A New Synthetic Route to Vinyl Sulfides Utilizing the Reaction of (Phenylthio)carbenes with Nitrile Anions

Toshiro Harada, Akio Karasawa, and Akira Oku*

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

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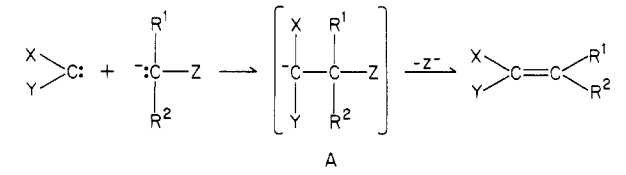
Reactions of nitrile anion ($LiCR^2R^3CN$) and (phenylthio)carbenes generated from 1-chloroalkyl phenyl sulfides ($R^1CH(Cl)SPh$) **2a–e** by the action of *n*-BuLi have been shown to be a useful synthetic route to vinyl sulfides ($PhSC(R^1)=CR^2R^3$) **3a–k** (34–91%). The nucleophilic attack of the nitrile anion on the carbenic species gave the presumed intermediate β-(phenylthio)-β-lithionitrile, which eliminated LiCN to give the expected vinyl sulfides. The application of the present reaction to the synthesis of cyclic vinyl sulfides was successful: the decomposition of the dianion of ω,ω-bis(phenylthio)alkanenitriles (**8b**, **8c**, **11**, and **14**) affording the corresponding 1-(phenylthio)cycloalkenes (**9**, **10**, **12**, and **15**) in 12–87% yields.

It is well-known that a variety of nucleophiles undergo addition reactions to carbenes (or carbenoids).[1] Among these, the addition of carbanions is of special importance for synthetic applications. However, there have been few reports on the utilization of this type of reaction.[2] This is partly due to the fact that the addition of a carbanion to carbenes (or carbenoids) generates another reactive nucleophile and hence it is difficult to control the initial reaction. In this context, we envisioned that the reaction of carbenic species with a carbanion bearing a suitable functional group Z, which not only stabilizes the anion but also serves as a good leaving group, would give the initial adduct A and that a facile elimination reaction would follow to give the corresponding olefin (Scheme I).[3,4]

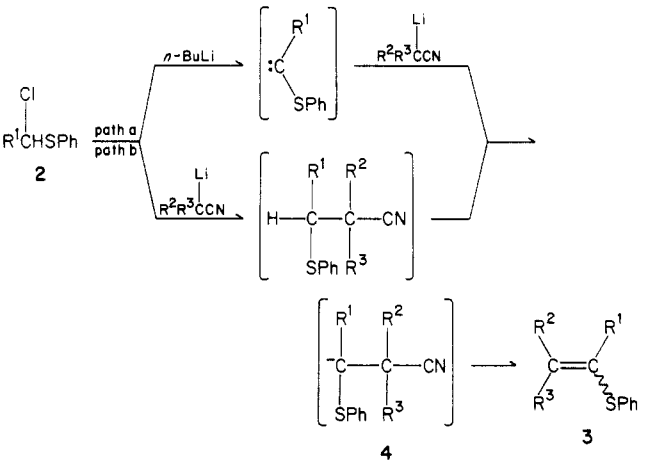
We report here the realization of the above scheme in the reaction of (phenylthio)carbenes (X = PhS, Y = alkyl)[4,5] with nitrile anions (Z = CN).[6] The reaction provides a new route to vinyl sulfides, which are useful synthetic intermediates.[7]

Scheme I



A

Scheme II

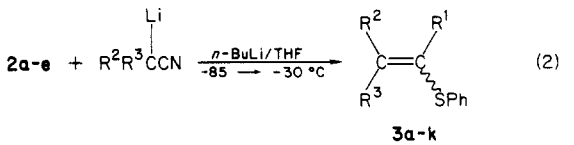


Results and Discussion

Intermolecular Reaction of Nitrile Anions with (Phenylthio)carbenes. Alkyl phenyl sulfides **1a–e** were converted quantitatively to the corresponding chlorides **2a–e** by the reaction with *N*-chlorosuccinimide (NCS) in CCl_4 (eq 1). A mixture of the chloride **2a–e** and a nitrile anion (2 equiv) in tetrahydrofuran (THF) was treated with *n*-BuLi at −85 °C and was gradually warmed up to −40 °C over a period of 3 h. After aqueous workup followed by silica gel chromatography, the corresponding vinyl sulfide **3a–k** was isolated in 34–91% yield (eq 2). The results of the reactions of various sulfides with nitriles are summarized in Table I.

