2.30–2.60 (m, 2 H), 2.64–2.94 (m, 2 H); ^{13}C NMR δ 167.9, 29.8, 23.0*, 22.7*, 24.1, 131.2, 156.5, 18.0; mass spectrum, *m/e* (intensity) EI 185.1 (100, M^+), 170.1 (50, $M^+ - CH_3$), 138.1 (60, $M^+ - SCH_3$).

Anal. Calcd for $C_8H_{11}NS_2$: C, 51.85; H, 5.98. Found: C, 51.76; H, 6.02.

5,6-Dihydro-3-(methylthio)-4*H*-cyclopent[*c*]isothiazole (13). Either general procedure B (heated to reflux for 0.75 h) or C (heated to reflux for 8 h) was used to obtained this isothiazole. Workup gave crude **13** in 75% (procedure D) and 85% (procedure E) yield. Purification by silica gel column chromatography (R_f 0.23, petroleum ether/10% ether, v/v) gave an analytically pure sample of **13**: IR 2999 (s), 2996 (s), 2926 (m), 2853 (w), 1427 (s), 1381 (s), 954 (m), 757 (s) cm^{-1}; ^1H NMR δ 2.48 (s, 3 H), 2.40–2.63 (m, 6 H); ^{13}C NMR δ 179.8, 29.3, 24.2, 28.7, 140.1, 151.7, 18.3; mass spectrum, *m/e* (intensity) CI 172.2 (100, $M^+ + 1$); EI 171.1 (100, M^+), 124.1 (60, $M^+ - SCH_3$).

Anal. Calcd for $C_7H_9NS_2$: C, 49.09; H, 5.30; S, 37.45. Found: C, 49.09; H, 5.32; S, 37.53.

3-Ethyl-4-methyl-5-(methylthio)isothiazole (14). Oxime **7** (688 mg, 3.34 mmol) dissolved in dry methylene chloride (3.5 mL) was added dropwise over a period of 25 min to a solution of $SOCl_2$ (0.3 mL) and pyridine (0.6 mL) at 0 °C under nitrogen and then the solution was stirred at room temperature for 9 h. Workup (R_f 0.16, petroleum ether/10% ether, v/v) gave crude **14** in 80% (≥95% by NMR) yield: IR (neat) 2976 (s), 2927 (m), 2877 (w), 1680 (m), 1516 (m), 1261 (vs), 1097 (s), 1015 (s), 966 (s), 810 (vs) cm^{-1}, ^1H NMR (200 MHz) δ 2.35 (s, 3 H), 2.44 (s, 3 H), 1.35 (t, J = 7.5 Hz, 3 H), 2.91 (q, J = 7.5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ 173.6, 27.2, 13.9, 15.3 (CH_3C=C), 123.9, 155.0, 21.6; mass spectrum, *m/e* (intensity) CI 174.2 (100, $M^+ + 1$); EI 173.1 (100, M^+), 158.1 (67, $M^+ - CH_3$).

Anal. Calcd for $C_7H_{11}NS_2$: C, 48.51; H, 6.40. Found: C, 48.60; H, 6.47.

5-(Methylthio)isothiazole (15). General procedure C was employed and afforded isothiazole **15** in 60% yield (≥95% pure by NMR, R_f 0.28, petroleum ether/10% ether, v/v): IR 2997 (s), 2926 (s), 1490 (m), 1443 (m), 1396 (vs), 1336 (m), 1286 (m), 970 (m), 907 (m), 828 (s), 804 (s), 725 (m) cm^{-1}; ^1H NMR δ 2.62 (s, 3 H), 7.02 (s, 1 H), 8.34 (s, 1 H); ^{13}C NMR (50.3 MHz) δ 164.0, 121.2, 157.6, 18.8; mass spectrum *m/e* (intensity) EI 131.1 (100, M^+).

Acknowledgment. Support for this work by the National Institutes of Health (PHS GM-36824-01) is gratefully acknowledged.

Registry No. **1**, 17649-90-0; **2**, 17649-89-7; **3**, 51507-08-5; **4**, 78263-38-4; **5**, 118631-08-6; **6**, 118631-09-7; **7**, 118631-10-0; **8**, 118631-11-1; **9**, 118631-12-2; **10**, 118631-13-3; **11**, 68289-72-5; **12**, 118631-14-4; **13**, 118631-15-5; **14**, 118631-16-6; **15**, 45438-78-6.

Formation of Thiocarbonyl Compounds in the Reaction of Ebselen Oxide with Thiols

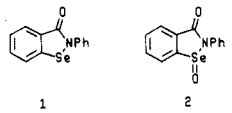
Richard S. Glass,* Firdous Farooqui, Mahmood Sabahi, and Kenneth W. Ehler

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

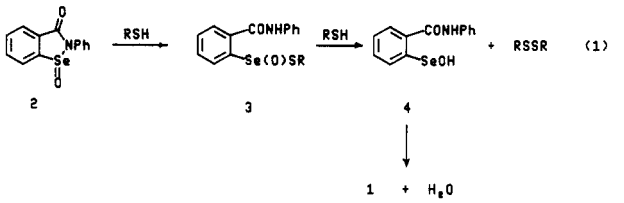
Received June 20, 1988

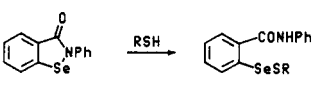
Reaction of α-toluenethiol with Ebselen oxide, **2**, affords dibenzyl disulfide and seleno sulfide **5**, R = $PhCH_2$. In the course of this reaction, thiobenzaldehyde is formed and can be trapped with cyclopentadiene in 90% yield. Reaction of 2-propene-1-thiol with **2** afforded thioacrolein dimer in 69% yield and seleno sulfide **5**, R = CH_2-CH=CH_2. Trapping, stereochemical, and isotopic exchange studies were used to determine if in the reaction of **2** with 1-heptanethiol, cyclohexanethiol, and *N*-acetyl-D,L-cysteine thiocarbonyl compounds heptanethial, cyclohexanethione, and 2-acetamino-3-thioxopropanoic acid (α-thioformyl-*N*-acetylglycine), respectively, are also formed. These studies showed that free thiocarbonyl compounds are not formed in these reactions.

The selenium heterocycle 2-phenyl-1,2-benziso-selenazol-3(2*H*)-one, **1** (Ebselen, PZ 51),[1] is a remarkably good catalyst for the oxidation of glutathione (GSH) to GSSG by hydroperoxides.[2] Interest in this catalytic activity has been stimulated because of its possible relevance to the mechanism of action of the selenium-containing enzyme glutathione peroxidase.[3] Ebselen is readily oxidized to the corresponding oxide **2** by hydrogen peroxide.[4] The rapid reactions of Ebselen oxide, **2**, with thiols have been reported[4,5] to give Ebselen and the corresponding disulfides by the suggested pathway shown in eq 1. Ebselen, **1**, further reacts with thiols to give the corresponding seleno sulfides **5**. In a related reaction of α-toluenethiol



1 2





(1) Kamigata, N.; Iizuka, H.; Izuoka, A.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2179.

