Substitution Reactions of Carbon Nucleophiles with β-(Phenylseleno)vinyl Sulfone Se Oxides[1]

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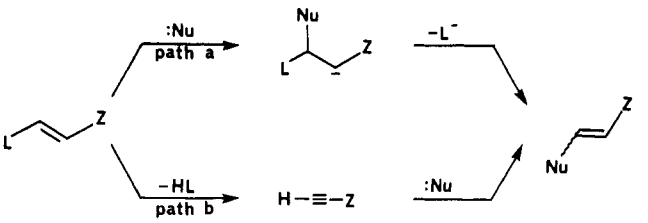
Selenoxides **2**, obtained from the selenosulfonation and peracid oxidation of acetylenes, reacted with various nucleophiles to afford the products of overall substitution of the PhSeO moiety. Anions of dimethyl malonate, ethyl acetoacetate, malononitrile, 1-(trimethylsilyl)propyne, 1,3-dithiane, and KCN were successfully employed in this manner, producing γ-sulfonyl-substituted α,β-unsaturated dicarbonyls **6**, **7**, **12**, and **14**, dinitrile **8**, enynes **9** and **16**, ketene dithioacetal **10**, and β-cyanovinyl sulfone **13**, respectively. The reaction proceeds chiefly by elimination of the selenoxide to an acetylenic or allenic sulfone, followed by Michael addition of the nucleophile, and isomerization of the double bond to the corresponding allylic sulfone. Weak nucleophiles such as the conjugate bases of nitromethane or acetylacetone failed to undergo Michael addition and resulted in the isolation of the unaltered acetylenic or allenic sulfone intermediate.

Vinylic compounds containing an electron-withdrawing or -delocalizing group Z and a leaving group L in the β-position undergo overall substitution when treated with suitable nucleophiles[2] (Scheme I). In general, the mechanism consists of a Michael addition followed by β-elimination (addition–elimination, path a) or by elimination to an intermediate acetylene which then functions as a Michael acceptor in a subsequent addition step (elimination–addition, path b).

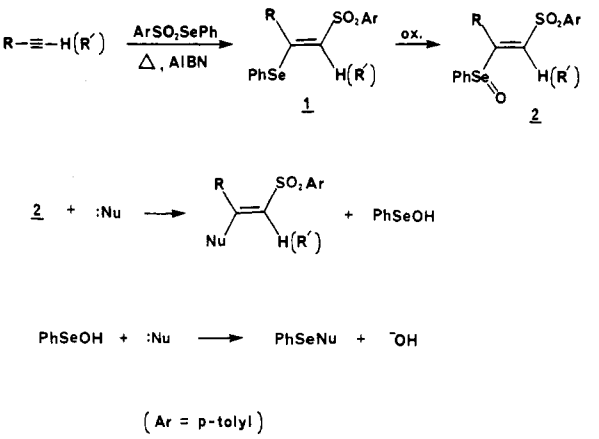
β-(Phenylseleno)vinyl sulfones **1** and their selenoxides **2** are readily available from the free-radical selenosulfonation of acetylenes.[3] The sulfone group of such compounds is expected to stabilize an adjacent carbanion,[4] and the selenolate,[5] or the potentially more reactive selenoxide moiety, should function as a leaving group (i.e., Z = SO_2Ar and L = SePh or OSePh) in path a of Scheme I. Moreover, selenoxides **2** are known to eliminate to acetylenic sulfones,[3a,c] which in turn have been reported to act as Michael acceptors with various nucleophiles.[6] This suggests that path b might also prove viable with selenoxides **2**. This realization prompted us to investigate the possibility of performing overall substitutions such as those depicted in a general sense in Scheme I with compounds **1** and **2**.

To date, we have observed that alcohols[3a] and amines[7] are capable of effecting such reactions with selenoxides **2**, affording enol ethers **3** or ketals **4** (from a second Michael addition to **3**) and enamines **5**, respectively. Extension of the procedure to carbon-centered nucleophiles[8] would be of particular synthetic value as the overall sequence shown

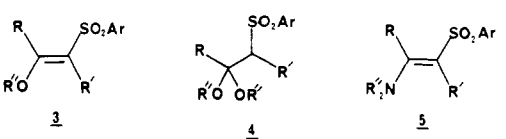
Scheme I



Scheme II



in Scheme II would permit the formation of a new carbon-carbon bond at the 2-position of an acetylenic precursor. We now report our results in this area.



Results and Discussion

Substitution Reactions. Initial experiments in which β-selenovinyl sulfones **1** were treated with a variety of carbon nucleophiles proved fruitless as only the unreacted starting materials or the corresponding allylic sulfone isomers could be isolated. Consequently, we turned our attention to the selenoxide derivatives **2**, which proved considerably more reactive. The results are summarized

(1) We gratefully acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada.