(1)

a, R^1=H; **b**, R^1=Me; **c**, R^1=Et; **d**, R^1=*n*-Pr; **e**, R^1=Ph



(2)

The reactions of aryl-substituted acetonitrile anions generally proceeded efficiently. For example, the reaction of phenylacetonitrile anion and α-naphthylacetonitrile anion with 1-chloropropyl phenyl sulfide (**2c**) gave the corresponding vinyl sulfides **3c** and **3g**, in 91% and 70% yield, respectively (entries 3 and 7). While the yield decreased in the reaction of sterically hindered isobutyronitrile anion (entry 13), the reactions of both acetonitrile anion and propionitrile anion gave the corresponding sulfides in relatively good yields (entries 9, 11, and 12). As

(1) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; Chapter 11.
(2) (a) Easton, N. R.; Dillard, R. D. *J. Org. Chem.* **1962**, *27*, 3602. (b) Gunther, H.; Bothner-By, A. A. *Chem. Ber.* **1963**, *96*, 3112. (c) Kitatani, K.; Yamamoto, H.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2158. (d) Cohen, T.; Ouellette, D.; Daniewski, W. M. *Tetrahedron Lett.* **1978**, 5063. (e) Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 5035.
(3) (a) Oda, R.; Ito, Y.; Okano, M. *Tetrahedron Lett.* **1964**, 7. (b) Ito, Y.; Okano, M.; Oda, R. *Tetrahedron* **1964**, *22*, 2615.
(4) (a) Schöllkopf, U.; Lehmann, G. J.; Paust, J.; Härtl, H.-D. *Chem. Ber.* **1964**, *97*, 1527. (b) Köbrich, G. *Angew. Chem., Int. Ed. Engl*, **1972**, *11*, 473.
(5) Block, E. "Reactions of Organosulfur Compounds"; Academic Press: New York, 1978.
(6) Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React. (N.Y.)* **1984**, *31*, 1.
(7) (a) "Organic Compounds of Sulfur, Selenium, and Tellurium", The Chemical Society, London; Vol. 6, 1981; p 31. (b) Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357. (c) For a recent leading reference, see: Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075.

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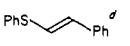
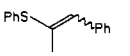
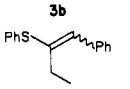
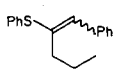
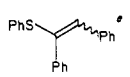
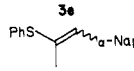
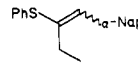
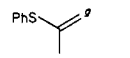
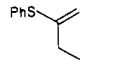
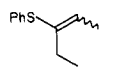
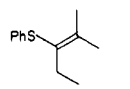
Table I. Reaction of Nitrile Anions with (Phenylthio)carbenes[a]

entry	nitrile	sulfide	product	yield,[b] %	isomer ratio[c]
1	$PhCH_2CN$	$PhSCH_3$ (**1a**)	 **3a**	52	[1.0:0]
2	$PhCH_2CN$	$PhSCH_2CH_3$ (**1b**)	 **3b**	73	[2.1:1]
3	$PhCH_2CN$	$PhS(CH_2)_2CH_3$ (**1c**)	 **3c**	91	[1.7:1]
4	$PhCH_2CN$	$PhS(CH_2)_3CH_3$ (**1d**)	 **3d**	75	[1.3:1]
5	$PhCH_2CN$	$PhSCH_2Ph$ (**1e**)	 **3e**	46	*f*
6	α-$NaphCH_2CN$	$PhSCH_2CH_3$ (**1b**)	 **3f**	77	*f*
7	α-$NaphCH_2CN$	$PhS(CH_2)_2CH_3$ (**1c**)	 **3g**	70	*f*
8	CH_3CN	$PhSCH_2CH_3$ (**1b**)	 **3h**	46	
9[h]				53	
10	CH_3CN	$PhS(CH_2)_2CH_3$ (**1c**)	 **3i**	55	
11[h]				70	
12	CH_3CH_2CN	$PhS(CH_2)_2CH_3$ (**1c**)	 **3j**	60	[2.2:1]
13	$(CH_3)_2CHCN$	$PhS(CH_2)_2CH_3$ (**1c**)	 **3k**	34	

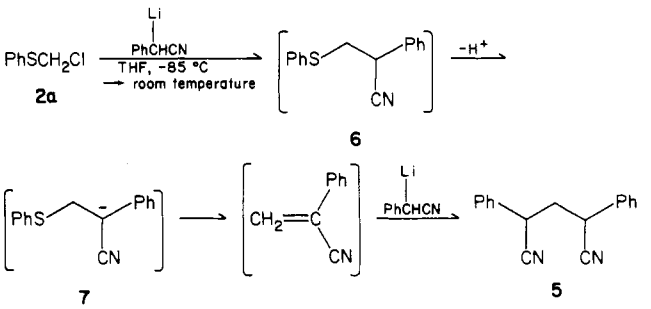
[a] Reactions were carried out as described in the Experimental Section. Unless otherwise noted a hexane solution of *n*-BuLi, free of lithium halides, was employed. [b] Isolated yields. [c] The identification of *E* and *Z* isomers was not performed. [d] Oida, T.; Tanimoto, S., Ikehira, H.; Okano, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 959. [e] Campaigne, E.; Leal, J. R. *J. Am. Chem. Soc.* **1954**, *76*, 1272. [f] The isomer ratio was not determined. [g] Gröbel, B.-T.; Seebach, D. *Chem. Ber.* **1977**, *110*, 867. [h] An ether solution of *n*-BuLi containing LiBr was used.

shown in entry 1, the reaction starting with chloromethyl phenyl sulfide (**2a**) proceeded less effectively than other chloroalkyl sulfides due to a concomitant involvement of the direct alkylation of nitrile anion (vide infra).

In the present reaction a hexane solution of *n*-BuLi, free of lithium halide, was generally used as a base. When an ether solution of *n*-BuLi containing LiBr was used instead, the yields of vinyl sulfides were slightly improved (entries 9 and 11).