(2) (a) Muller, A.; Cadenas, E.; Graf, P.; Sies, H. *Biochem. Pharmacol.* **1984**, *33*, 3235. (b) Wendel, A.; Fausel, M.; Safayhi, H.; Tiegs, G.; Otter, R. *Ibid.* **1984**, *33*, 3241. (c) Wendel, A.; Fausel, M.; Safayhi, H.; Tiegs, G.; Otto, R. In *Selenium in Biology and Medicine*; Combs, G. F., Jr., Spallholz, J. E., Levander, D. A, Oldfield, J. E., Eds.; Van Nostrand Reinhold: New York, 1987; Part A, pp 153–159.

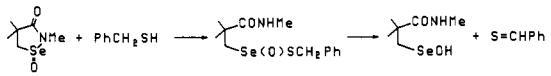
(3) Ganther, H. E.; Kraus, R. J. *Meth. Enzymol.* **1984**, *107*, 593. Epp, O.; Ladenstein, R.; Wendel, A. *Eur. J. Biochem.* **1983**, *133*, 51. Ganther, H. E. *Chem. Scr.* **1975**, *8A*, 79.

(4) Fischer, H.; Dereu, N. *Bull. Chem. Soc. Belg.* **1987**, 757.

(5) Kamigata, N.; Takata, M.; Matsuyama, H.; Kobayashi, M. *Sulfur Lett.* **1986**, *5*, 1.

0022-3263/89/1954-1092$01.50/0

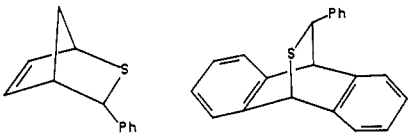
with seleninamide **6** under basic conditions, thiobenzaldehyde was reportedly formed[6] by a syn elimination of the presumed intermediate thiolseleninate as shown below. This paper reports our studies on the formation of thiocarbonyl compounds in the reaction of thiols with Ebselen oxide.



6

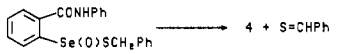
Results and Discussion

Reaction of **2** with α-toluenethiol in a 1:3 molar ratio in dichloromethane afforded dibenzyl disulfide in 77% isolation yield and seleno sulfide **5**, R = $PhCH_2$, in 80% isolated yield. Since a transient blue color was observed in this reaction, it was conjectured that thiobenzaldehyde might be an intermediate. Consequently, the reaction was carried out in the presence of cyclopentadiene, which is known to trap thiobenzaldehyde as adduct **7**.[7] In the



7 8

event, adduct **7** was obtained in 90% isolated yield as a mixture of isomers and seleno sulfide **5**, R = $PhCH_2$, in 84% isolated yield. A reasonable mechanism for the production of thiobenzaldehyde is first formation of thioseleninate **3**, R = $PhCH_2$, followed by elimination of selenenic acid **4**, perhaps by a syn pathway.[6] Since under

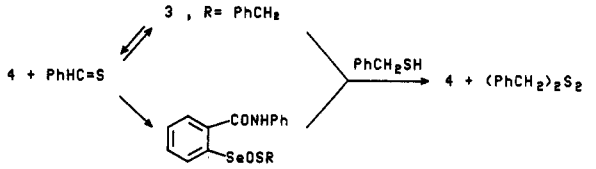


the conditions of this reaction in the absence of cyclopentadiene, dibenzyl disulfide is formed in high yield, thiobenzaldehyde must be converted to this product. The simplest possibility for this transformation is the reaction of thiobenzaldehyde and α-toluenethiol to form dibenzyl disulfide (eq 2). To adduce evidence on this point, the

$$PhCH{=}S + PhCH_2SH \rightarrow PhCH_2SSCH_2Ph \quad (2)$$

adduct of anthracene and thiobenzaldehyde **8**, which is known to decompose thermally to anthracene and thiobenzaldehyde,[8] was heated at reflux in xylene in the presence of α-toluenethiol. Anthracene was formed in high yield, but dibenzyl disulfide, which is stable under the reaction conditions, was produced in only low yield. This demonstrates that formation of dibenzyl disulfide by direct, uncatalyzed reaction of thiobenzaldehyde and α-toluenethiol, under these reaction conditions, is not a major pathway. This suggests that the direct reaction of thiobenzaldehyde and α-toluenethiol, under the conditions of the reaction of Ebselen oxide, **2**, and α-toluenethiol (even though the temperature in this reaction and that with adduct **8** are different) is not the major route by which the thiobenzaldehyde formed in this reaction is converted to product. Consequently, selenenic acid **4**, which is formed concomitantly with thiobenzaldehyde, may have catalyzed the reaction shown in eq 2. Conceivable pathways for this

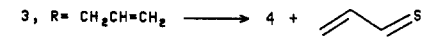
Scheme I



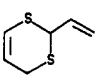
9

catalysis are summarized in Scheme I. Recombination of thiobenzaldehyde and selenenic acid **4** to regenerate thiolseleninate **3**, R = $PhCH_2$, followed by slow reaction of this thiolseleninate with α-toluenethiol is possible.[9] However, rearrangement of this thiolseleninate to its isomer **9**, R = $PhCH_2$, followed by reaction with α-toluenethiol is an alternative sequence analogous to that suggested previously in a related system.[10] Indeed, selenenic–sulfenic mixed anhydride **9**, R = $PhCH_2$, could be formed directly from selenenic acid **4** and thiobenzaldehyde followed by recombination with opposite regiochemistry.[10]

The reaction of 2-propene-1-thiol (allyl mercaptan) with **2** was studied. α-Elimination of expected adduct **3**, R = $CH_2CH{=}CH_2$ would give thioacrolein as shown in eq 3.



(3)



10

Such cycloelimination is analogous to the formation of thioacrolein from allicin **11a** and 5-methyl 2-propenethiosulfinate **11b** as shown in eq 4.[11] Thioacrolein is

$$RS(O)SCH_2CH{=}CH_2 \rightarrow RSOH + S{=}CHCH{=}CH_2 \quad (4)$$

11a, R = $CH_2{=}CHCH_2$
11b, R = CH_3

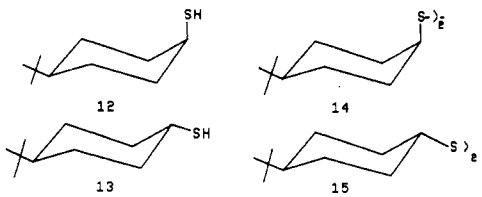
known[12] to dimerize to a mixture consisting predominantly of dimer **10**. The reaction of 2-propene-1-thiol and **2** was monitored by ^1H NMR spectroscopy. With a 3:1 ratio respectively of reactants, adduct **5**, R = $CH_2CH{=}CH_2$, dimer **10**, and unreacted thiol were the major constituents immediately formed in this fast reaction, and there was no significant change on standing. Essentially the same result was obtained by using a 2:1 ratio, respectively, of reactants except no 2-propene-1-thiol remained. Analysis of this latter reaction by ^1H NMR spectroscopy revealed the formation of dimer **10** in 69% yield and the absence of diallyl disulfide. Chromatographic purification of the mixture formed on reacting 2-propene-1-thiol and **2** in a 2:1 molar ratio, respectively, afforded pure dimer **10**, which was characterized by IR, ^1H NMR, and MS analyses, and seleno sulfide **5**, R = $CH_2CH{=}CH_2$, isolated in 84% yield.

