

tricyclic ketone **2** is principally triplet-state derived. (d) The bicyclic ketone **4** is principally singlet-state derived.

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**Registry No.** 1, 81447-74-7; 2, 37939-83-6; 3, 694-98-4; 4, 54074-60-1; 6, 81447-75-8.

### Organoselenium Chemistry. Characterization of Reactive Intermediates in the Selenoxide Syn Elimination: Selenenic Acids and Selenolseleninate Esters

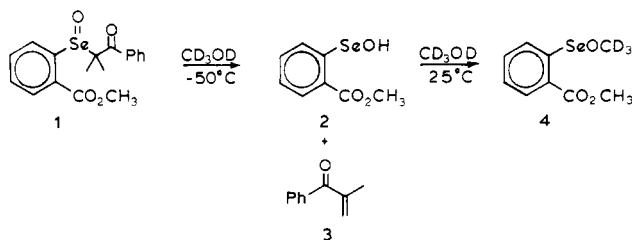
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Selenenic acids (RSeOH) and their derivatives are presumed intermediates in a number of important reactions: selenoxide syn eliminations,<sup>1,2</sup> [2,3]sigmatropic rearrangements of allylic and propargylic selenoxides,<sup>3</sup> oxidation of selenols and diselenides,<sup>1b,4</sup> reduction of seleninic acids (RSeO<sub>2</sub>H).<sup>5,6</sup> A selenenic acid may also be at the active site of the redox selenoenzyme glutathione peroxidase<sup>7</sup> as part of a selenocysteine residue. With the exception of a series of *o*-nitrobenzene and anthraquinone derivatives,<sup>6</sup> selenenic acids are unstable and disproportionate to diselenides and seleninic acids.

We have examined the syn elimination of several selenoxides to establish whether selenenic acids could be observed and their chemistry studied. Compound **1**<sup>8</sup> was chosen as a precursor to



(1) (a) Jones, D. N.; Mundy, D.; Whitehouse, R. D. *J. Chem. Soc., Chem. Commun.* **1970**, 86. (b) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697.

(2) For recent reviews see: (a) Reich, H. J. "Oxidation of Organic Compounds, Part C"; Trahanovsky, W., Ed.; Academic Press: New York, 1978; p 1. (b) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22. (c) Clive, D. L. *J. Tetrahedron* **1978**, *34*, 1049.

(3) (a) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7154. (b) Reich, H. J. *J. Org. Chem.* **1975**, *40*, 2570. (c) Reich, H. J.; Shah, S. K. *J. Am. Chem. Soc.* **1977**, *99*, 263.

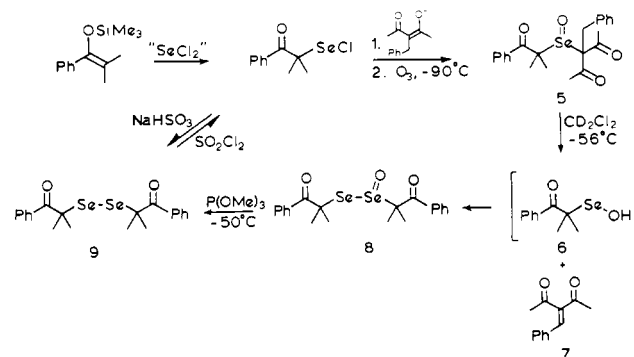
(4) (a) Hori, T.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1689. (b) Shimizu, M.; Takeda, R.; Kuwajima, I. *Tetrahedron Lett.* **1979**, 419, 3461. (c) Gancarz, R. A.; Kice, J. L. *Tetrahedron Lett.* **1981**, 22, 1661.

(5) Labar, D.; Krief, A.; Hevesi, L. *Tetrahedron Lett.* **1978**, 3967.