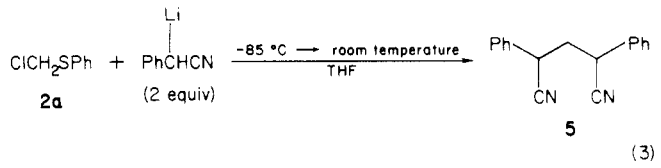
According to Schöllkopf et al., (phenylthio)carbene was generated by the reaction of chloromethyl phenyl sulfide (**2a**) with *n*-BuLi.[4] The present reaction could then proceed through a mechanism involving a carbenic intermediate as outlined in path a in Scheme II. Alternatively, the formation of vinyl sulfides can also be explained by a mechanism involving the alkylation of the nitrile anion by α-chloroalkyl phenyl sulfide, followed by the base-induced elimination of HCN from the resulting β-(phenylthio)nitriles (path b in Scheme II). The latter mechanism, however, is unlikely because the acidity of the proton α to the cyano group is estimated to be higher than that of the proton α to the phenylthio group; for example, the absolute equilibrium acidities (pK_a) of phenylacetonitrile and benzyl phenyl sulfide in Me_2SO are reported to be 21.9 and 30.0, respectively.[8]

Scheme III



This assumption was verified by the reaction of chloromethyl phenyl sulfide (**2a**) with lithiophenylacetonitrile (2 equiv) (eq 3) in the absence of *n*-BuLi. The formation of 2,4-diphenylglutaronitrile (**5**) (63% yield) shows that the initially formed β-(phenylthio)nitrile (**6**) undergoes a facile deprotonation not at the position α to the phenylthio group but at the position α to the cyano group; the resulting anion (**7**) liberates benzenethiolate ion to afford

(8) Bordwell, F. G.; Bares, J. E.; Bartmess, J. E.; Drucker, G. E.; Gerhold, J.; McCollum, G. J.; Puy, M. V. D.; Vanier, N. R.; Matthews, W. S. *J. Org. Chem.* **1977**, *42*, 326.



(3)

2-phenylacrylonitrile, which is then converted to **5** by the conjugate addition of the nitrile anion (Scheme III).[9] The result illustrated in eq 3 strongly suggests that the present reaction proceeds through a mechanism involving the nucleophilic attack of a nitrile anion on (phenylthio)carbene to generate the β-lithio-β-phenylthio nitrile intermediate **4** (path a).

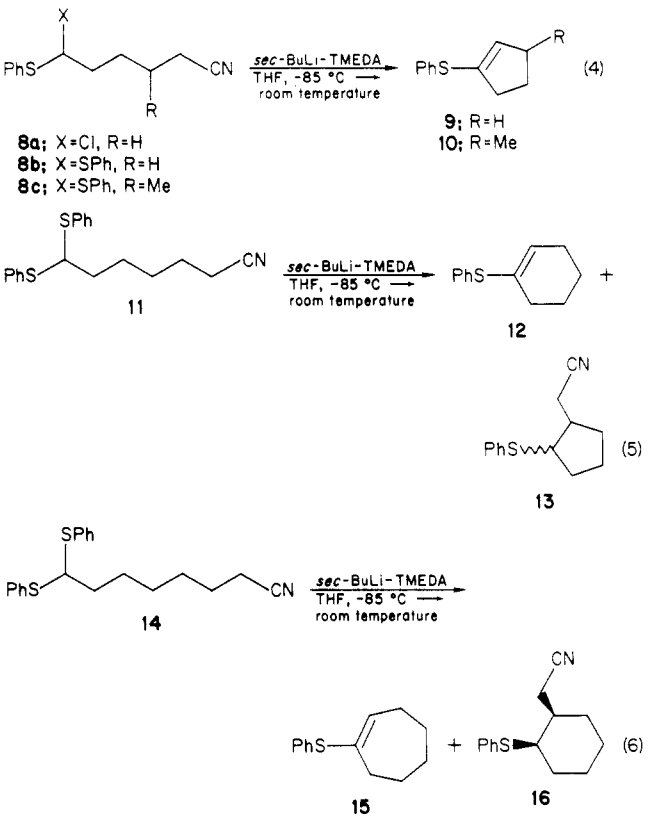
The intermediate carbanion **4**, one kind of homoenolate anion,[10] cannot be generated by the deprotonation of β-(phenylthio)nitrile (e.g., **6**). Therefore, we would stress that the present type of carbene reaction also has the potential for generating carbanions that are difficult to be prepared by a simple deprotonation reaction.

Intramolecular Cyclization Reaction. In order to apply the present reaction to the synthesis of cyclic vinyl sulfides, we first examined the intramolecular reaction starting with 6-chloro-6-(phenylthio)hexanenitrile (**8a**; X = Cl) (eq 4). However, the yield of the desired 1-(phenylthio)cyclopentene (**9**)[7c] was not satisfactory.