(2) For reviews, see: (a) Rappoport, Z. In *Advances in Physical Organic Chemistry*; Gold, V., Ed.; Academic Press: New York, 1969; Vol. 7, pp 1–114. (b) Patai, S.; Rappoport, Z. *The Chemistry of Alkenes*; Patai, S., Ed.; Wiley: New York, 1964; pp 525–546. (c) Modena, G. *Acc. Chem. Res.* **1971**, *4*, 73.

(3) (a) Back, T. G.; Collins, S.; Kerr, R. G. *J. Org. Chem.* **1983**, *48*, 3077. (b) Back, T. G.; Collins, S.; Gokhale, U.; Law, K.-W. *Ibid.* **1983**, *48*, 4776. (c) Miura, T.; Kobayashi, M. *J. Chem. Soc., Chem. Commun.* **1982**, 438.

(4) Block, E. *Reactions of Organosulfur Compounds*, Academic Press: New York, 1978; Chapter 2.

(5) Marshall, D. R.; Thomas, P. J. Stirling, C. J. M. *J. Chem. Soc., Perkin Trans 2* **1977**, 1898.

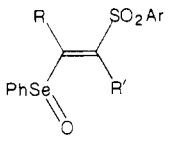
(6) For recent examples, see: (a) Bury, A.; Joag, S. D.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1986**, 124. (b) Ohnuma, T.; Hata, N.; Fujiwara, H.; Ban, Y. *J. Org. Chem.* **1982**, *47*, 4713.

(7) Back, T. G.; Collins, S.; Law, K.-W. *Can. J. Chem.* **1985**, *63*, 2313.

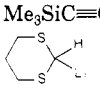
(8) For the formally related substitution reactions of selenides **1** with organocuprates, see the preceding paper.

0022-3263/87/1952-4265$01.50/0

Table I. Reactions of Nucleophiles with Selenoxides 2[a]

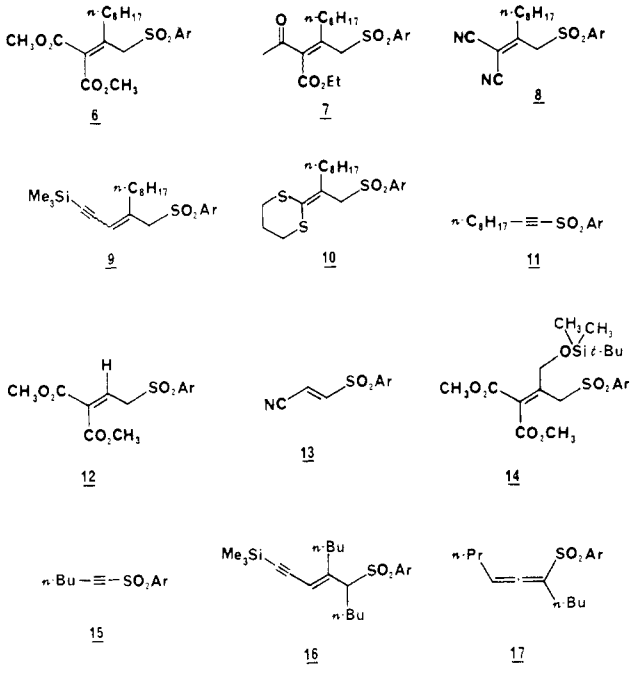


2

entry	selenoxide no.	R	R′	nucleophile[b]	conditions[c] temp	time (h)	product no.	yield (%)[d]
1	**2a**	n-C_8H_{17}	H	$Na^+{}^-CH(CO_2Me)_2$	rt	16	**6**	71
2	**2a**			$Na^+CH_3(O)C^-CHCO_2Et$	rt	1	**7**	71
3	**2a**			$Na^+{}^-CH(CN)_2$	rt	1	**8**	42
4	**2a**			$Me_3SiC{\equiv}CCH_2Li$	rt	2	**9**	84
5	**2a**				−25 °C	1.5	**10**	37
6	**2a**			$Na^+{}^-CH_2NO_2$	0 °C	0.75	**11**	88
7	**2a**			$CH_3(O)C^-CHC(O)CH_3\,Na^+$	rt	1	**11**	89
8	**2b**	H	H	$Na^+{}^-CH(CO_2Me)_2$[e]	rt	1	**12**	87
9	**2b**			KCN[f,g]	rt	2	**13**	56
10	**2c**	CH_2OSiMe_2-t-Bu	H	$Na^+{}^-CH(CO_2Me)_2$	rt	1	**14**	72
11	**2d**	n-Bu	H	KCN[f]	rt	2.5	**15**	82
12	**2e**	n-Bu	n-Bu	$Me_3SiC{\equiv}CCH_2Li$	−70 °C	0.5	**16**	79
13	**2e**			$Na^+CH_3(O)C^-CHCO_2Et$	rt	16	**17**	85
14	**2e**			$Na^+{}^-CH_2NO_2$	0 °C	0.75	**17**	81

[a] Ar = p-tolyl. [b] Two molar equivalents of the nucleophile were employed unless otherwise indicated. [c] All reactions were performed in THF solution; rt = room temperature. [d] Isolated yields are reported. [e] Three equivalents of the nucleophile were employed. [f] Ten equivalents of KCN were employed along with a catalytic amount of 18-crown-6. [g] We thank K.-W. Law for this result: Law, K.-W., M.S. Thesis, University of Calgary, 1985, p 65.

