of silica gel (5 g) eluted with benzene (50–100 mL). Concentration of the eluant affords the products in Tables I and II.

7-Methoxybenz[*a*]anthracene (4c). To a solution of sodium methoxide prepared from sodium (500 mg, 22 mmol) in absolute methanol (25 mL) under nitrogen was added **4b** (700 mg, 2.45 mmol). The resulting suspension was heated at reflux for 1 h, cooled, treated cautiously with dimethyl sulfate (10 mL), and stirred at room temperature for 20 h. The reaction mixture was poured into 5% aqueous NaOH (300 mL), and stirred for an additional hour. The product was removed by filtration, dried, and filtered through a short column of silica gel eluted with benzene–hexane (1:1). Evaporation of the solvent afforded **4c** (500 mg, 89%), mp 109–110 °C (lit.[24] 110.5–111.0 °C).

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Registry No. 1, 84-11-7; 2, 484-17-3; 3, 84-65-1; 4, 2498-66-0; **4a**, 56-55-3; **4b**, 25040-01-1; **4c**, 6366-20-7; **4d**, 60699-25-4; 5, 2051-10-7; 6, 3228-74-8; anthracene, 120-12-7; chrysene, 218-01-9; dibenz[*a*,*c*]-anthracene, 215-58-7; phenanthrene, 85-01-8; 9-acetoxyphenanthrene, 957-82-4; 1-hydroxynaphthalene, 90-15-3; naphthalene, 91-20-3; 7,12-dihydrobenz[*a*]anthracene, 2498-66-0; HI, 10034-85-2.

(24) Fieser, L. F.; Hershberg, E. B. *J. Am. Chem. Soc.* **1937**, *59*, 1028.

Stereochemistry and Mechanism of the Base-Induced Loss of Thiophenol from 1,1,3-Tris(phenylthio)alkanes to Form Cyclopropanone Dithioketals

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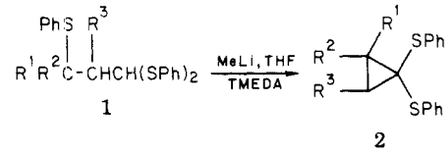
The indicated aspects of the title reaction were investigated by subjecting *trans*-2-(bis(phenylthio)-methyl)-1-(phenylthio)cyclohexane (**9**) and the corresponding cis isomer (**5**) to the action of methyllithium for 50 h and quenching the mixtures with deuterium oxide. The trans isomer gave the ring-closed product (**10**) in 51% yield, and 29% of the undeuterated starting material was recovered. The cis isomer gave a variety of decomposition products, 13% of starting material which was completely deuterated at the thioacetal carbon atom, and no ring-closed product (**10**). It is concluded that the ring closure is an intramolecular nucleophilic displacement of phenylthiolate ion by the thioacetal anion.

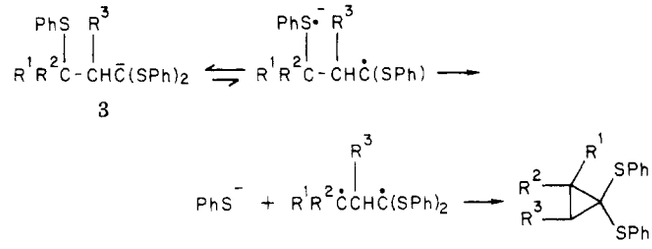
It has recently been found that cyclopropanone bis(phenylthio)ketals (**2**) are produced in excellent yields by the loss of thiophenol from 1,1,3-tris(phenylthio)alkanes (**1**) induced by methyllithium in a tetrahydrofuran (THF) solution containing tetramethylethylenediamine (TMEDA).[1] The recently developed synthesis of complex cyclopropanone thioketals by a connective version of this ring closure[2] and the reductive lithiation of the ring-closed products to sulfur-stabilized anions[3] suggest that this type of ring closure will have considerable synthetic utility, and we have thus carried out an investigation of its stereochemistry and mechanism, a study which was also designed to allow an assessment of its potential for preparing cyclopropanone dithioketals fused to larger rings.