Recently, Cohen et al. have reported the generation of (phenylthio)carbenes from the anions of diphenyl dithioacetals bearing an additional negative charge, such as oxyanion, enolate anion, and anion of dithioacetal.[2d,11] The generation of (phenylthio)carbene bearing a nitrile anion moiety might then be successfully achieved by the decomposition of the dianion of the corresponding ω,ω-bis(phenylthio)nitrile. Actually, in our experiments, the efficiency of the cyclization was greatly improved by the use of 6,6-bis(phenylthio)hexanenitrile (**8b**; X = SPh) as a starting material. When **8b** was treated with 3 equiv of *sec*-BuLi–TMEDA in THF at −85 °C for 1 h and the resulting dianion warmed to a room temperature, 1-(phenylthio)cyclopentene (**9**)[7c] was obtained in 87% yield (eq 4).

Similarly, the 3-methyl derivative **8c** cyclized to give 3-methyl-1-(phenylthio)cyclopentene (**10**) in 56% yield (eq 4). Since other procedures for the preparation of **10** from 3-methylcyclopentanone cannot avoid the formation of the regioisomeric byproduct 4-methyl-1-(phenylthio)cyclopentene, the methodological advantage of the present reaction thus has been clearly demonstrated by the exclusive formation of **10**.[7,12] Six-membered ring formation starting from 7,7-bis(phenylthio)heptanenitrile (**11**) also proceeded successfully to give 1-(phenylthio)cyclohexene (**12**)[7c] in 46% yield (eq 5). On the other hand, seven-membered ring formation proceeded to give 1-(phenylthio)cycloheptene (**15**)[13] only in low yield (14%) (eq 6).

Also observed was the formation of byproducts *trans*- and *cis*-2-(phenylthio)cyclopentylacetonitrile (**13**) (25%) and *cis*-2-(phenylthio)cyclohexylacetonitrile (**16**) (9%) in the six- and seven-membered ring formation reactions, respectively. We have recently disclosed an enhanced reactivity of the C–H bond adjacent to oxyanion in the carbenic insertion reaction.[14] Moreover, the general



character of this activation effect in other anionic systems was demonstrated in the regioselective insertion by (phenylthio)carbene into the β C–H bond of an alkyllithium.[15] Therefore, the formation of these byproducts may be explained in terms of the insertion of (phenylthio)carbene into the activated C–H bond α to the nitrile anion site.

Conclusion

Vinyl sulfides are known to be one of the most versatile synthetic intermediates for structural transformations as shown by a growing number of reports on their synthetic applications.[7] In this regard, the reaction of nitrile anions with (phenylthio)carbenes provides the following advantage for the synthesis of vinyl sulfides over other methods:[7] (1) The necessary starting materials, sulfides and nitriles, are easily available in laboratories. (2) The procedure is simple and does not require acidic reaction conditions. (3) Above all, the synthesis of vinyl sulfides is accomplished simultaneously with the regiocontrolled carbon chain construction.

Prior to our study, the utilization of the reaction of phosphorus or sulfur ylides with dihalocarbenes in the synthesis of *gem*-dihaloalkenes has been reported,[3] and the dimerization of carbenoids has been shown to proceed through an analogous mechanism.[4] Therefore, the present synthetic method depicted in Scheme I seems to possess wide applicability to various combinations between carbenes (or carbenoids) and carbanions bearing a suitable leaving group Z. Further studies are in progress.

Experimental Section

Infrared spectra were measured on a JASCO IRA-1 grating spectrophotometer. ^{1}H NMR spectra were recorded on a Varian

(9) Hoffmann, K.; Kebrle, J.; Schmid, H. J. *Helv. Chem. Acta* **1957**, *40*, 387.
(10) Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205.
(11) (a) Cohen, T.; Ritter, R. H.; Ouellette, D. *J. Am. Chem. Soc.* **1982**, *104*, 7142. (b) Cohen, T.; Yu, L.-C. *Ibid.* **1983**, *105*, 2811.
(12) See, for example: Barillier, D.; Strobel, M. P.; Morin, L.; Paquer, D. *Tetrahedron* **1983**, *39*, 767.
(13) Newman, H.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2785.
(14) (a) Harada, T.; Oku, A. *J. Am. Chem. Soc.* **1981**, *103*, 5965. (b) Harada, T.; Akiba, E.; Oku, A. *Ibid.* **1983**, *105*, 2771. (c) Harada, T.; Nozaki, Y.; Oku, A. *Tetrahedron Lett.* **1983**, *24*, 5665. (d) Harada, T.; Nozaki, Y.; Yamaura, Y.; Oku, A. *J. Am. Chem. Soc.* **1985**, *107*, 2189.
(15) Harada, T.; Maeda, H.; Oku, A. *Tetrahedron Lett.* **1985**, *26*, 6489.