(6) Reich, H. J.; Jasperse, C. P. *J. Am. Chem. Soc.* **1987**, *109*, 5549.
(7) Vedejs, E.; Eberlein, T. H.; Mazur, D. J.; McClure, C. K.; Perry, D. A.; Ruggeri, R.; Schwartz, E.; Stults, J. S.; Varie, D. L.; Wilde, R. G.; Wittenberger, S. *J. Org. Chem.* **1986**, *51*, 1556.
(8) Baldwin, J. E.; Lopez, R. C. G. *J. Chem. Soc., Chem. Commun.* **1982**, 1029.
(9) Kice, J. L.; Lee, T. W. S. *J. Am. Chem. Soc.* **1978**, *100*, 5094.
(10) Reich and Jasperse[6] suggested that the thiolseleninate $tBuSSe(O)CH_2C(Me)_2CONHMe$ reacted with tBuSH to give tBuSStBu by rate-determining isomerization of the thiolseleninate to the corresponding selenenic–sulfenic mixed anhydride. Such isomerization requires a pathway not involving elimination to a selenenic acid and thiocarbonyl compound and recombination because such elimination is not possible in this case.
(11) Block, E.; O'Connor, J. *J. Am. Chem. Soc.* **1974**, *96*, 3929. Baldwin, J. E.; Lopez, R. G. *Tetrahedron* **1983**, *39*, 1487. Block, E.; Ahmad, S. *J. Am. Chem. Soc.* **1984**, *106*, 8295. Block, E.; Ahmad, S.; Catalfano, J. L.; Jain, M. K.; Apitz-Castro, R. *Ibid.* **1986**, *108*, 7045.
(12) Bock, H.; Mohmand, S.; Hirabayashi, T.; Semkow, A. *J. Am. Chem. Soc.* **1982**, *104*, 312. Bock, H.; Mohmand, S.; Hirabayashi, T.; Semkow, A. *Chem. Ber.* **1982**, *115*, 1339.

These results support the formation of thioacrolein according to eq 3. However, this thiocarbonyl compound irreversibly dimerizes and does not form diallyl disulfide even in the presence of excess 2-propene-1-thiol. The high yield of thioacrolein dimer obtained in the reaction of **2** with 2-propene-1-thiol suggests that this may be a synthetically useful method for generating thioacrolein.

To determine whether α-elimination of thioseleninates **3** was a general reaction, attempts were made to trap other thiocarbonyl compounds. 1-Heptanethiol was next studied to determine if it underwent elimination to form the corresponding thioaldehyde. Reaction of 1-heptanethiol with **2** in a 3:1 molar ratio in dichloromethane produced *n*-heptyl disulfide in 90% isolated yield and seleno sulfide **5**, R = $(CH_2)_6CH_3$, in 87% isolated yield. When this reaction was carried out in a 2:1 molar ratio of 1-heptanethiol to **2**, the same products were obtained in lower yield along with unreacted **2**. In the presence of cyclopentadiene, the same products were produced and there was no evidence for the formation of the cycloadduct from heptanethial and cyclopentadiene. The lack of evidence for the formation of the corresponding thioaldehyde from 1-heptanethiol, in contrast to that obtained with α-toluenethiol and 2-propene-1-thiol, may be due to either of two reasons. α-Elimination of thiolseleninates **3**, R = $PhCH_2$, and **3**, R = $CH_2CH{=}CH_2$ may be favored because the hydrogen removed is activated, i.e., benzylic and allylic respectively, whereas, there is no such activation in thiolseleninate **3**, R = $(CH_2)_6CH_3$. Alternatively, heptanethial is formed in the reaction of 1-heptanethiol with **2**, but it undergoes disulfide formation faster than cycloaddition with cyclopentadiene. To eliminate this latter possibility, two other tests for detecting the intermediacy of thiocarbonyl compounds in the reaction of aliphatic thiols with Ebselen oxide were devised and used as outlined below.

Cyclohexanethiol reacts with **2** in a 3:1 molar ratio, respectively, to afford the corresponding disulfide isolated in 58% yield and seleno sulfide **5**, R = C_6H_{11}, isolated in 86% yield. If α-elimination of the presumed thiolseleninate intermediate **3**, R = C_6H_{11}, occurred to give cyclohexanethione followed by recombination with selenenic acid **4** and subsequent disulfide formation, it was surmised that such a sequence could be revealed by a stereochemical test. Since in this sequence the α-hydrogen is removed and then replaced, loss of stereochemical integrity is expected. However, reaction of *cis*- or *trans*-4-*tert*-butylcyclohexanethiol[13] **12** or **13**, respectively, with **2** in a 3:1 molar ratio produced *cis*- or *trans*-disulfides[14] **14** or **15**, respectively (and *no cis,trans*-disulfide), and the



corresponding seleno sulfides **5**, R = *cis*-4-*tert*-butylcyclohexyl, and **5**, R = *trans*-4-*tert*-butylcyclohexyl, in good yields. That is, this reaction is completely *stereospecific* within the limits of experimental error. The absence of isomerization at C(1) excludes the intermediacy of free 4-*tert*-butylcyclohexanethione.

A second test for detecting α-elimination of thiolseleninates **3** to thiocarbonyl compounds was based on isotopic exchange. If the thiol allowed to react with **2** was deuterated in the α-position, α-elimination would afford selenenic acid **4** with SeOD instead of SeOH and the thiocarbonyl compound. If this reaction were carried out in hydroxylic solvent and if H/D exchange of the acidic selenenic acid were fast (with solvent or the adjacent amide moiety), then recombination of the selenenic acid and the thiocarbonyl compound should provide an α-hydrogen atom in place of an α-deuterium atom.