(6) (a) Rheinboldt, H.; Giesbrecht, E. *Chem. Ber.* **1955**, *88*, 666, 1037, 1974. The material identified by these authors as *o*-nitrobenzeneselenenic acid is actually the selenenic anhydride (ArSeOSeAr). Authentic selenenic acid can be prepared by hydrolysis of the anhydride (Reich, H. J.; Willis, W. W.; Wollowitz, S., unpublished results. Kice, J. L.; McAfee, F.; Slebocka-Tilk, H., private communication). (b) Rheinboldt, H.; Giesbrecht, E. *Chem. Ber.* **1956**, *89*, 631. (c) Jenny, W. *Helv. Chim. Acta* **1958**, *41*, 317.

(7) For recent reviews see: Sunde, R. A.; Hoekstra, W. G. *Nutr. Rev.* **1980**, *38*, 265. Stadtman, T. C. *Adv. Enzymol.* **1979**, *48*, 1. Stadtman, T. C. *Annu. Rev. Biochem.* **1980**, *49*, 93.

### Scheme I



the selenenic acid **2**. There was reason to believe that **2** might be stable, since *o*-benzoylbenzeneselenenic acid has been reported.<sup>6b</sup> The decomposition of selenoxide **1** at -50 °C in CD<sub>3</sub>OD followed first-order kinetics (*t*<sub>1/2</sub> ≈ 13 min), giving only two products, the enone **3** and a compound we believe to be the selenenic acid **2**. The <sup>77</sup>Se NMR chemical shift of **2** (1091 ppm)<sup>10</sup> is different from that of the related seleninic acid (1220) and diselenide (458) and quite similar to the chemical shift of the stable<sup>6a</sup> *o*-nitrobenzeneselenenic acid (1053).<sup>11</sup> Compound **2** is stable in methanol below 25 °C but does react slowly at 25 °C (*t*<sub>1/2</sub> = 2 h) with solvent to give the methyl selenenate ester **4**. The identity of the selenenate ester was confirmed by carrying out the elimination of selenoxide **1** in protiomethanol. Solvent removal and dissolution in methanol-*d*<sub>4</sub> allowed observation of the <sup>1</sup>H NMR spectrum ( $\delta$  4.07, <sup>3</sup>J<sub>Se-H</sub> = 7 Hz), in which the OCH<sub>3</sub> signal gradually disappeared as transesterification replaced methoxy with deuterio-methoxy. Selenenic acid **2** was much less stable in CD<sub>2</sub>Cl<sub>2</sub> than in CD<sub>3</sub>OD solvent.<sup>12</sup>

A second compound studied was the selenoxide **5**, a possible precursor to the aliphatic selenenic acid **6**. Compound **5** was prepared as shown in Scheme I. It decomposes at -52 °C in CD<sub>3</sub>OD and at -60 °C in CD<sub>2</sub>Cl<sub>2</sub> (*t*<sub>1/2</sub> ≈ 18 min). The reaction was followed by low-temperature NMR spectroscopy (-50 to -80 °C). In addition to the enedione **7**, only one other product was observed. It shows four methyl resonances (<sup>1</sup>H:  $\delta$  1.80, 1.84, 1.94, 1.96; <sup>13</sup>C:  $\delta$  20.9, 24.3, 28.4, 29.37) in a 1:1:1:1 ratio, two sets of *ortho*-aryl protons at  $\delta$  7.72, 7.87, as well as <sup>13</sup>C resonances for two carbonyl groups ( $\delta$  200.6, 202.3) and two aliphatic quaternary carbons ( $\delta$  52.4, 76.5). The <sup>77</sup>Se NMR spectrum showed two signals at 862 and 540 ppm.<sup>10</sup> On the basis of this spectral information, in particular the observation of two sets of diastereotopic methyl groups (indicating the presence of a center of chirality) and the Se NMR shift (see below), we assign the selenolseleninate structure **8** to this species. Further supporting evidence is provided by the clean and quantitative reduction of **8** to the diselenide **9**<sup>13</sup> with trimethyl phosphite and its conversion to selenenamide **10**<sup>13</sup> on treatment with dimethylamine.<sup>14</sup> No

(8) This selenoxide was prepared by the reaction of *o*-carbomethoxybenzeneselenenyl chloride<sup>9</sup> with the enolate of isobutyrophenone, followed by ozonization.