Chart I



in Table I; the structures of the products **6–17** are shown in Chart I.

The required selenoxides **2** were prepared fresh for each experiment by the m-chloroperbenzoic acid (MCPBA) oxidation of the precursor selenides. Although the selenoxides are generally stable enough to isolate, they undergo selenoxide elimination slowly at room temperature and rapidly at elevated temperatures or in the presence of base.[3a]

In general, a twofold or greater excess of the nucleophile was employed as the substitution reaction shown in Scheme II produces benzeneselenenic acid (PhSeOH) as a byproduct. Since this compound[9] is capable of reacting with various nucleophiles, up to 1 equiv of the latter can thus be consumed unproductively. In some cases, byproducts were observed with spectral properties consistent with the structures of the expected selenenylated nucleophiles, but were not investigated further.

The reactions of selenoxides **2** with active methylene compounds gave generally good yields of the desired substitution products **6–8**, **12**, and **14** (entries 1–3, 8, and 10). In each case, isomerization of the double bond occurred to permit conjugation with the carbonyl or cyano groups, resulting in allylic instead of vinylic sulfone products. Similarly, the propargyllithium reagent in entries 4 and 12 furnished the corresponding enynes **9** and **16**. The former product was obtained as a separable 71:29 mixture of geometric isomers **9a** and **9b**, whereas the latter appeared to be homogeneous. The dithiane anion afforded the ketene dithioacetal **10**, albeit in modest yield (entry 5). Further investigation of this reaction revealed that reduction of selenoxide **2a** (R = n-C_8H_{17}, R′ = H) was taking place at the expense of substitution to produce the selenide **1a** and, presumably, sulfoxide derivatives of the dithiane. No improvement resulted when 2-lithio-2-(trimethylsilyl)-1,3-dithiane was used in place of 2-lithio-1,3-dithiane in entry 5. Similarly, we observed that **2a** was reduced quantitatively to **1a** by benzenethiol, which was itself converted to diphenyl disulfide.[10]

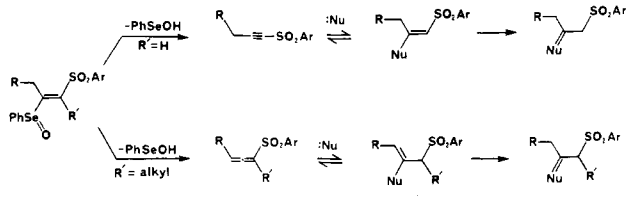
Milder nucleophiles derived from relatively strong conjugate acids such as nitromethane (pK_a = 10.2)[11] and acetylacetone (pK_a = 9)[12] failed to effect substitution with

(9) Electrophilic behavior ascribed to selenenic acids may actually be due to the corresponding anhydrides or to other disproportionation intermediates: (a) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697. (b) Hori, T.; Sharpless, K. B. *Ibid.* **1978**, *43*, 1689. (c) Reich, H. J.; Willis, W. W., Jr.; Wollowitz, S. *Tetrahedron Lett.* **1982**, *23*, 3319. (d) Kice, J. L.; McAfee, F.; Slebocka-Tilk, H. *Ibid.* **1982**, *23*, 3323.

(10) The oxidation of thiols to disulfides with bis(p-methoxyphenyl) selenoxide has been reported: Ogura, F.; Yamaguchi, H.; Otsubo, T.; Tanaka, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 641.

(11) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 61.

Scheme III



selenoxide **2a**, and only the corresponding acetylenic sulfone elmination product **11** was isolated (entries 6 and 7). Potassium cyanide proved to be a marginal nucleophile, affording the desired β-cyanovinyl sulfone **13** in moderate yield from the unsubstituted selenoxide **2b** (R = R′ = H) (entry 9) but providing only the acetylenic sulfone **15** from the more hindered selenoxide **2d** (R = *n*-Bu, R′ = H) (entry 11). Very strong nucleophiles such as alkyllithiums or the dianion of ethyl acetoacetate[13] gave complex mixtures of products with **2a**, which were not further investigated. Surprisingly, however, several moderately powerful nucleophiles such as acetylides, ketone enolates, and α-metalated nitriles also afforded complex product mixtures of little synthetic utility.

Since selenoxides **2a–d** were all derived from terminal acetylenes, we investigated selenoxide **2e** (R = R′ = *n*-Bu), in order to determine whether substitution reactions could also be performed on substrates obtained from disubstituted acetylenes. Our results indicate that relatively strong nucleophiles such as the metalated propargyllithium in entry 12 react in the desired sense, affording the substitution product **16** in good yield. However, the enolate of ethyl acetoacetate, which had been successfully employed with selenoxide **2a** in entry 2, produced only the allenic sulfone elimination product **17** with **2e** (entry 13) and not the corresponding substitution product. The same result occurred with the nitromethane anion Na^+–CH_2NO_2 (entry 14). Evidently, weak and even moderate nucleophiles are not suitable for substitution reactions with more highly substituted selenoxides such as **2e**.