1 2

It has been demonstrated[4] that the thioacetal proton of 1 (R^1 = Me; R^2 = R^3 = H) can be removed by methyllithium, and it is assumed that the anion **3** (Scheme I) is an intermediate in the ring closure. A direct intramolecular "S_N2" reaction with explusion of the thiophenoxide ion appeared questionable (1) because this ion has apparently never been observed as a leaving group in an S_N2 reaction and (2) because of very high yields, 100 and 90%, respectively, observed in the ring closures of 1 (R^1 = R^2 = Me; R^3 = H)[3] and 1 (R^1 = Me; R^2 = SPh; R^3 = H), where

Scheme I



the nucleophile and the carbon bearing the leaving group are both tertiary.[1] A mechanism involving expulsion of thiophenoxide ion from the negatively charged carbon atom of **3** to form a carbene,[5] intramolecular capture of the carbene by the 3-thiophenoxy group to form a four-member ring ylide,[6] and Stevens rearrangement of the ylide to produce the cyclopropane product[6] was excluded by a labeling experiment in which it was demonstrated that the thiophenoxide group on the 3-carbon atom is the one that is lost.[1]

There is still at least one more alternative to the intramolecular nucleophilic displacement. Sulfur-stabilized anions appear to be capable of one-electron donation to suitable acceptors,[7,8] and phenylthioethers can apparently

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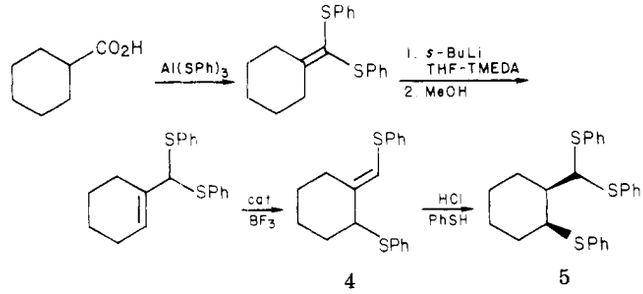
(2) Cohen, T; Weisenfeld, R. B.; Gapinski, R. E., submitted.
(3) Cohen, T.; Daniewski, W. M.; Weisenfeld, R. B. *Tetrahedron Lett.* **1978**, 4665.
(4) Cohen, T.; Mura, A. J., Jr.; Shull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218.
(5) Cohen, T.; Ouellette, D.; Daniewski, W. M. *Tetrahedron Lett.* **1978**, 5063.
(6) Kondo, K.; Ojima, I. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1490.
(7) Baarschers, W. H.; Loh, T. L. *Tetrahedron Lett.* **1971**, 3483. Seebach, D. *Synthesis* **1969**, 17. Meyers, C. Y.; Mathews, W. S.; Ho, L. L.; Kolb, V. M.; Parady, T. E. In "Catalysis in Organic Syntheses 1977"; Smith G. V., Ed.; Academic Press: New York, 1977; p 197.
(8) We interpret the recently reported alkylation of a sulfur-stabilized anion by *tert*-butyl bromide as proceeding by an electron transfer to the alkyl halide followed by expulsion of bromide ion and combination of the *tert*-butyl radical with the sulfur-stabilized radical. Gräfing, R.; Verkruijsse, H. D.; Brandsma, L. *J. Chem. Soc., Chem. Commun.* **1978**, 596.

0022-3263/79/1944-4816$01.00/0

Scheme II



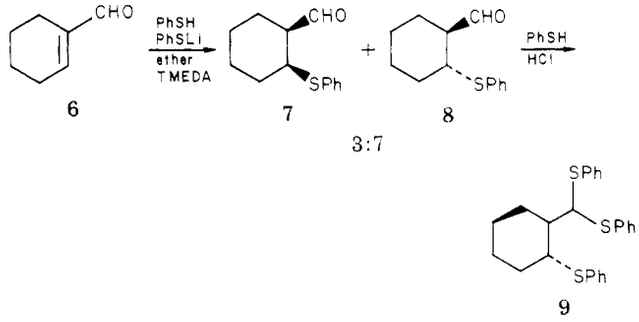
accept an electron from a suitable donor with cleavage of the resulting radical anion to produce a carbon radical and phenylthiolate anion.[9] An electron transfer from the thioacetal anion to the 3-phenylthio group may be expected to be facilitated by the proximity of the donor and acceptor. Even a very unfavorable equilibrium for this process could result in product if phenylthiolate ejection were irreversible, as it probably would be due to the great efficiency of 1,3-diradical ring closure[10] (Scheme I). Such a mechanism would admirably account for the high yields in the cases in which R^1 and R^2 are bulky groups.