(9) Lesser, R.; Schoeller, A. *Chem. Ber.* **1914**, *47*, 2505. Lesser, R.; Weiss, R. *Chem. Ber.* **1913**, *46*, 2540.

(10) All <sup>77</sup>Se chemical shifts are reported in ppm downfield from Me<sub>2</sub>Se.

(11) For previous studies of <sup>77</sup>Se NMR chemical shifts see: (a) McFarlane, W.; Wood, R. J. *J. Chem. Soc., Dalton Trans.* **1972**, 1397. (b) Lardon, M. A. In "Organic Selenium Compounds: Their Chemistry and Biology"; Klayman, D. L., Günther, W. H. H., Eds.; Wiley-Interscience: New York, 1973; p 933. (c) Odom, J. D.; Dawson, W. H.; Ellis, P. D. *J. Am. Chem. Soc.* **1979**, *101*, 5815 and references therein. (d) Llabres, G.; Baiwir, M.; Piette, J.-L.; Christiaens, L. *Org. Magn. Reson.* **1981**, *15*, 152.

(12) Similar observations had been made for sulfenic acids: Shelton, J. R.; Davis, K. E. *Int. J. Sulfur Chem.* **1973**, *8*, 205.

(13) Selenium-77 NMR (CD<sub>2</sub>Cl<sub>2</sub>): **9**,  $\delta$  559, 25 °C; **10**, 986, -42 °C; **13**, 289, 25 °C.

(14) Compound **10** could also be prepared by reaction of the selenenyl chloride with dimethylamine. Benzeneselenenic acid reacts in situ with secondary amines to form selenenamides.<sup>1b,15</sup>

(15) Reich, H. J.; Renga, J. M. *J. Org. Chem.* **1975**, *40*, 3313.

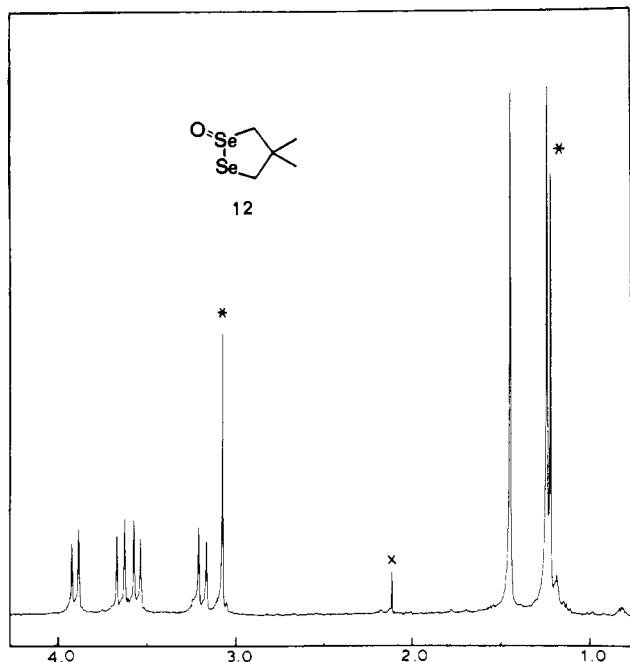
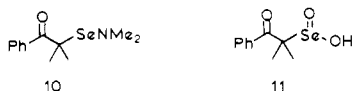


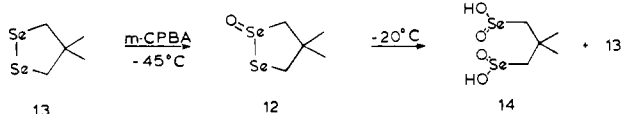
Figure 1.  $^1\text{H}$  NMR spectrum (270 MHz,  $-50^\circ\text{C}$ ,  $\text{CD}_2\text{Cl}_2$ ) of **12**. The singlets at  $\delta$  1.22 and 3.08 marked with an asterisk are those of **13**.