N-Acetyl-D,L-β,β-dideuterocysteine **16** was prepared by a modification of the reported synthesis of D,L-β,β-dideuterocysteine.[15] *N*-Acetyl-D,L-β,β-dideuterocysteine reacts rapidly with **2** in a 3:1 molar ratio in either methanol or aqueous dioxane. To facilitate chromatographic separation, the reaction mixture was treated with diazomethane. Seleno sulfide **5**, R = $CD_2CH(NHAc)CO_2Me$, was obtained in 63–91% yield and methyl *N*-acetyl-D,L-β,β-dideuterocystinate **17** in 80–96% yield as outlined in eq 5. Authentic seleno sulfide **5**, R = $CH_2CH(NHAc)CO_2Me$, was prepared by the reaction of **1** with methyl *N*-acetyl-D,L-cysteinate. After chromatographic separation of the disulfide **17** produced in this reaction, ^1H NMR spectroscopic analysis[16] revealed no detectable exchange of the α-deuterium atoms. This result shows that α-elimination does not occur in this reaction, assuming that recombination of selenenic acid **4** with the thiocarbonyl compound is slower than H/D exchange.

$$\mathbf{2} + \underset{\mathbf{16}}{HO_2CCH(NHAc)CD_2SH} \rightarrow \mathbf{5},\ R = CD_2CH(NHAc)CO_2Me + \underset{\mathbf{17}}{[MeO_2CCH(NHAc)CD_2S]_2} \quad (5)$$

In conclusion, free thiocarbonyl compounds are formed in the reaction of α-toluenethiol and 2-propene-1-thiol with Ebselen oxide, **2**, but not in the reaction of 1-heptanethiol, cyclohexanethiol, or *N*-acetyl-D,L-cysteine with **2**. The reactions observed and intermediates suggested in the reactions of all the thiols studied with **2** are outlined in Scheme II.

Experimental Section

All melting points are uncorrected and were taken in open glass capillary tubes with a Thomas-Hoover melting point apparatus. IR spectra were obtained on a Perkin-Elmer Model 983 infrared spectrometer. ^1H NMR spectra were measured at 250 MHz with a Bruker WM250 NMR spectrometer and at 500 MHz with a Bruker AM500 NMR spectrometer on samples containing tetramethylsilane as internal standard. Mass spectra were measured with a Finnegan MAT 90 or Varian 311A mass spectrometers. GC–MS analyses were done with a Hewlett-Packard Ultra-2 system with a 25 × 0.2 mm fused silica column packed with 5% phenyl methyl silicone.

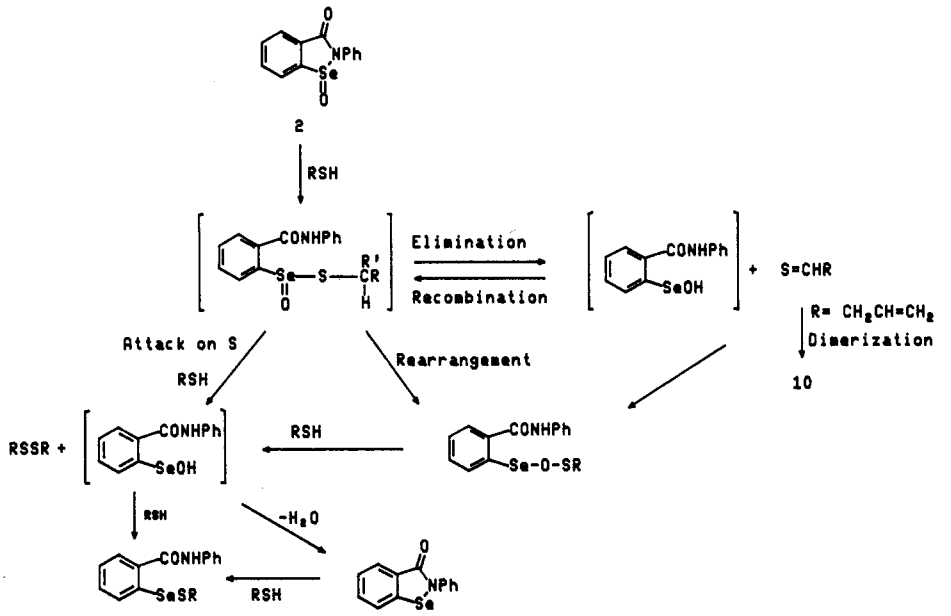
Preparative TLC was done on 20 × 20 cm glass plates prepared with silica gel GF (Analtech) on an absorbent layer 0.75 mm thick. Column chromatography was done using silica gel (60 Å pore size, 75–125 μm) supplied by Analtech.

Reagent grade dichloromethane was distilled from P_2O_5 before use. Diallyl mercaptan and diallyl disulfide were obtained from Aldrich Chemical Co., Milwaukee, WI. Ebselen, **1**, was prepared by the procedure of Kamigata et al.,[1] and it was oxidized to Elselen oxide, **2**, by the method of Fischer and Dereu.[4]

Reaction of Ebselen Oxide (2) with α-Toluenethiol. To a solution of **2** (60 mg, 0.206 mmol) dissolved in anhydrous dichloromethane (4 mL) was added α-toluenethiol (76.7 mg, 0.618 mmol) with stirring. A transient blue color was observed during the addition. After the mixture was stirred for 0.5 h, the solvent was evaporated, and the residue was purified by preparative TLC

(13) Eliel, E. L.; Kandasamy, D. *J. Org. Chem.* **1976**, *41*, 3899.
(14) These materials were shown to be identical with authentic compounds prepared by the procedures in the literature.[13]
(15) Upson, D. A.; Hruby, V. J. *J. Org. Chem.* **1976**, *41*, 1353.
(16) Jones, J. B.; Wigfield, D. C. *Can. J. Chem.* **1966**, *44*, 2522.

Scheme II



with 20% ethyl acetate in hexane as eluant. Seleno sulfide **5**, R = $PhCH_2$ (65 mg, 80%), identical with material prepared as below, and dibenzyl disulfide (39 mg, 77%), mp 67–68 °C, identical with authentic sample, were obtained in this way.

Reaction of 2 with α-Toluenethiol in the Presence of Cyclopentadiene. To a solution of **2** (20 mg, 0.068 mmol) dissolved in anhydrous dichloromethane (3 mL) was added freshly distilled cyclopentadiene (9.07 mg, 0.137 mmol) followed by α-toluenethiol (25.6 mg, 0.206 mmol) with stirring. After being stirred for 1 h the reaction mixture was concentrated on a rotary evaporator, and the residue was purified by preparative TLC, eluting with 20% ethyl acetate in hexane. Seleno sulfide **5**, R = $PhCH_2$ (23 mg, 84%), and adduct **7** (12 mg, 90%) as a mixture of exo and endo isomers (3:1) identical spectroscopically with that reported in the literature[7] was obtained in this way.