XL-200 or a Varian T-60A spectrometer. Mass spectra were measured on a Hitachi M-80 or a Shimazu QP-1000 mass spectrometer. Microanalyses were performed by the Microanalysis Center of Kyoto University. Short-path (bulb-to-bulb) distillations were carried out with a Kugelrohr apparatus, and all boiling points are correspond to the bath temperature. Silica gel (Wakogel C-300) was used as an absorbent in flash chromatography. Starting nitriles, tetramethylethylenediamine (TMEDA), and CH_2Cl_2 were dried over CaH_2, distilled, and stored over 4-Å molecular sieves. *n*-BuLi (1.62 M, hexane solution) and *sec*-BuLi (1.29 M, cyclohexane solution) were purchased from Nakarai Chemical Co. and Aldrich Chemical Co., respectively, and were used after titration. Starting sulfides (**1a–e**) were prepared by the alkylation of thiophenol with alkyl bromides.[16]

General Procedure for the Intermolecular Reaction of Nitrile Anions with (Phenylthio)carbenes. To a solution of alkyl sulfide **1a–e** (1 mmol) in CCl_4 (1 mL) was added *N*-chlorosuccinimide (NCS) (1.1 mmol), and the mixture was stirred at a room temperature for several hours. The completion of the reaction was monitored by ^1H NMR analysis. After the removal of succinimide by filtration followed by the evaporation of the solvent in vacuo, the crude chloro sulfide **2a–e** thus obtained was used without further purification. To a solution of a nitrile (2 mmol) in THF (4 mL) was slowly added 2.2 mmol of *n*-BuLi at −85 °C under a nitrogen atmosphere, and the mixture was stirred for 1 h. To this mixture was added a THF (1 mL) solution of **2a–e** and then *n*-BuLi (1.1 mmol). After being stirred for 0.5 h at the same temperature, the resulting solution was allowed to warm to −30 °C over a period of 3 h, quenched by the addition of water, and extracted twice with ethyl acetate. Concentration of the dried (sodium sulfate) extracts in vacuo followed by purification by flash chromatography using petroleum ether as eluent gave vinyl sulfides **3a–k**. The physical and spectral data of new compounds are as follows.

(*E*)- and (*Z*)-1-Phenyl-2-(phenylthio)propene (3b): bp 168 °C (2 mmHg); ^1H NMR (200 MHz, $CDCl_3$) δ 2.05 (3 H for the minor isomer, d, *J* = 1.3 Hz), 2.16 (3 H for the major isomer, d, *J* = 1.3 Hz), 6.72 (1 H for the major isomer, br s), 6.74 (1 H for the minor isomer, br s), 7.20–7.62 (10 H, m); IR (liquid film) 2960 (s), 1590 (s), 920 (m), 745 (s), 695 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 226 (M^+, 85), 167 (37), 116 (29), 115 (100), 91 (69). Anal. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.24. Found: C, 79.71; H, 6.19.

(*E*)- and (*Z*)-1-Phenyl-2-(phenylthio)-1-butene (3c): oil; ^1H NMR (200 MHz, $CDCl_3$) δ 1.23 (3 H for the minor isomer, t, *J* = 7.2 Hz), 1.31 (3 H for the major isomer, t, *J* = 7.2 Hz), 2.42 (2 H for the minor isomer, br q, *J* = 7.2 Hz), 2.56 (2 H for the major isomer, q, *J* = 7.2 Hz), 6.78 (1 H for the major isomer, br s), 6.91 (1 H for the minor isomer, br s), 7.24–7.74 (10 H, m); IR (liquid film) 2980 (s), 1585 (m), 1070 (s), 1025 (s), 840 (m), 740 (s), 690 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 240 (M^+, 63), 211 (29), 167 (35), 91 (100); exact mass calcd for $C_{16}H_{16}S$ 240.0974, found 240.0977.

(*E*)- and (*Z*)-1-Phenyl-2-(phenylthio)-1-pentene (3d): oil; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (3 H for the major isomer, t, *J* = 6.4 Hz), 0.91 (3 H for the minor isomer, t, *J* = 6.4 Hz), 1.54–1.71 (2 H, m), 2.28 (2 H for the major isomer, br t, *J* = 6.4 Hz), 2.43 (2 H for the minor isomer, m), 6.67 (1 H for the minor isomer, br s), 6.82 (1 H for the minor isomer, br s), 7.18–7.65 (10 H, m); IR (liquid film) 2975 (s), 1585 (s), 1025 (s), 805 (m), 740 (s), 690 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 254 (M^+, 25), 167 (20), 135 (26), 129 (34), 115 (80), 91 (100); exact mass calcd for $C_{17}H_{18}S$ 254.1130, found 254.1129.

(*E*)- and (*Z*)-1-(1-Naphthyl)-2-(phenylthio)propene (3f): oil; ^1H NMR (60 MHz, CCl_4) δ 1.95 (3 H for the major isomer, d, *J* = ~1 Hz), 2.08 (3 H for the minor isomer, d, *J* = ~1 Hz), 6.93–8.03 (13 H, m); IR (liquid film) 1580 (s), 845 (s), 805 (s), 780 (s), 740 (s), 690 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 276 (M^+, 72), 243 (33), 228 (24), 167 (54). Anal. Calcd for $C_{19}H_{16}S$: C, 82.58; H, 5.84. Found: C, 82.78; H, 5.77.

(*E*)- and (*Z*)-1-(1-Naphthyl)-2-(phenylthio)-1-butene (3g): 195–200 °C (0.4 mmHg); ^1H NMR (200 MHz, $CDCl_3$) δ 1.08 (3 H for the major isomer, t, *J* = 7.5 Hz), 1.22 (3 H for the minor isomer, t, *J* = 7.5 Hz), 2.33 (2 H for the major isomer, q, *J* = 7.5 Hz), 2.41 (2 H for the minor isomer, br q, *J* = 7.5 Hz), 6.98 (1 H for the major isomer, s), 7.20–8.00 (12 H, m); IR (liquid film) 2940 (s), 1590 (s) 789 (s), 750 (s), 695 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 290 (M^+, 42), 229 (23), 165 (100), 152 (23); exact mass calcd for $C_{20}H_{18}S$ 290.1130, found 290.1133.