NMR signals assignable to the selenenic acid **6** were observed during these studies.



Compound **8** is moderately stable at  $-50^\circ\text{C}$  ( $t_{1/2} \approx 1$  h), decomposing to several products including enone **3** (57%), seleninic acid **11** (8%), diselenide **9** (18%), and two other products thought to be polyselenides (25%, 4%). These products account for 80% of the selenoxide **5** used. The formation of the enone **3** can be considered diagnostic of the Se-oxide grouping in **8**, which should share with selenoxides,<sup>1</sup> seleninic acids, seleninate esters,<sup>16</sup> and their sulfur analogues<sup>17a</sup> the capability for pericyclic syn elimination. Compound **8** is the first example of an observable selenoseleninate ester, although a thiol-seleninate ester has been detected during a study of the reaction of thiols with benzene-seleninic acids.<sup>18</sup> Thiol-sulfonates are much more stable, and a number have been isolated.<sup>12,17</sup>

Further support for the assignment of structure **8** is provided by the spectroscopic properties of the cyclic selenoseleninate **12**, which is formed by oxidation of 4,4-dimethyl-1,2-diselenolane (**13**)



with 1 equiv of *m*-chloroperbenzoic acid at  $-45^\circ\text{C}$ . The proton NMR spectrum (Figure 1) is particularly characteristic, showing two AB quartets for the methylene protons and two singlets for the diastereotopic methyl groups.<sup>19</sup> The  $^{77}\text{Se}$  NMR spectrum ( $\text{CD}_2\text{Cl}_2$ ,  $-56^\circ\text{C}$ ) has resonances at 273 and 693 ppm.<sup>10,13</sup> The strong downfield shift of one of the selenium resonances is expected from other comparisons<sup>11a</sup> and was also observed for selenol-

seleninate **8**.<sup>20</sup> Compound **12** decomposes at  $-20^\circ\text{C}$  to give  $\sim 65\%$  yield of diselenide **13** and a precipitate of the seleninic acid **14**, the expected disproportionation products.<sup>21</sup>

**Summary.** The selenoxide syn elimination occurs at temperatures below  $-50^\circ\text{C}$  in certain carbonyl derivatives. Under these conditions normally unstable species such as selenenic acids or their dimeric dehydration products, the selenoseleninates, can be observed and characterized spectroscopically ( $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{77}\text{Se}$  NMR) and chemically. A cyclic selenoseleninate has also been prepared by partial oxidation of a diselenide.

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**Registry No.** **1**, 81360-85-2; **2**, 81360-86-3; **3**, 769-60-8; **4**, 81360-87-4; **5**, 81360-88-5; **7**, 4335-90-4; **8**, 81360-89-6; **9**, 81360-90-9; **10**, 81360-91-0; **11**, 81360-92-1; **12**, 81360-93-2; **13**, 81360-94-3; **14**, 81360-95-4; 1-phenyl-1-trimethylsilyloxy-1-isobutene, 39158-85-5; 2-chloroselenyl-2-methylpropionophenone, 81360-96-5; 3-benzyl-2,4-pentanedione, 1134-87-8.

(20) Oxidation of diselenide **9** with either ozone or peracid has not given selenoseleninate **8** as a major product. 4,4'-Difluorodiphenyl diselenide also gave no intermediates during oxidation with *tert*-butylhydroperoxide.<sup>4c</sup>

(21) Bergson, G. (*Acta Chem. Scand.* **1961**, *15*, 1611) has suggested that 1,2-diselenolane-4-carboxylic acid is oxidized to a marginally stable ( $t_{1/2} = 5$ –10 min at room temperature) selenoseleninate.