Synthesis of Seleno Sulfide 5, R = $PhCH_2$. To a solution of Ebselen, **1** (100 mg, 0.364 mmol), dissolved in dichloromethane (10 mL) was added α-toluenethiol (54 mg, 0.44 mmol) with stirring at room temperature. After the mixture was stirred for 1 h, the solvent was removed by rotary evaporation. The residue was washed with ether and recrystallized from benzene–petroleum ether to give seleno sulfide **5**, R = $PhCH_2$ (101 mg, 67%), as colorless crystals: mp 128–9 °C; IR (KBr) 3302 (NH), 1620 (CO), 1592 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.90 (2 H, s, CH_2), 7.11–7.60 (13 H, m, Ar H), 7.79 (1 H, s, NH), 8.11 (2 H, dd, J = 8.0, 1.0 Hz).

Decomposition of Anthracene–Thiobenzaldehyde Adduct 8 in the Presence of α-Toluenethiol. A sample of the anthracene–thiobenzaldehyde adduct **8** (10 mg, 0.033 mmol), prepared according to the procedure of Baldwin and Lopez,[8] and α-toluenethiol (8.3 mg, 0.078 mmol) dissolved in xylene (0.8 mL) were stirred and heated at reflux for 1 h. The solution was concentrated carefully on a rotary evaporator, and the residue was analyzed by ^1H NMR spectroscopy. Piperonal (0.01 mmol) was added as a standard, and anthracene (73%), dibenzyl disulfide (14%), α-toluenethiol (37%), and unidentified products were observed. When adduct **8** was allowed to decompose in the absence of α-toluenethiol no significant amount of dibenzyl disulfide was detected by ^1H NMR spectroscopic analysis.

Reaction of 2 with 2-Propene-1-thiol. To a solution of **2** (58 mg, 0.20 mmol) dissolved in anhydrous dichloromethane (5 mL) was added a solution of purified 2-propene-1-thiol (48 μL, 44 mg) in anhydrous dichloromethane (3 mL) with stirring at room temperature. After 1 h the reaction mixture was concentrated by rotary evaporation, and the residue was purified by preparative TLC, eluting with 5% ethyl acetate in hexanes. Seleno sulfide **5**, R = $CH_2CH{=}CH_2$ (58 mg, 84%) was obtained as a colorless solid: mp 185 °C dec; IR (KBr) 3212 (NH), 1634 (CO), 1595 (CONH), 1521, 1436, 1326 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.35 (2 H, d, J = 7.3 Hz), 4.95 (1 H, d, J = 9.9 Hz), 5.02 (1 H, d, J = 17.0 Hz), 5.75 (1 H, ddd, J = 17.0, 9.9, 7.3 Hz), 7.05 (1 H, t, J = 7.3 Hz), 7.14–7.27 (3 H, m), 7.42 (1 H, t, J = 7.3 Hz), 7.49 (2 H, d, J = 7.3 Hz), 7.60 (1 H, d, J = 7.3 Hz), 8.01 (1 H, br s, NH), 8.22 (1 H, d, J = 8.0 Hz); MS, m/z 351 (9.8), 350 (7.8), 349 (41), 348 (4), 347 (20), 346 (7.4), 345 (7.2), 277 (11.9), 276 (15.7), 275 (48, M – C_3H_5S), 274 (15.1), 273 (25), 272 (13.3), 271 (9.9), 195 (100).

This reaction was also monitored by ^1H NMR spectroscopy in the following way. In each of two NMR tubes was placed a solution of **2** (5.8 mg, 0.020 mmol) dissolved in dideuteriodichloromethane (0.2 mL) and cooled in an ice–water bath. A solution of 2-propene-1-thiol (3.2 μL, 0.040 mmol) dissolved in dideuteriodichloromethane (0.2 mL) was added to one NMR tube, and a solution of 2-propene-1-thiol (4.8 μL, 0.060 mmol) in dideuteriodichloromethane (0.2 mL) was added to the other. ^1H NMR spectra were taken at various time intervals, and the sample containing the 3:1 molar ratio of 2-propene-1-thiol to **2** showed peaks due to thiol even after 48 h at room temperature. Analysis of the ^1H NMR spectrum of the sample containing the 2:1 molar ratio of 2-propene-1-thiol to **2** revealed the formation of thioacrolein dimer **10** in 69% yield. Comparison of this ^1H NMR spectrum with that of authentic diallyl disulfide showed no trace of this material in the reaction mixture. Analysis of this reaction mixture by TLC also failed to reveal the presence of any diallyl disulfide.

Reaction of 2 with 1-Heptanethiol. To a solution of **2** (20 mg, 0.068 mmol) dissolved in anhydrous dichloromethane (3 mL) was added 1-heptanethiol (27.2 mg, 0.206 mmol) with stirring. After 0.5 h at room temperature, the reaction mixture was concentrated on a rotary evaporator and purified by preparative TLC, eluting with 20% ethyl acetate in hexane. Seleno sulfide **5**, R = $(CH_2)_6CH_3$ (24.3 mg, 87%), identical with material made as recorded below, and diheptyl disulfide (17 mg, 90%), identical with authentic material, were obtained in this way.

Synthesis of Seleno Sulfide 5, R = $(CH_2)_6CH_3$. To a solution of Ebselen, **1**, (150 mg, 0.545 mmol) dissolved in chloroform (10 mL) was added 1-heptanethiol (144 mg, 1.09 mmol) with stirring. After 1 h at room temperature, the solvent was evaporated with a rotary evaporator, and the residue was recrystallized with ethyl acetate–petroleum ether to give seleno sulfide **5**, R = $(CH_2)_6CH_3$ (187 mg, 85%): mp 110–111 °C; IR (KBr) 3306 (NH), 2922, 1625 (CO), 1596 (CONH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78 (3 H, t, J = 6.9 Hz, CH_3), 1.08–1.32 (8 H, m), 1.55 (2 H, tt, J = 7.3, 6.6 Hz), 2.68 (2 H, t, J = 7.3 Hz, SCH_2), 7.01–7.16 (2 H, m, Ar H), 7.19–7.61 (7 H, m, Ar H), 7.99 (1 H, br s, NH), 8.22 (2 H, dd, J = 7.1, 1.0 Hz, Ar H); MS, m/z 407, 406. Anal. Calcd for $C_{20}H_{25}NOSSe$: C, 59.11; H, 6.16; N, 3.45; S, 7.88. Found: C, 58.93; H, 6.23; N, 3.43; S, 7.91.

Reaction of 2 with Cyclohexanethiol. To a solution of **2** (26 mg, 0.089 mmol) dissolved in anhydrous dichloromethane (5 mL) was added cyclohexanethiol (31.2 mg, 0.268 mmol) with

stirring. After 1 h, the reaction mixture was concentrated by rotary evaporator, and the residue was purified by preparative TLC, eluting with 10% ethyl acetate in hexane to give dicyclohexyl disulfide (12 mg, 58%), identical with authentic sample, and seleno sulfide **5**, R = C_6H_{11} (30 mg, 86%): mp 120–121 °C; IR (KBr) 3312 (NH), 1624 (CO), 1590 (CONH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06–1.90 (10 H, m), 2.61–2.72 (1 H, m, CHS), 7.06–7.62 (7 H, m, Ar H), 7.87 (1 H, br s, NH), 8.28 (1 H, dd, J = 8.1, 0.9 Hz).