Mechanism. Scheme I presents two general mechanisms for overall substitution reactions such as those summarized in Table I. Previous work has demonstrated that the elimination of selenoxides **2**, when they are derived from terminal acetylenes, to acetylenic sulfones is relatively facile,[3a,c] particularly under basic conditions such as those employed here.[3a] Indeed, in the case of entries 6, 7, and 11, the acetylenic sulfones **11** and **15** were the principal isolated products. It is therefore evident that much, and possibly all, of the selenoxide reacts by elimination in the initial step. In order to test the feasibility of the second step, which involves the Michael addition of the nucleophile to the acetylenic sulfone, we performed a simple control experiment. The enolate of dimethyl malonate was treated with an authentic sample of acetylenic sulfone **11** under conditions simulating those of entry 1, and the same product **6** was isolated in 98% yield. We therefore conclude that under the conditions of Table I, the starting selenoxides react mostly, and possibly exclusively, by the elimination–addition mechanism shown in Scheme III, analogous to path b in Scheme I.[14] The failure of species that are weaker nucleophiles (or better leaving groups) to form substitution products (entries 6, 7, and 11) can then be attributed to their inability to react with the initially produced acetylenic sulfones or to an unfavourable equilibrium in the Michael addition step.

Similar considerations apply to selenoxide **2e**, which is derived from a disubstituted acetylene. Although this compound cannot produce an acetylenic sulfone by elimination because of the absence of a vinylic hydrogen atom, its elmination to the allenic sulfone **17** has been previously reported.[3b] A control experiment demonstrated that **17** reacts with the nucleophile $Me_3SiC{\equiv}CCH_2Li$ under the same conditions as those employed in entry 12 in Table I to afford the same product **16** in 86% yield. These results again point to an elimination–addition sequence as the principal pathway for product formation (Scheme III).

Although the one-pot conversion of selenoxides **2** to the substitution products in Table I is particularly convenient, it is evident that these products can be similarly prepared from acetylenic or allenic sulfones obtained from other sources.[6]

Conclusions. Acetylenes can be conveniently converted to γ-sulfonyl-substituted α,β-unsaturated dicarbonyls and dinitriles, enynes, and ketene dithioacetals by the sequence of selenosulfonation, oxidation to selenoxides **2**, and reaction with appropriate carbo-centered nucleophiles. Evidence suggests that the overall substitution of selenoxides **2** proceeds mainly by an elimination–addition mechanism, followed by isomerization of the vinyl sulfone moiety to the corresponding allylic sulfone.

Experimental Section

Spectroscopic instruments and chromatographic (GC and preparative TLC) methods were as described in the preceding article. Tetrahydrofuran was freshly distilled from lithium aluminum hydride before each experiment and all reactions were carried out under argon. The nucleophiles in entries 1–3, 6–8, 10, 13, and 14 are prepared by treating the corresponding conjugate acid with sodium hydride in THF, whereas those in entries 4, 5, and 12 were generated from the reaction of 1,3-dithiane[15] or 1-(trimethylsilyl)propyne[16] with *n*-butyllithium in THF. β-(Phenylseleno)vinyl sulfones **1a**, **1b**, and **1e** were obtained according to previously published procedures.[3] Compounds **1c** and **1d** were prepared as described below. All other reagents were purchased from commercial sources and purified by standard methods as necessary.

(*E*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-(phenylseleno)-3-(*p*-tolylsulfonyl)-2-propene (1c). Propargyl alcohol was converted to its *tert*-butyldimethylsilyl ether by the method of Corey and Venkateswarlu.[17] The silyl ether (3.40 g, 20 mmol) and *Se*-phenyl *p*-tolueneselenosulfonate (6.22 g, 20 mmol) were refluxed 30 h in 30 mL of benzene. Small portions (ca. 10 mg) of azobis(isobutyronitrile) (AIBN) were added at intervals of 8 h. The reaction mixture was then filtered through Celite to remove a small amount of insoluble material, evaporated in vacuo, and crystallized from hexane and then ethanol to afford 7.79 g (81%) of **1c**: mp 104–105 °C; IR (Nujol) 1595, 1570, 1308, 1147 cm^{-1}; ^1H NMR (200 MHz) δ 7.6–7.3 (complex, 9 H), 5.52 (t, J = 2.2 Hz, 1 H), 5.01 (d, J = 2.2 Hz, 2 H), 2.41 (s, 3 H), 0.94 (s, 9 H), 0.12 (s, 6 H); mass spectrum, m/e (relative intensity) 482 (M^+, ^{80}Se, <1), 480 (M^+, ^{78}Se, <1), 467 ($M^+ - CH_3$, ^{80}Se, 1.2), 465 ($M^+ - CH_3$, ^{78}Se, <1), 425 ($M^+ - t$-Bu, ^{80}Se, 77), 423 ($M^+ - t$-Bu, ^{78}Se, 42), 149 (100). Anal. Calcd for $C_{22}H_{30}O_3SSeSi$: C, 54.86; H, 6.28. Found: C, 55.06; H, 6.19.