In order to distinguish between a direct displacement and an electron transfer mechanism, we have studied the action of methyllithium on the cis (**5**) and trans (**9**) isomers of 1-(bis(phenylthio)methyl)-2-(phenylthio)cyclohexane. Whereas ring closure by the electron transfer mechanism should be possible in the anions derived from both **5** and **9**, only that from the trans isomer **9** should be capable of an intramolecular nucleophilic displacement resulting in inversion of configuration at the carbon atom bearing the thiophenoxide leaving group; such a displacement in the cis isomer **5** would lead to a three-member ring fused in a trans manner to a six-member ring, a system of intolerable strain.

The cis isomer (**5**) was prepared in 90% yield by hydrogen chloride catalyzed addition of thiophenol to **4**, which is available in 84% yield from cyclohexanecarboxylic acid (Scheme II), as described previously.[11] The formation of the cis product resulting from addition of a proton to 2-substituted alkylidenecyclohexanes is not unexpected,[12] although the complete stereospecificity is gratifying.

The trans isomer **9** was prepared in 94% yield by passing a stream of hydrogen chloride into a solution of *trans*-2-(phenylthio)cyclohexanecarboxaldehyde (**8**) dissolved in thiophenol. The trans aldehyde **8** constituted 70% of a mixture of the cis **7** and trans **8** aldehydes obtained in 88% yield by treatment of 1-cyclohexene-2-carboxaldehyde (**6**)[13] with thiophenol in the presence of lithium phenylthiolate (Scheme III); the same mixture is obtained when the cis isomer **7**, first produced when the enal **6** is treated with thiophenol in the presence of triethylamine,[14] is allowed to equilibrate for 3 days in this medium at 25 °C. Chromatography of this 3:7 mixture of **7** and **8** on silica gel provides the pure trans aldehyde **8** and a small quantity of the cis isomer **7**; the latter decomposes on the column

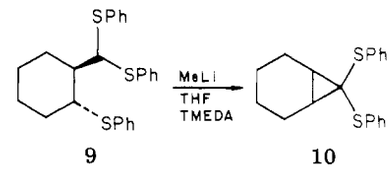
Scheme III



to **6** by trans-diaxial elimination of thiophenol, whereas the trans isomer is stable under these conditions.

In confirmation of the configurations assigned to **7** and **8**, the widths at half height of the NMR signal due to the protons on the sulfur-bearing carbon atoms of **7** and **8** are 8 and 20 Hz, respectively; the former value is expected[15] for an equatorial proton, thus indicating an axial phenylthio group and a cis configuration, while the latter value is characteristic of an axial proton, revealing the phenylthio group of **8** as equatorial and the configuration as trans. These assignments are corroborated by the ^1H NMR spectra of the tris(phenylthio) compound **9**, derived from **8**, and of its geometric isomer **5**; the widths at half-height of the signals due to the protons attached to the ring carbon atom bearing the phenylthio group are 7 Hz for **5** and 20 Hz for **9**.

When the trans isomer **9** was treated at 0 °C with excess methyllithium in THF containing TMEDA for 50 h and the reaction mixture was quenched with D_2O, 7,7-bis(phenylthio)bicyclo[4.1.0]heptane (**10**) was produced in 51% yield, and 29% of unreacted, undeuterated (NMR) **9** was recovered. The spectral characteristics of **10** are identical with those of an authentic sample prepared by the method of Braun and Seebach.[16] The recovery of undeuterated starting material clearly indicates that the proton removal is the rate-determining step. Thus, the considerably slower reaction rate compared with previous examples (high yields were typically obtained after only 2 h in simple cases[1]) is due not to sluggish ring closure of the thioacetal anion but to a low rate of proton removal presumably caused by greater steric hindrance.



In the crucial experiment, the cis isomer **5** was subjected to the same reaction conditions for 50 h. Starting material (13%), completely deuterated at the thioacetal carbon atom, was recovered along with an extensive array of other unidentified products; no detectable quantity of the ring-closed product **10** was formed. When the reaction was allowed to proceed for only 7 h, 30% of the decomposition products was detected, and recovered starting material was found to be 85% deuterated. Thus, the deprotonation step is somewhat faster in the cis case, but the thioacetal anion does not ring close; instead, it undergoes slow decomposition processes and can readily be detected by deuteration.