Reaction of 2 with *cis*-4-*tert*-Butylcyclohexanethiol. To a solution of **2** (15.8 mg, 0.054 mmol) dissolved in anhydrous dichloromethane (2 mL) was added a solution of *cis*-4-*tert*-butylcyclohexanethiol (28 mg, 0.16 mmol), prepared according to the method of Eliel and Kandasamy,[13] dissolved in anhydrous dichloromethane (2 mL) with stirring and under an atmosphere of argon. Monitoring the reaction by ^1H NMR spectroscopy and TLC indicated that the reaction was complete in less than 1 h. After 1 h the reaction mixture was concentrated on a rotary evaporator, and the residue was chromatographed on a silica gel column (15 g, 55 × 1 cm). Elution with hexanes afforded *cis*-disulfide **14** (14 mg, 77%), identical with authentic compound by IR, ^1H NMR, and TLC analyses. Elution with ethyl acetate–hexanes (1:1) provided seleno sulfide **5**, R = *cis*-4-*tert*-butylcyclohexyl (21 mg, 84%), as a colorless solid: mp 140–141 °C; IR (KBr) 3366 (NH), 1642 (CO), 1596 (CONH), 1525, 1436 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.87 (9 H, s, t-Bu), 1.44–1.54 (5 H, m), 1.68 (2 H, tt, J = 3.9, 13.4 Hz), 2.12 (2 H, br d, J = 14.2 Hz), 3.23 (1 H, br s, CHS), 7.18 (1 H, dt, J = 1.0, 7.8 Hz, H4′), 7.33 (1 H, dt, J = 1.1, 7.8 Hz, H4), 7.39 (2 H, t, J = 7.8 Hz), 7.53 (1 H, dt, J = 1.1, 8.2 Hz, H3), 7.63 (2 H, dd, J = 1.0, 7.8 Hz), 7.67 (1 H, d, J = 7.8 Hz, H5), 7.84 (1 H, br s, NH), 8.35 (1 H, d, J = 8.2 Hz, H2); MS, m/z 449 (1.6), 448 (1.8), 447 (6.5), 446 (1.0), 445 (3.7), 444 (1.3), 443 (1.3), 276 (58, $M^+ - C_{10}H_{19}S$), 275 (47), 274 (35), 273 (29), 93 (100), calcd for $C_{23}H_{29}NOSSe$ 447.11358, found 447.11276.

Reaction of 2 with *trans*-4-*tert*-Butylcyclohexanethiol. The reaction was carried out in the same way as that for the reaction of **2** with *cis*-4-*tert*-butylcyclohexanethiol except that the trans isomer was used in place of the cis isomer. The crude reaction product was chromatographed on a silica gel column (15 g, 55 × 1 cm). Elution with hexanes afforded *trans*-disulfide **15** (16 mg, 88%), identical with authentic material[13] by IR, ^1H NMR, and TLC analyses. Elution with ethyl acetate–hexanes (1:1) gave seleno sulfide **5**, R = *trans*-4-*tert*-butylcyclohexyl (22 mg, 94%), as an off-white solid: mp 133–134.5 °C; IR (KBr) 3291 (NH), 1637 (CO), 1595 (CONH), 1561, 1437, 1322 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.80 (9 H, s, t-Bu), 0.98–1.06 (2 H, m), 1.22–1.37 (3 H, m), 1.78 (1 H, d, J = 9.7 Hz), 1.85 (1 H, d J = 12.3 Hz), 2.14 (2 H, br d, J = 13.3 Hz), 2.62 (1 H, tt, J = 3.8, 12.3 Hz, CHS), 7.17 (1 H, dt, J = 1.0, 7.6 Hz, H4′), 7.31 (1 H, dt, J = 1.0, 7.6 Hz, H4), 7.38 (2 H, t, J = 7.6 Hz, H3′,5′), 7.43 (1 H, t, J = 7.6 Hz, H3), 7.63 (2 H, dd, J = 1.0, 7.6 Hz, H2′,6′), 7.68 (1 H, d, J = 7.6 Hz, H5), 7.95 (1 H, br s, NH), 8.11 (1 H, dd, J = 1.0, 7.6 Hz, H2); MS, m/z 449 (1.6), 448 (1.8), 447 (6.9), 446 (1.0), 445 (3.8), 444 (1.4), 443 (1.4), 277 (23, $M^+ - C_{10}H_{19}S$), 276 (55), 275 (29), 93 (100), calcd for $C_{23}H_{29}NOSSe$ 447.11358, found 447.11397.

Synthesis of Ethyl *N*-Acetyl-*S*-benzyl-D,L-β,β-dideuterocysteinate. A solution of sodium α-toluenethiolate was prepared by adding α-toluenethiol (2.26 mL, 19.1 mmol) to a freshly prepared solution of sodium ethoxide made by adding sodium metal (0.44 g, 19 mmol) to absolute ethanol (30 mL), under a dry argon atmosphere. A solution of diethyl α-acetamido-α-[(trimethylammonio)dideuteromethyl]malonate iodide (7.7 g, 19.1 mmol, 98+% dideuterated), prepared according to the method of Upson and Hruby,[15] dissolved in absolute ethanol (30 mL) was added to the solution of sodium α-toluenethiolate heated at reflux. The reaction mixture was stirred and heated at reflux for 6 days. At the end of this time, the mixture was allowed to cool and then concentrated to an oil with a rotary evaporator. The oil was dissolved in chloroform and washed with cold, distilled water (13 mL), the aqueous layer was back-extracted with chloroform (10 mL), and the combined chloroform layers were dried over anhydrous potassium carbonate. After drying, the organic layer was filtered and concentrated by rotary evaporation to an oil, which was crystallized from ethyl acetate–hexanes to give colorless crystalline ethyl *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteinate (3.84 g, 50% yield): mp 73.5–74.5 °C; IR (KBr) 3333 (NH), 3025, 3007, 2983, 2936, 2916, 1726 (ester C=O), 1648 (amide C=O), 1524, 1241, 1035, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.26 (3 H, t, J = 7.3 Hz, CH_3CH_2), 1.98 (3 H, s, CH_3CO), 2.88 (0.04 H, br m, 2% β-CH_2S), 3.69 (2 H, s, $PhCH_2S$), 4.19 (2 H, q, J = 7.3 Hz, CH_3CH_2), 4.77 (1 H, d, J = 7.7 Hz, α-CH), 6.22 (1 H, br d, J = 7.7 Hz, NH), 7.29 (5 H, m, C_6H_5).