(*E*)-2-(Phenylseleno)-1-(*p*-tolylsulfonyl)-1-hexene (1d). The preceding procedure was employed to produce the title compound in 81% yield: mp 61–62.5 °C (from hexane); IR (KBr) 1596, 1567, 1314, 1304, 1141 cm^{-1}; ^1H NMR (200 MHz) δ 7.7–7.3 (complex, 9 H), 5.86 (s, 1 H), 2.84 (t, J = 8 Hz), 2.43 (s, 3 H), 1.65–1.25 (complex, 4 H), 0.90 (t, J = 7 Hz, 3 H); mass spectrum,

(12) Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439.
(13) Weiler, L. *J. Am. Chem. Soc.* **1970**, *92*, 6702.
(14) On the basis of this evidence, we cannot rule out the possibility that some of the product arises from a competing addition–elimination pathway.
(15) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075.
(16) Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041.
(17) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

m/e (relative intensity) 394 (M^+, ^{80}Se, 3), 392 (M^+, ^{78}Se, 2), 157 ($Ph^{80}Se^+$, 58), 155 ($Ph^{78}Se^+$, 34), 91 ($C_7H_7^+$, 100). Anal. Calcd for $C_{19}H_{22}O_2SSe$: C, 58.01; H, 5.65. Found: C, 58.46; H, 5.71.

Selenoxides 2a–e. All selenoxides were prepared according to the following procedure. The corresponding selenide and 1.3 molar equiv of MCPBA were stirred in dichloromethane solution for 15 min. The solution was then rapidly washed with aqueous K_2CO_3 and water, and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo to afford the crude selenoxide, which was suitable for further use.

Reactions of Nucleophiles with Selenoxides 2 (see Table I). In general, the nucleophile in THF solution was cooled to −30 °C or −78 °C and the selenoxide in THF was added via syringe. The solution was warmed to the temperature shown in the table and stirred for the indicated time. The reaction was then quenched with water, and the solution was washed with aqueous NaCl, dried over anhydrous $MgSO_4$, and evaporated in vacuo. Details of purification procedures as well as spectral and analytical data for the products are given below. A typical procedure for the preparation of diester **6** is provided in detail.

Typical Procedure. Diester 6 (Entry 1). Sodium hydride (25 mg, 0.50 mmol) in 1 mL of THF was cooled to −30 °C. Dimethyl malonate (57 μL, 0.50 mmol) was added via syringe. Selenoxide **2a**, prepared from selenide **1a** (112 mg, 0.25 mmol), in 2 mL of THF was added. The reaction mixture was stirred at −30 °C for 1.5 h, at which time TLC indicated chiefly starting material to be present. The solution was then stirred for 16 h at room temperature, washed with aqueous NaCl, dried ($MgSO_4$), and evaporated in vacuo. Preparative TLC (15% ethyl acetate–hexane) afforded 75 mg (71%) of the diester **6** as a colorless oil, R_f 0.34: IR (Film) 1730, 1630, 1595, 1323, 1152 cm^{-1}; ^1H NMR (200 MHz) δ 7.77 (d, J = 8 Hz, 2 H), 7.34 (d, J = 8 Hz, 2 H), 4.62 (s, 2 H), 3.79 (s, 3 H), 3.50 (s, 3 H), 2.44 (s, superimposed on t, J = 7 Hz, total 5 H), 1.3 (complex, 12 H), 0.88 (crude t, 3 H); mass spectrum, m/e (relative intensity) 424 (M^+, 1.4), 269 ($M^+ - SO_2Ar$, 35), 91 ($C_7H_7^+$, 100). Anal. Calcd for $C_{22}H_{32}O_6S$: C, 62.23; H, 7.61. Found: C, 62.51; H, 7.47.

Keto Ester 7 (Entry 2). The product was isolated as an inseparable mixture of E/Z isomers by preparative TLC in benzene to give a colorless oil, R_f 0.17: IR (film) 1722, 1703, 1622, 1598, 1321, 1304, 1153, 1133 cm^{-1}; ^1H NMR (200 MHz) δ 7.79 (complex, 2 H), 7.35 (d, J = 8 Hz, 2 H), 4.65 and 4.43 (two singlets with ratio of intensity 3:2, total 2 H), 4.29 and 3.98 (two quartets, J = 7 Hz, integrating in the ratio of 2:3, total 2 H), 2.45 (s superimposed on m), 2.29 (s superimposed on m), 2.04 (s, total integrated intensity for signals at δ 2.45–2.04 = 8 H), 1.2 (complex, superimposed on t at δ 1.17, J = 7 Hz, total 15 H), 0.88 (crude t, 3 H); mass spectrum, m/e (relative intensity) 267 ($M^+ - SO_2Ar$, 46), 91 ($C_7H_7^+$, 53), 43 (100); chemical ionization (NH_3), 423 ($M^+ + 1$, 82); exact mass calcd for $M^+ - SO_2Ar$, $C_{16}H_{27}O_3$ 267.1960, found 267.1946.