2-(Phenylthio)-1-butene (3i): oil; ^1H NMR (60 MHz, CCl_4) δ 1.10 (3 H, t, *J* = 7.4 Hz), 2.22 (2 H, br q, *J* = 7.4 Hz), 4.82 (1 H, br s), 5.07 (1 H, br s), 7.12–7.53 (5 H, m); IR (liquid film) 2950 (s), 1620 (s), 1595 (m), 910 (m), 865 (s), 750 (s), 695 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 164 (M^+, 46), 150 (23), 135 (100), 110 (35), 91 (30); exact mass calcd for $C_{10}H_{12}S$ 164.0661, found 164.0653.

(*E*)- and (*Z*)-3-(Phenylthio)-2-pentene (3j): oil; ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (3 H, t, *J* = 6.8 Hz), 1.74 (3 H for the minor isomer, br t, *J* = 6.8 Hz), 1.86 (3 H for the major isomer, d t, *J* = 1.3 and 6.7 Hz), 2.10–2.28 (2H, m), 5.87 (1 H for the minor isomer, br t, *J* = 6.8 Hz), 5.98 (1 H for the major isomer, t q, *J* = 1.2 and 6.7 Hz), 7.08–7.36 (5 H, m); IR (liquid film) 2930 (s), 1590 (m), 740 (m), 690 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 178 (M^+, 74), 149 (56), 110 (100), 73 (100); exact mass calcd for $C_{11}H_{14}S$ 178.0817, found 178.0802.

2-Methyl-3-(phenylthio)-2-pentene (3k): oil; ^1H NMR (60 MHz, CCl_4) δ 1.00 (3 H, t, *J* = 7.0 Hz), 1.87 (3 H, s), 1.98 (3 H, s), 2.25 (2 H, br q, *J* = ~7 Hz), 7.03–7.40 (5 H, m); IR (liquid film) 2980 (s), 1640 (s), 1590 (s), 740 (s), 690 cm^{-1} (s); mass spectrum, *m/e* (relative intensity) 192 (M^+, 7), 119 (14), 110 (19), 55 (100); exact mass calcd for $C_{12}H_{16}S$ 192.0974, found 192.0953.

Reaction of Chloromethyl Phenyl Sulfide (2a) with Lithiophenylacetonitrile. To a solution of phenylacetonitrile (234 mg, 2.0 mmol) in THF (4 mL) was added *n*-BuLi (2.2 mmol) at −85 °C under a nitrogen atmosphere, and the mixture was stirred for 1 h. A THF (1 mL) solution of chloromethyl phenyl sulfide (**2a**), which was prepared from thioanisole (**1a**) (124 mg, 1.0 mmol) as described above, was added to the solution of lithiophenylacetonitrile at the same temperature. The resulting solution was warmed up to room temperature under stirring for 12 h. The reaction mixture was quenched by the addition of water and extracted twice with ethyl acetate. Concentration of the dried (sodium sulfate) extract, followed by flash chromatography (50% benzene/cyclohexane) gave 155 mg (63%) of 2,4-diphenylglutaronitrile (**5**)[17] as a mixture of *dl* and meso isomers. **5**: oil; ^1H NMR (200 MHz, $CDCl_3$) δ 2.33 (1 H for meso isomer, dt, *J* = 13.5 and 8.0 Hz), 2.40 (2 H for *dl* isomer, dd, *J* = 7.7 and 8.6 Hz), 2.65 (1 H for meso isomer, dt, *J* = 13.5 and 8.0 Hz), 3.73 (2 H for meso isomer, t, *J* = 8.0 Hz), 4.05 (2 H for *dl* isomer, br t, *J* = ~8 Hz), 7.26–7.50 (10 H, m); mass spectrum, *m/e* (relative intensity) 246 (M^+, 1.6), 245 (0.9), 130 (20), 117 (100), 116 (24).

Preparation of 6,6-Bis(phenylthio)hexanenitrile (8b). To a stirred solution of 5-(phenylthio)-1-pentanol (392 mg, 2.0 mmol) and triethylamine (292 μL, 2.1 mmol) in CH_2Cl_2 (2.5 mL) was added methanesulfonyl chloride (163 μL, 2.1 mmol) at 0 °C. After 10 min, the reaction mixture was diluted with petroleum ether and filtered through a cotton plug. Solvents were removed in vacuo to give the crude mesylate, which was then dissolved in DMF (10 mL). To this solution was added sodium cyanide (147 mg, 3.0 mmol) and sodium iodide (60 mg, 0.4 mmol), and the mixture was heated at 110 °C for 1 h. After the addition of water followed by extraction with ether, the combined organic layer was washed 3 times with water, dried over sodium sulfate, and concentrated in vacuo. The crude material was purified by flash chromatography (15% ethyl acetate/petroleum ether) to give 285 mg (70%) of 6-(phenylthio)hexanenitrile as an oil; ^1H NMR (60 MHz, CCl_4) δ 1.43 (6 H, m), 2.28 (2 H, br t, 2.90 (2 H, br t), 7.10–7.53 (5 H, m).