Synthesis of *N*-Acetyl-*S*-benzyl-D,L-β,β-dideuterocysteine. On heating a suspension of ethyl *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteinate (1.6 g, 5.6 mmol) in 1 N aqueous sodium hydroxide solution (7 mL, 7.0 mmol) to 65 °C for 2 min, a clear, colorless solution was obtained. After 2 h at room temperature, the solution was extracted with diethyl ether (2 × 10 mL) and acidified to pH 2.8 with 3 N aqueous hydrochloric acid solution. Colorless crystals of *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteine (1.3 g, 90%) were so obtained: mp 155.5–156 °C. The same reaction starting with ethyl *N*-acetyl-*S*-benzyl-D,L-cysteinate gave colorless crystals of *N*-acetyl-*S*-benzyl-D,L-cysteine: mp 155–156 °C; ^1H NMR (CD_3OD, 250 MHz) δ 1.98 (3 H, s, CH_3CO), 2.79 (2 H, *ABX*, J_{AB} = 14.0 Hz, J_{AX} = 8.4 Hz, J_{BX} = 4.9 Hz, β-CH_2S), 3.65 (2 H, s, $PhCH_2S$), 4.60 (1 H, AB*X*, J_{AX} = 8.3 Hz, J_{BX} = 4.9 Hz, α-CH), 7.31 (5 H, m, C_6H_5).

Synthesis of *N*-Acetyl-D,L-β,β-dideuterocysteine (16). Sodium (240 mg, 10.4 mmol) was added portionwise to a solution of *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteine (1.3 g, 5.1 mmol) in liquid ammonia (approximately 100 mL) freshly distilled from sodium in a 250-mL three-necked round-bottom flask. After the last portion of sodium metal was added, the blue color persisted for 30 min. Sufficient additional sodium metal slivers were added until a blue color was again obtained, and after 15 min, ammonium chloride (100 mg) was added. The ammonia was evaporated under argon over 4 h. Argon-purged distilled water (2 mL) was added to the residue, and the solution was extracted under argon with argon-purged diethyl ether (2 × 40 mL). The aqueous solution was acidified to about pH 2.2 with argon-purged 3 N aqueous hydrochloric acid solution, saturated with sodium chloride, and extracted under argon with argon-purged ethyl acetate (3 × 50 mL). The organic extracts were dried over anhydrous magnesium sulfate and concentrated by rotary evaporation to produce *N*-acetyl-D,L-β,β-dideuterocysteine (605 mg, 72%) as colorless crystals: mp 129–130 °C; IR (KBr) 3341 (NH), 2565 (br, SH), 1722 (ester C=O), 1595 (amide C=O), 1536, 1427, 1337, 765 cm^{-1}; ^1H NMR (CD_3COCD_3, 250 MHz) δ 1.89 (1 H, s, SH), 2.00 (3 H, s, CH_3CO), 2.9–3.0 (0.04 H, br m, 2% β-CH_2S), 4.68 (1 H, d, J = 7.6 Hz, α-CH), 7.52 (1 H, br s, NH).

Reaction of 2 with *N*-Acetyl-D,L-β,β-dideuterocysteine (16). To a solution of **2** (20 mg, 0.07 mmol) dissolved in methanol, dichloromethane, or aqueous 1,4-dioxane was added a solution of *N*-acetyl-D,L-β,β-dideuterocysteine (34 mg, 0.21 mmol) dissolved in the respective solvent. In one case, a solution of **2** dissolved in methanol was added to a solution of *N*-acetyl-D,L-β,β-dideuterocysteine dissolved in methanol. In all cases, the reaction was monitored by TLC on silica gel, eluting with two different solvent systems: methanol–1-butanol–water (1:7:2) and ethyl acetate. In each case, reaction was complete in 5–10 min after the addition with no Ebselen oxide, **2**, remaining. After the mixture was allowed to stand overnight, a freshly prepared solution of diazomethane in diethyl ether was added with dry ice–acetone cooling. In the case of the reaction in aqueous dioxane, the solvents were first removed under vacuum, the residue was dissolved in a few milliliters of methanol, and the solution was treated with ethereal diazomethane. Excess diazomethane was decomposed by the addition of acetic acid, and the reaction mixture was purified by preparative TLC, eluting with ethyl acetate. This gave a mixture of the diastereomers of methyl *N*-acetyl-D,L-β,β-dideuterocystinate [(88% in methanol, 96% in dichloromethane, 68% in aqueous dioxane, and 80% in methanol with inverse addition): ^1H NMR ($CDCl_3$, 250 MHz) δ 2.07, 2.08 (3 H, s, CH_3CO), 3.22 (0.03 H, br m, 2% β-CH_2S), 3.78 (3 H, s, CH_3O), 4.78 (1 H, d, J = 7.3 Hz, α-CH), 6.62 (1 H, t, J = 7.3 Hz, NH).[16] (In the case of the reaction in aqueous dioxane, ^1H NMR analysis indicated less than 2.2% proton exchanged for deuterium and less than 1.5% exchange in the other cases)] and β,β-dideutero seleno sulfide **5**, R = $CD_2CH(NHAc)CO_2Me$, identical (except for the deuterium atoms in place of hydrogen atoms) with that prepared below.

Synthesis of Methyl *N*-Acetyl-D,L-cysteinate. A solution of *N*-acetyl-D,L-cysteine (363 mg, 2.22 mmol), prepared in the same way as *N*-acetyl-D,L-β,β-dideuterocysteine outlined above, dissolved in methanol (3 mL) was added to an excess of freshly prepared diazomethane solution in diethyl ether cooled in a dry ice–acetone bath. The minimum amount of glacial acetic acid was added to discharge the yellow color. The resulting clear, colorless solution was concentrated with a rotary evaporator to an oil, which resisted crystallization (but whose spectra were identical with those of authentic crystalline methyl *N*-acetyl-L-cysteinate): IR (neat) 3279 (NH), 2563 (w, SH), 1736 (ester C=O), 1658 (amide C=O), 1537, 1216, 1042 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.37 (1 H, t, J = 9.0 Hz, SH), 2.08 (3 H, s, CH_3CO), 3.02 (2 H, dd, J = 3.9, 9.1 Hz, β-CH_2S), 3.80 (3 H, s, CH_3O), 4.90 (1 H, dt, J = 3.9, 7.7 Hz, α-CH), 6.54 (1 H, br s, NH).