Dinitrile 8 (Entry 3). The product was isolated by preparative TLC in benzene as a viscous pale yellow oil, R_f 0.32; GC purity, 94%: IR (film) 2234, 1596, 1331, 1154 cm^{-1}; ^1H NMR (200 MHz) δ 7.79 (d, J = 8 Hz, 2 H), 7.44 (d, J = 8 Hz, 2 H), 4.26 (s, 2 H), 2.86 (t, J = 8 Hz, 2 H), 2.50 (s, 3 H), 1.6 (m, 2 H), 1.3 (complex, 10 H), 0.89 (crude t, 3 H); mass spectrum, m/e (relative intensity) 358 (M^+, 0.5), 155 ($ArSO_2^+$, 100), 91 ($C_7H_7^+$, 98); exact mass calcd for $C_{20}H_{26}N_2SO_2$ 358.1715, found 358.1718.

Enyne 9 (Entry 4). The product was obtained as a 71:29 mixture of geometric isomers and separated by preparative TLC in 15% ethyl acetate–hexane. The major isomer was a pale yellow oil, R_f 0.42; GC purity, 95%: IR (film) 2130, 1598, 1320, 1151, 1134 cm^{-1}; ^1H NMR (200 MHz) δ 7.74 (d, J = 8 Hz, 2 H), 7.35 (d, J = 8 Hz, 2 H), 5.24 (s, 1 H), 3.77 (s, 2 H), 2.46 (s, 3 H), 2.40 (t, J = 7 Hz, 2 H), 1.3 (complex, 12 H), 0.88 (crude t, 3 H), 0.18 (s, 9 H); mass spectrum, m/e (relative intensity) 404 (M^+, 3), 91 ($C_7H_7^+$, 72), 73 (100); exact mass calcd for $C_{23}H_{36}O_2SSi$ 404.2205, found 404.2209.

The minor isomer was a colorless oil, R_f 0.54; GC purity, 97% IR (film) 2129, 1598, 1322, 1154, 1133 cm^{-1}; ^1H NMR (200 MHz) δ 7.73 (d, J = 8 Hz, 2 H), 7.29 (d, J = 8 Hz, 2 H), 5.45 (s, 1 H), 4.14 (s, 2 H), 2.42 (s, 3 H), 2.37 (t, J = 7 Hz, 2 H), 1.3 (complex, 12 H), 0.86 (crude t, 3 H), 0.10 (s, 9 H); mass spectrum, m/e (relative intensity) 404 (M^+, 3), 91 ($C_7H_7^+$, 44), 73 (100); exact mass calcd for $C_{23}H_{36}O_2SSi$ 404.2205, found 404.2208.

Ketene Dithioacetal 10 (Entry 5). The product was isolated by preparative TLC in 15% ethyl acetate–hexane as a pale yellow oil, R_f 0.34: IR (film) 1651, 1597, 1568, 1317, 1301, 1151, 1131 cm^{-1}; ^1H NMR (200 MHz) δ 7.77 (d, J = 8 Hz, 2 H), 7.33 (d, J = 8 Hz, 2 H), 4.18 (s, 2 H), 2.84 (t, J = 6 Hz, 2 H), 2.60 (t, J = 6.5 Hz, 2 H), 2.45 (s, superimposed on t, total 5 H), 2.00 (m, 2 H), 1.3 (complex, 12 H), 0.88 (crude t, 3 H); mass spectrum, m/e (relative intensity) 257 ($M^+ - SO_2Ar$, 83), 159 (93), 91 ($C_7H_7^+$, 95), 41 (100). Anal. Calcd for $C_{21}H_{32}O_2S_3$: C, 61.11; H, 7.83. Found: C, 61.18; H, 7.71.

1-(*p*-Tolylsulfonyl)-1-decyne (11) (Entries 6 and 7). The product was isolated by flash chromatography on silica gel, elution with dichloromethane, and identified by comparison (IR, NMR) with an authentic sample.[3a]

Diester 12 (Entry 8). When the reaction mixture in THF was washed with aqueous NaCl in the usual manner, much of the product was extracted into the aqueous phase. The latter was then acidified to pH ~ 3 with aqueous HCl and extracted several times with ether. The combined organic extracts were dried over anhydrous $MgSO_4$ and evaporated to afford the crude product as a colorless oil. Attempts to further purify the product by chromatography or bulb-to-bulb distillation resulted in decomposition. The crude product had the following: IR (film) 1732, 1651, 1597, 1322, 1286, 1146 cm^{-1}; ^1H NMR (200 MHz) δ 7.67 (d, J = 8 Hz, 2 H), 7.29 (d, J = 8 Hz, 2 H), 6.91 (t, J = 8 Hz, 1 H), 4.18 (d, J = 8 Hz, 2 H), 3.72 (s, 3 H), 3.59 (s, 3 H), 2.38 (s, 3 H) [Impurity signals were observed at δ 3.71 and 3.68, integrating at ca. 10% of those at 3.72 and 3.59.]; mass spectrum, m/e (relative intensity) 312 (M^+, 4), 281 (M^+ – OMe, 100); exact mass calcd for $C_{14}H_{16}O_6S$ 312.0668, found 312.0682.