To a stirred suspension of NaH (1.5 mmol) in 2.5 mL of THF was added thiophenol (143 mg, 1.3 mmol) at 0 °C under a nitrogen atmosphere, and the mixture was stirred for 0.5 h. To the resulting suspension was added 6-chloro-6-(phenylthio)hexanenitrile (**8a**), which was prepared from 6-(phenylthio)hexanenitrile (205 mg, 1.0 mmol) by the action of NCS as described above. The mixture was stirred for 24 h at room temperature, brine was added, and the total mixture was extracted twice with ethyl acetate and dried

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over sodium sulfate. The crude mixture was purified by flash chromatography (benzene) to give 232 mg (74%) of **8b** as an oil: ^{1}H NMR (60 MHz, CCl_4) δ 1.47–1.93 (6 H, m), 2.18 (2 H, br t, J = ~6 Hz), 4.32 (1 H br t), 7.10–7.53 (10 H, m); IR (liquid film) 2960 (m), 2270 (m), 1595 (s), 1035 (s), 750 (s), 695 cm^{-1} (s).

By a similar procedure ω,ω-bis(phenylthio)nitriles **8c**, **11**, and **14** were prepared starting from the corresponding ω-(phenylthio)alkanol. Yields of products and their spectral data together with those of intermediate ω-(phenylthio)nitriles are summarized below.

3-Methyl-6,6-bis(phenylthio)hexanenitrile (8c): 35% overall yield from the corresponding ω-(phenylthio)alkanol; oil; ^{1}H NMR (60 MHz, CCl_4) δ 1.02 (3 H, d, J = 5.8 Hz), 1.53–1.60 (4 H, m), 2.05–2.30 (2 H, m), 4.25 (1 H, br t), 7.17–7.63 (5 H, m); IR (liquid film) 2960 (s), 2275 (m), 1595 (s), 1035 (s), 750 (s), 695 cm^{-1} (s).

7-(Phenylthio)heptanenitrile: 76% yield; oil; ^{1}H NMR (60 MHz, CCl_4) δ 1.17–1.83 (8 H, m), 2.14 (2 H, br t), 2.80 (2 H, br t), 6.93–7.30 (5 H, m); IR (liquid film) 2985 (s), 2285 (m), 1605 (s), 750 (s), 695 cm^{-1} (s).

7,7-Bis(phenylthio)heptanenitrile (11): 65% yield; bp 220 °C (0.07 mmHg); ^{1}H NMR (60 MHz, CCl_4) δ 1.33–1.90 (8 H, m), 2.17 (2 H, br t, J = ~6 Hz), 4.27 (1 H, br t, J = ~6 Hz), 7.13–7.50 (10 H, m); IR (liquid film) 2960 (s), 2240 (s), 740 (s), 690 cm^{-1} (s).

8-(Phenylthio)octanenitrile: 80% yield; waxy solid; ^{1}H NMR (60 MHz, CCl_4) δ 1.17–1.83 (10 H, m), 2.18 (2 H, br t), 2.83 (2 H, br t), 7.07–7.36 (5 H, m); IR (liquid film) 2940 (s), 2250 (m), 745 (s), 690 cm^{-1} (s).

8,8-Bis(phenylthio)octanenitrile (14): 77% yield; bp 195–205 °C (0.03 mmHg); ^{1}H NMR (60 MHz, CCl_4) δ 1.23–1.90 (10 H, m), 2.18 (2 H, br t, J = ~6 Hz), 4.28 (1 H, br t, J = ~6 Hz), 7.13–7.50 (10 H, m); IR (liquid film) 2955 (s), 2260 (m), 1590 (s), 745 (s), 695 cm^{-1} (s).

General Procedure for the Intramolecular Cyclization Reaction. To a solution of ω,ω-bis(phenylthio)nitrile (1.0 mmol) and TMEDA (3.0 mmol) in THF (10 mL) was added *sec*-BuLi (cyclohexane solution, 3 mmol) at −85 °C under a nitrogen atmosphere. The mixture was stirred at this temperature for 1 h, then allowed to warm gradually to a room temperature, and stirred further for 12 h. After aqueous workup, product(s) was isolated by means of flash chromatography (petroleum ether/benzene, gradient). Physical and spectral data of new compounds are as follows.

3-Methyl-1-(phenylthio)cyclopentene (10): oil; ^{1}H NMR (60 MHz, CCl_4) δ 1.03 (3 H, d, J = 6.6 Hz), 1.80–2.87 (5 H, m), 5.50 (1 H, m), 7.07–7.47 (5 H, m); IR (liquid film) 2940 (s), 1590 (m), 815 (s), 740 (s), 690 cm^{-1} (s); mass spectrum, m/e (relative intensity) 190 (M^+, 33), 175 (22), 147 (11), 110 (12), 81 (100); exact mass calcd for $C_{12}H_{14}S$ 190.0817, found 190.0815.