Synthesis of Seleno Sulfide 5, R = $CH_2CH(NHAc)CO_2Me$. To a stirred solution of Ebselen, 1 (115 mg, 0.42 mmol), dissolved in dichloromethane (7 mL) under an argon atmosphere, was added a solution of methyl *N*-acetyl-D,L-cysteinate (68 mg, 0.42 mmol) dissolved in dichloromethane (2 mL). The solvent was removed with a rotary evaporator to obtain a pale yellow oil, which was crystallized from ethyl acetate–hexanes to give seleno sulfide **5**, R = $CH_2CH(NHAc)CO_2Me$ (115 mg, 61%), as a white solid: mp 141–142 °C dec; IR (KBr) 3278 (NH), 1742, 1731 (ester C=O), 1648, 1632 (amide C=O), 1596, 1530, 1437, 1327, 783, 757 cm^{-1}; ^1H NMR ($CDCl_3$ with 20% CD_3CN, 250 MHz) δ 1.93 (3 H, s, CH_3CO), 3.23 (2 H, *AB*X, J_{AB} = 13.8 Hz, J_{AX} = 6.3 Hz, J_{BX} = 4.8 Hz, β-CH_2S), 3.69 (3 H, s, CH_3O), 4.72 (1 H, m, α-CH), 6.64 (1 H, d, J = 7.6 Hz), 7.16 (1 H, AA'BB'X, J_{BX} = 7.4 Hz, H4'), 7.37 (3 H, m, H5,3',5'), 7.56 (1 H, t, J = 7.9 Hz, H4), 7.66 (2 H, AA'BB'X, J_{AB} = 7.7 Hz, H2',6'), 7.85 (1 H, d, J = 7.9 Hz, H6), 8.24 (1 H, d, J = 7.9 Hz, H3). Anal. Calcd for $C_{19}H_{20}N_2O_4SSe$: C, 50.55; H, 4.47; N, 6.21. Found: C, 50.65; H, 4.35; N, 6.23.

Registry No. **1**, 60940-34-3; **2**, 104473-83-8; **5** (R = $PhCH_2$), 114744-69-3; **5** (R = $CH_2CH{=}CH_2$), 118398-38-2; **5** (R = $(CH_2)_6CH_3$), 118398-39-3; **5** (R = C_6H_{11}), 118398-40-6; **5** (R = *cis*-4-*tert*-butylcyclohexyl), 118398-41-7; **5** (R = *trans*-4-*tert*-butylcyclohexyl), 118398-42-8; **5** (R = $CD_2CH(NHAc)CO_2Me$), 118398-43-9; **5** (R = $CH_2CH(NHAC)CO_2Me$), 118398-44-0; *exo*-**7**, 95417-00-8; *endo*-**7**, 95416-99-2; **8**, 84040-16-4; **10**, 80028-57-5; **12**, 53273-25-9; **13**, 60260-88-0; **14**, 60305-05-7; **15**, 60260-89-1; **16**, 118398-45-1; **17** (diastereomer 1), 118398-46-2; **17** (diastereomer 2), 118456-63-6; $PhCH_2SH$, 100-53-8; $(PhCH_2)_2S_2$, 150-60-7; cyclopentadiene, 542-92-7; anthracene, 120-12-7; 2-propene-1-thiol, 870-23-5; 1-heptanethiol, 1639-09-4; diheptyl disulfide, 10496-16-9; cyclohexanethiol, 1569-69-3; dicyclohexyl disulfide, 2550-40-5; ethyl *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteinate, 118398-47-3; sodium α-toluenethiolate, 3492-64-6; diethyl α-acetamido-α-[(trimethylammonio)dideuteromethyl]malonate iodide, 57866-76-9; *N*-acetyl-*S*-benzyl-D,L-β,β-dideuterocysteine, 118398-48-4; ethyl *N*-acetyl-*S*-benzyl-D,L-cysteinate, 118456-64-7; *N*-acetyl-*S*-benzyl-D,L-cysteine, 19538-71-7; *N*-acetyl-D,L-cysteine, 7218-04-4; methyl *N*-acetyl-D,L-cysteinate, 118398-49-5.

Cycloadditions of Isoquinolinium Salts: Vinyl Sulfide Dienophiles for the Syntheses of 1-Naphthaldehydes and Tetralins

Ram B. Gupta,[†] Richard W. Franck,*[,†] Kay D. Onan,[‡,§] and Clifford E. Soll[†]

Department of Chemistry, Hunter College/CUNY 695 Park Ave., New York, New York 10021, and Department of Chemistry, Northeastern University, 360 Huntington Ave., Boston, Massachusetts 02115

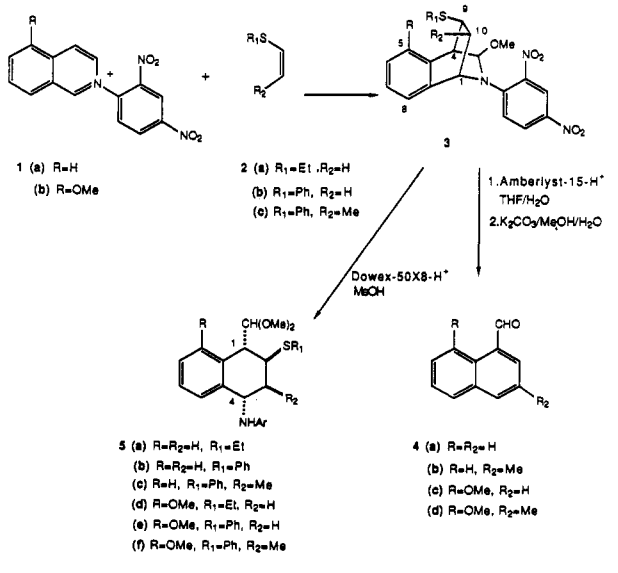
Received May 17, 1988

Vinyl sulfides are used as dienophiles in the Bradsher cycloaddition reaction. Processing of the cycloadducts leads to either tetralins or naphthaldehydes. The tetralins are formed with high stereoselectivity. The configuration of the products is confirmed by an X-ray structure determination. Removal of sulfur from the tetralin products affords materials that are the equivalent of having used simple alkenes as dienophiles.

Vinyl sulfides have emerged as versatile substrates in synthetic methodology.[1] Of particular significance is their ability to participate as electron-rich alkenes in cycloaddition reactions.[2] Recently, Denmark[3] reported their use in the intramolecular inverse-electron-demand (IED) Diels–Alder reactions of α,β-unsaturated aldehydes, and Posner[4] has used these sulfur dienophiles in cycloadditions to pyrones.

The IED reactions of two closely related systems, acridizinium and isoquinolinium ions, discovered by Bradsher,[5] have been the subject of extensive investigation.[6] Dienophiles shown to participate in these reactions include alkenes, dienes, styrenes, benzyne, vinyl ethers, vinyl silyl ethers, enamines, ynamines, ketene acetals, and ketene aminals. Conspicuous by their absence, however, are reports on the use of vinyl sulfides in the Bradsher cycloaddition. We now describe our results, which remedy the omission and which have significance for the synthetic community.

Scheme I



Thus, when isoquinolinium salt **1** was treated with vinyl sulfide **2** in anhydrous methanol containing calcium car-

[†] Hunter College/CUNY.
[‡] Northeastern University.
[§] Correspondence concerning the X-ray crystallography should be addressed to K.D.O.

0022-3263/89/1954-1097$01.50/0