(*E*)-3-(*p*-Tolylsulfonyl)propenenitrile (13) (Entry 9).[18] The product was isolated by preparative TLC in 50% ethyl acetate–hexane, R_f 0.61, mp 128–132 °C (lit.[18a] mp 132–134 °C), and was identical with an authentic sample.

Diester 14 (Entry 10). The product was isolated by preparative TLC in 18% ethyl acetate–hexane as a colorless oil, R_f 0.29: IR (film) 1728, 1640, 1597, 1324, 1155, 1125 cm^{-1}; ^1H NMR (200 MHz) δ 7.76 (d, J = 8 Hz, 2 H), 7.34 (d, J = 8 Hz, 2 H), 4.77 (s, 2 H), 4.39 (s, 2 H), 3.79 (s, 3 H), 3.56 (s, 3 H), 2.44 (s, 3 H), 0.89 (s, 9 H), 0.06 (s, 6 H); mass spectrum, m/e (relative intensity) 399 ($M^+ - t$-Bu, 47), 243 (75), 91 ($C_7H_7^+$, 78), 89 (100). Anal. Calcd for $C_{21}H_{32}O_7SSi$: C, 55.24; H, 7.08. Found: C, 55.05; H, 7.42.

1-(*p*-Tolylsulfonyl)-1-hexyne (15) (Entry 11). The product was isolated by preparative TLC in 17% ethyl acetate–hexane as a colorless oil, R_f 0.41; GC purity, >99%: IR (film) 2201, 1596, 1330, 1160 cm^{-1}; ^1H NMR (200 MHz) δ 7.88 (d, J = 8 Hz, 2 H), 7.37 (d, J = 8 Hz, 2 H), 2.46 (s, 3 H), 2.36 (t, J = 7 Hz, 2 H), 1.6–1.2 (complex, 4 H), 0.88 (t, J = 7 Hz, 3 H); mass spectrum, m/e (relative intensity) 236 (M^+, 50), 155 ($ArSO_2^{\bullet+}$, 62), 139 (92), 91 ($C_7H_7^+$, 100); exact mass calcd for $C_{13}H_{16}O_2S$ 236.0871, found 236.0870.

Enyne 16 (Entry 12). The product was isolated by preparative TLC in benzene as a pale yellow oil, R_f 0.40; GC purity, >90%: IR (film) 2132, 1598, 1316, 1303, 1147, 1108 cm^{-1}; ^1H NMR (200 MHz) δ 7.70 (d, J = 8 Hz, 2 H), 7.33 (d, J = 8 Hz, 2 H), 5.41 (s, 1 H), 3.56 (dd, J = 11, 3.5 Hz, 1 H), 2.45 (s, 3 H), 2.0 (m, 2 H), 1.65 (m, 2 H), 1.3 (complex, 8 H), 0.9 (complex, 6 H), 0.19 (s, 9 H); mass spectrum, m/e (relative intensity) 404 (M^+, <1), 249 ($M^+ - SO_2Ar$, 21), 91 ($C_7H_7^+$, 30), 73 (100); chemical ionization (NH_3), 405 ($M^+ + 1$, 22); exact mass calcd for $M^+ - SO_2Ar$ $C_{16}H_{29}Si$ 249.20385, found 249.2034.

6-(*p*-Tolylsulfonyl)-4,5-decadiene (17) (Entries 13 and 14). The product was isolated by either flash chromatography over silica gel, elution with dichloromethane, or by preparative TLC in benzene, R_f 0.29. It was identified by comparison with an authentic sample[3b] (IR, NMR).

Control Experiments. Reaction of 1-(*p*-Tolylsulfonyl)-1-decyne (11) with the Enolate of Dimethyl Malonate. The acetylenic sulfone 11 (73 mg, 0.25 mmol) was treated with the enolate of dimethyl malonate (0.50 mmol) under same conditions as in entry 1 of the table. The reaction was then worked up as in entry 1 to afford 104 mg (98%) of the diester **6**, identical in

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all respects with the previous sample.

Reaction of 6-(*p*-Tolylsulfonyl)-4,5-decadiene (17) with $Me_3SiC{\equiv}CCH_2Li$. The allenic sulfone **17** (73 mg, 0.25 mmol) was treated with 0.50 mmol of the nucleophile under the same conditions as in entry 12 of the table. The same workup then furnished 87 mg (86%) of enyne **16**, indentical in all respects with the previous sample.