The results thus appear definitive. The anion of the trans isomer **9** rapidly ring closes, while that of the cis

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(11) Cohen, T.; Gapinski, R. E.; Hutchins, R. R. *J. Org. Chem.* **1979**, *44*, 3599.
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(13) Taguchi, H.; Tanaka, S.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* **1973**, 2465.
(14) Predominant, although not necessarily exclusive, formation of the cis adduct as the kinetic product is expected from the work of Abramovitch.[12b]
(15) Pinkus, J. L.; Cohen, T. *J. Org. Chem.* **1968**, *33*, 3538 and references cited therein.
(16) Braun, M.; Seebach, D. *Chem. Ber.* **1976**, *109*, 669.

isomers **5** undergoes no detectable ring closure. We must conclude, therefore, that the ring closure is merely a very efficient intramolecular S_N2 process. The reason for the high yields[1,3] compared to similar ring closures to cyclopropanone dithioketals in which halide or tosylate is the leaving group[16,17] may be the stability of the alkyl phenylthioether group at the 3-position toward alkyllithiums; halide and tosylate groups at this position may be exchanged for lithium and/or undergo 1,2-eliminations in the presence of alkyllithiums.

The findings reported here place an obvious restriction on the use of this ring closure reaction to produce certain fused cyclopropanone thioketals; a trans orientation of the thioacetal and phenylthio groups will be necessary for all but fairly large rings. When the groups are trans disposed as in the case of **9**, the ring closure occurs quite cleanly. A minor inconvenience in this case is the long reaction time required. While an attempt to increase the reaction rate by replacing methyllithium with *n*-butyllithium succeeded in leading to more rapid deprotonation, the yield of product was seriously reduced by partial lithium–phenylthio exchange between **10** and the base;[18] such destruction of the product may be responsible for the fairly poor yield of **10** observed upon treatment of *trans*-2-(bis(phenylthio)methyl)-1-(tosyloxy)cyclohexane with *n*-butyllithium.[16]

Experimental Section

^{1}H NMR spectra were taken on a Varian T-60 instrument with tetramethylsilane as an internal standard. IR spectra were recorded on a Beckman IR-8 spectrophotometer. High-resolution mass spectra were obtained on a Varian CH-5 instrument.

***cis*-2-(Bis(phenylthio)methyl)-1-(phenylthio)cyclohexane (5).** Anhydrous hydrogen chloride was passed through a solution of 1.01 g (3.24 mmol) of (*E*)-1-[(phenylthio)methylidene]-2-(phenylthio)cyclohexane (**4**)[11] in 4.0 mL (38 mmol) of thiophenol for 4 h at 25 °C. The reaction mixture was taken up in ether and washed with 5% aqueous sodium hydroxide until no thiophenoxide could be detected by precipitation of diphenyl disulfide upon addition of hypochlorite bleach solution. The organic phase was dried over magnesium sulfate and removed in vacuo to give a yellowish oil. The latter was passed rapidly through a silica gel wash column (5% ethyl acetate in hexanes) to provide 1.24 g (90%) of **5** as a pale yellow oil: ^{1}H NMR (CCl_4) δ 1.0–2.6 (m, 9 H, $(CH_2)_4$), 4.0–4.2 (m, 1 H, HCSPh), 4.63 (d, J = 10 Hz, 1 H, $HC(SPh)_2$), 7.0–7.6 (m, 15 H, aromatic); IR (CCl_4) 1585 cm^{-1}; m/e (obsd) 422.1160, m/e (calcd for $C_{25}H_{26}S_3$) 422.1197.

***cis*-(7) and *trans*-2-(Phenylthio)cyclohexanecarboxaldehyde (8).** To a solution of 0.80 mL (860 mg, 7.8 mmol) of thiophenol dissolved in 10 mL of anhydrous ether was added 0.23 mL (0.25 mmol) of a 1.1 M solution of low halide methyllithium in ether and 20.0 μL (15.4 mg, 13 mmol) of TMEDA. The latter caused partial dissolution of the lithium thiophenoxide. A solution of 500 mg (4.54 mmol) of cyclohexenecarboxaldehyde in 5 mL of ether was added, and the mixture was stirred for 1.5 h at 25 °C. The mixture was extracted with 5% aqueous sodium hydroxide until no thiophenoxide was present in the aqueous wash. Removal of the ether from the dried ($MgSO_4$) extract gave 876 mg (88%) of a pale yellow oil consisting of a 3:7 mixture (NMR) of the cis **7** and the trans **8** isomers. The isomers were separated by medium-pressure liquid chromatography on a silica gel column, using 5% ethyl acetate in hexanes as eluent. Cis aldehyde **7**: ^{1}H NMR (CCl_4) δ 1.1–2.3 (m, 8 H, $(CH_2)_4$), 2.3–2.7 (m, 1 H, HCCHO), 3.5–3.7 (m, 1 H, HCSPh), 7.0–7.4 (m, 5 H, aromatic), 9.70 (s, 1 H, CHO); IR ($CHCl_3$) 1720 cm^{-1} (C=O); m/e (obsd) 220.0920, m/e (calcd for $C_{13}H_{16}OS$) 220.0922. Trans aldehyde **8**: ^{1}H NMR (CCl_4) δ 1.0–2.4 (m, 9 H, $(CH_2)_4CHCHO$), 2.8–3.4 (m, 1 H, HCSPh), 7.1–7.5 (m, 5 H, aromatic), 9.55 (d, J = 2.5 Hz, 1 H, CHO); IR ($CHCl_3$) 1710 cm^{-1} (C=O); m/e (obsd) 220.0906, m/e (calcd for $C_{13}H_{16}OS$) 220.0922.