## Remarkably Enhanced Charge-Transfer Interaction in Stable Single-Compartment Vesicles

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The characterization and chemical application of synthetic bilayer membranes constitute a rapidly growing research area in recent years.<sup>2–7</sup> Several recent studies are concerned with the extent of spatial organization of surfactant molecules when they are assembled into bilayer aggregates.<sup>8,9</sup> We have recently shown that amphiphiles involving an amino acid residue (L-Ala or L-His) interposed between a polar head group and an aliphatic double chain form *stable single-compartment vesicles* in aqueous media.<sup>10,11</sup> We have also successfully identified for these bilayer

(1) To whom correspondence should be addressed.

(2) (a) Kunitake, T.; Okahata, Y. *J. Am. Chem. Soc.* **1977**, *99*, 3860–3861. (b) Kunitake, T.; Okahata, Y.; Tamaki, K.; Kumamaru, F.; Takayanagi, M. *Chem. Lett.* **1977**, 387–390. (c) Kunitake, T.; Okahata, Y. *Ibid.* **1977**, 1337–1340. (d) Kunitake, T.; Nakashima, N.; Shimomura, M.; Okahata, Y.; Kano, K.; Ogawa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6642–6644.

(3) (a) Lim, Y. Y.; Fendler, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 4023–4029. (b) Kano, K.; Romero, A.; Djermouni, B.; Ache, H. J.; Fendler, J. H. *Ibid.* **1979**, *101*, 4030–4037. (c) Infelta, P. P.; Grätzel, M.; Fendler, J. H. *Ibid.* **1980**, *102*, 1479–1483. (d) Nomura, T.; Escabi-Perez, J. R.; Sunamoto, J.; Fendler, J. H. *Ibid.* **1980**, *102*, 1484–1488.

(4) Sunamoto, J.; Kondo, H.; Nomura, T.; Okamoto, H. *J. Am. Chem. Soc.* **1980**, *102*, 1146–1152.

(5) Mortara, R. A.; Quina, F. H.; Chaimovich, H. *Biochem. Biophys. Res. Commun.* **1978**, *81*, 1080–1086.

(6) Sudhölter, E. J. R.; Engberts, J. B. F. N.; Hoekstra, D. J. *Am. Chem. Soc.* **1980**, *102*, 2467–2469.

(7) Moriarty, R. M.; Schwartz, R. N.; Lee, C.; Curtis, V. J. *Am. Chem. Soc.* **1980**, *102*, 4257–4259.

(8) Czarniecki, M. F.; Breslow, R. *J. Am. Chem. Soc.* **1979**, *101*, 3675–3676.

(9) Russell, J. C.; Costa, S. B.; Seiders, R. P.; Whitten, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 5678–5679.

(10) Murakami, Y.; Nakano, A.; Fukuya, K. *J. Am. Chem. Soc.* **1980**, *102*, 4253–4254.

(11) Murakami, Y.; Nakano, A.; Yoshimatsu, A.; Fukuya, K. *J. Am. Chem. Soc.* **1981**, *103*, 728–730.

(16) Both **11** and its methyl ester decompose at room temperature to give **3**, **9**, and other products. See also: Sharpless, K. B.; Gordon, K. M. *J. Am. Chem. Soc.* **1976**, *98*, 300.

(17) (a) Block, E.; O'Connor, J. J. *Am. Chem. Soc.* **1974**, *96*, 3929. (b) Kice, J. L.; Large, G. B. *Ibid.* **1968**, *90*, 4069. (c) Takata, T.; Kim, Y. H.; Oae, S. *Tetrahedron Lett.* **1978**, 4303.

(18) Kice, J. L.; Lee, T. W. S. *J. Am. Chem. Soc.* **1978**, *100*, 5094.

(19) The  $^{13}\text{C}$  NMR spectrum also supports the assigned structure:  $\delta$  ( $\text{CD}_2\text{Cl}_2$ ,  $-56^\circ\text{C}$ ) 25.8 (q), 27.0 (q), 47.4 (t), 50.6 (s), 71.4 (t).