Registry No. **1a**, 86409-85-0; **1b**, 86409-89-4; **1c**, 108895-55-2; **1d**, 108918-97-4; **1e**, 87517-80-4; **2a**, 86409-98-5; **2b**, 86409-95-2; **2c**, 108895-56-3; **2d**, 108895-57-4; **2e**, 87517-81-5; **6**, 108895-58-5; (*E*)-**7**, 108895-59-6; (*Z*)-**7**, 108895-60-9; **8**, 108895-61-0; (*E*)-**9**, 108895-62-1; (*Z*)-**9**, 108895-63-2; **10**, 108895-64-3; **11**, 86409-91-8; **12**, 108895-65-4; **13**, 19542-67-7; **14**, 108895-66-5; **15**, 108895-67-6; **16**, 108895-68-7; **17**, 87517-82-6; $CH{\equiv}CCH_2OSi(Bu\text{-}t)Me_2$, 76782-82-6; $(MeO_2C)_2CH_2$, 108-59-8; $AcCH_2CO_2Et$, 141-97-9; $CH_2(CN)_2$, 109-77-3; $Me_3SiC{\equiv}CMe$, 6224-91-5; $SCH_2S(CH_2)_2CH_3$, 505-23-7; KCN, 151-50-8; NO_2Me, 75-52-5; Ac_2CH_2, 123-54-6; 1-hexyne, 693-02-7.

Sulfur-Bridged Cyclodecenones from Thioaldehyde Diels–Alder Adducts

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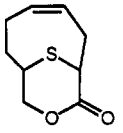
The adduct **7** of cyanothioformaldehyde with 2-(*tert*-butyldimethylsiloxy)-1,3-butadiene has been converted into allylic halides **15** and **20**. Upon heating with $NaI/K_2CO_3/CH_3CN$, the halides alkylate sulfur internally. The resulting sulfonium salts are deprotonated to give the ylides **30** or **28**, and 2,3-sigmatropic rearrangement affords the title compounds **21–23**. In the case of **20**, a single sulfur-bridged *Z*-cyclodecenone **23** is formed in 90% yield, while **15** gives a mixture of olefin *E,Z* isomers. This difference is attributed to conformational preferences of the more highly substituted olefin in ylide **28**. Efficient conversion of **23** into the monocyclic (*Z*)-4-methyl-8-(methylthio)cyclodec-4-enone (**25**) by S-methylation and zinc reduction is also reported.

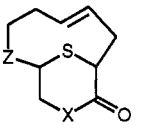
Medium-sized rings are accessible from cyclic sulfides by reactions that bridge the α and α' carbons of the sulfide with a carbon chain.[1-3] One technique for achieving this result is illustrated by the 2,3-sigmatropic shift of bicyclic sulfonium ylides **2** derived from sulfides **1**. The rearrangements to sulfur-bridged lactones **3** or **4** are interesting in the context of ylide stereochemistry and in principle could be used to make the parent medium rings by cleavage of carbon–sulfur bonds. However, the yields of

1 a X = O, Z = CH_2; b X = O, Z = bond; c X = CH_2, Z = CHOAc; d X = CH_2, Z = bond

2



3



4 X = O, Z = bond

5 X = CH_2, Z = CHOAc

3 or **4** are not high enough for preparative applications.[3] Somewhat better results are obtained with a carbocyclic periphery in the ylide, and **2c** affords the bridged cycloundecenone **5** in 60% yield.[2b] This technique has also been applied to highly complex substrates for cytochalasin synthesis with similar efficiency in the ring-expansion step.[2a] Further extensions to sulfur-bridged 10-membered carbocycles are of interest in the context of terpenoid target structures having the cyclodecane skeleton. To evaluate the potential of this approach, we have examined two representative substrates, which are the subject of this paper.

Previous efforts had not been able to identify the variables responsible for the relatively efficient rearrangement of **2c** vs. lactones **2a,b** (60% yield vs. 30%). Difficulties with **2a,b** could have been due to the sensitivity of the bridged, somewhat strained product to the reaction conditions (K_2CO_3/CH_3CN at 70 °C).[3] However, there remained the possibility that the improved behavior of **2c** was anomalous due to some conformational effect of the acetoxy substituent that had been incorporated to approximate the functionality of intermediates in cytochalasin synthesis.[2] To rule out this possibility in the 10-membered carbocycle series, we opted to study the unsubstituted ylide **2d**.

Preparation of starting materials begins with the known thioaldehyde adduct **7** (from NCCH=S + 2-siloxybutadiene).[4] A slight variation of the previously described method via photochemically induced fragmentation of phenacyl sulfide **6** was necessary for preparative-scale synthesis of **7**. The original method used tediuos chromatographic purification to remove acetophenone. To avoid this procedure, the mixture of **7** + acetophenone was reduced to aldehyde **8** (+ 1-phenylethanol) and converted into the Wittig product **9** without purification of inter-

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