***trans*-2-(Bis(phenylthio)methyl)-1-(phenylthio)cyclohexane (9).** Anhydrous hydrogen chloride was passed through a solution of 590 mg (2.68 mmol) of **8** dissolved in 2.5 mL (24 mmol) of thiophenol for 3 h. The reaction mixture was taken up in ether and washed with 5% sodium hydroxide until no thiophenoxide was present in the aqueous layer. Removal of the dried ($MgSO_4$) ether provided 1.06 g (94%) of **9** as a yellow oil: ^{1}H NMR (CCl_4) δ 1.0–2.7 (m, 9 H, $(CH_2)_4CHCH(SPh)_2$), 3.0–3.6 (m, 1 H, $HC(SPh)$), 5.42 (d, J = 3 Hz, 1 H, $HC(SPh)_2$), 7.0–7.6 (m, 15 H, aromatic); m/e (obsd) 422.1160, m/e (calcd for $C_{25}H_{26}S_3$) 422.1197.

Reaction of *trans*-2-(Bis(phenylthio)methyl)-1-(phenylthio)cyclohexane (9) with Methyllithium. To a solution of 218 mg (0.516 mmol) of **9** and 0.60 mL (0.46 g, 4.0 mmol) of TMEDA dissolved in 4.0 mL of anhydrous THF at 0 °C under argon was added 1.9 mL (2.1 mmol) of an ether solution of low halide methyllithium. After the solution had remained for 50 h at that temperature with stirring, excess D_2O was added. The mixture was washed with water, and the dried ($MgSO_4$) organic phase was concentrated in vacuo. The residue was subjected to medium-pressure liquid chromatography on silica gel, using 0.5% ethyl acetate in hexanes as eluent. The first fraction contained 79 mg (51%) of the ring-closed product **10**, mp 56–59 °C (mmp with an authentic sample[16] 57–59 °C); the mobility in thin-layer chromatography and the ^{1}H NMR spectrum were identical with those of the authentic sample. The second fraction consisted of 62 mg (29%) of unchanged **9**; within the error limits of NMR integration none of the thioacetal hydrogen atoms had been replaced with deuterium.

Reaction of *cis*-2-(Bis(phenylthio)methyl)-1-(phenylthio)cyclohexane (5) with Methyllithium. The experiment was performed in the same way as that described directly above, starting with 262 mg (0.621 mmol) of **5**. Medium pressure chromatography yielded five fractions containing the following weights (in mg): 8, 14, 42, 23, and 34. Although each of the first four fractions appeared homogeneous by TLC, the mass spectra indicated that each was a mixture; for example, a pair of major peaks in one fraction differed by 5 mass units. The fifth fraction consisted of recovered **5** (13%), the ^{1}H NMR spectrum of which lacked the doublet at σ 4.63 for the thioacetal proton.

Acknowledgment. We thank Dr. Robert Hutchins for supplying compound **4**, Mr. Daniel Ouellette for recording the high-resolution mass spectra, and the National Institutes of Health for support of this work (GM 22760).

Registry No. **4**, 71341-84-9; **5**, 71964-53-9; **6**, 1192-88-7; **7**, 71964-54-0; **8**, 71964-55-1; **9**, 71964-56-2; **10**, 58681-16-6; thiophenol, 108-98-5.

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(18) We had previously reported such exchange between cyclopropanone phenylthioketal and *tert*-butyllithium.[3]