; Rondon, N. G.; Wu, Y.-D.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257.

0022-3263/87/1952-4471$01.50/0