***trans*- and *cis*-[2-(Phenylthio)cyclopentyl]acetonitrile (13).** This compound was obtained as a 5.5:1 mixture of two isomers. Each isomer was isolated by means of preparative GC. Major isomer: oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.62–2.18 (6 H, m), 2.35 (1 H, dd, J = 14.4 and 8.0 Hz), 2.48 (1 H, m), 2.61 (1 H, dd, J = 14.4 and 5.2 Hz), 3.70 (1 H, br q, J = ~6.5 Hz), 7.20–7.40 (5 H, m); IR (liquid film) 2960 (s), 2260 (m), 1595 (s), 745 (s), 695 cm^{-1} (s); mass spectrum, m/e (relative intensity) 217 (M^+, 23), 110 (100), 67 (22). Minor isomer: oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.58–2.26 (7 H, m), 2.37 (1 H, dd, J = 16.8 and 6.5 Hz), 2.55 (1 H, dd, J = 16.8 and 4.4 Hz), 3.12 (1 H, br q, J = ~8 Hz), 7.19–7.42 (5 H, m); mass spectrum, m/e (relative intensity) 217 (M^+, 22), 110 (100), 67 (23); exact mass (mixture of two isomers) calcd for $C_{13}H_{15}NS$ 217.0927, found 217.0909.

***cis*-[2-(Phenylthio)cyclohexyl]acetonitrile (16)**: oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.12 (8 H, m), 2.12 (1 H, m), 2.44 (1 H, dd, J = 16.8 and 8.8 Hz), 2.62 (1 H, dd, J = 16.8 and 8.0 Hz), 3.51 (1 H, m, width at half height = ~6 Hz), 7.16–7.48 (5 H, m); IR (liquid film) 2950 (s), 2250 (m), 1590 (s), 1030 (s), 740 (s), 695 cm^{-1} (s); mass spectrum, m/e (relative intensity) 231 (M^+, 11.5), 110 (100), 81 (29), 79 (11); exact mass calcd for $C_{14}H_{17}NS$ 231.1083, found 231.1082.

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Registry No. **1a**, 100-68-5; **1b**, 622-38-8; **1c**, 874-79-3; **1d**, 1126-80-3; **1e**, 831-91-4; **2a**, 7205-91-6; **2b**, 13557-24-9; **2c**, 87514-10-1; **2d**, 72653-47-5; **2e**, 7693-31-4; **3a**, 7214-53-1; (*E*)-**3b**, 23261-39-4; (*Z*)-**3b**, 41796-43-4; (*E*)-**3c**, 66164-65-6; (*Z*)-**3c**, 66164-53-2; (*E*)-**3d**, 99965-66-9; (*Z*)-**3d**, 99965-71-6; **3e**, 24466-59-9; (*E*)-**3f**, 99965-67-0; (*Z*)-**3f**, 99965-72-7; (*E*)-**3g**, 99965-68-1; (*Z*)-**3g**, 99965-73-8; **3h**, 7594-43-6; **3i**, 99965-69-2; (*E*)-**3j**, 99965-70-5; (*Z*)-**3j**, 99965-74-9; **3k**, 85895-10-9; (±)-**5**, 19657-49-9; *meso*-**5**, 15146-07-3; **8a**, 99965-77-2; **8b**, 99965-78-3; **8c**, 99965-79-4; **9**, 37053-16-0; **10**, 99965-85-2; **11**, 99965-90-9; **12**, 4922-47-8; *trans*-**13**, 99965-86-3; *cis*-**13**, 99965-87-4; **14**, 99965-84-1; **15**, 64741-11-3; **16**, 99965-88-5; $PhCH_2CN$, 140-29-4; CH_3CN, 75-05-8; CH_3CH_2CN, 107-12-0; $(CH_3)_2CHCN$, 78-82-0; $PhS(CH_2)_3CH(CH_3)CH_2OH$, 99965-80-7; $PhS(CH_2)_6OH$, 99965-82-9; $PhS(CH_2)_7OH$, 99965-89-6; α-$naphCH_2CN$, 132-75-2; thiophenol, 108-98-5; 5-(phenylthio)-1-pentanol, 57774-95-5; 5-(phenylthio)-1-pentyl mesylate, 99965-75-0; 6-(phenylthio)hexanenitrile, 99965-76-1; 7-(phenylthio)heptanenitrile, 99965-81-8; 8-(phenylthio)octanenitrile, 99965-83-0.

Thietane Alkylations. A General Synthesis of 3-Halopropyl Benzyl Sulfides[1]

David C. Palmer and Edward C. Taylor*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544

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Reaction of thietane with benzyl halides yields 3-halopropyl benzyl sulfides in good to excellent yield.

Some 58 years have elapsed since Bennett and Hock demonstrated that the reaction of thietane (**1**) with methyl iodide did not yield 1,1-dimethylthietanediylium diiodide (**2**) as originally proposed, but rather *S,S*-dimethyl-3-(iodopropyl)sulfonium iodide (**5**).[2] They proposed that this compound arose by attack by iodide ion on the initially formed *S*-methylthietanium iodide (**3**) to yield 3-iodopropyl methyl sulfide (**4**), which underwent subsequent alkylation with methyl iodide.[3] Since that time, only a few additional reports have appeared on the reaction of

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