Sulfilimines and Sulfenamides Derived from N-Chlorobenzimidates and Sulfur Nucleophiles

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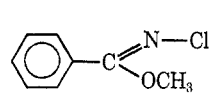
Received January 12, 1970

N-Haloimidates were first prepared in 1896 by Stieglitz[1] through the chlorination of ethyl benzimidate hydrochloride with cold, aqueous sodium hypochlorite solution. Subsequently, additional examples of N-chloro- and N-bromoimidates were reported[2-4] using the same general synthetic procedure. Direct halogenation of the free basic imidate esters with bromine,[5] iodine,[5] and *t*-butyl hypochloride[6] have also been described. Additionally, Stieglitz has reported[2,7] an elegant synthesis of N-haloimidates by treating N-chlorobenzamides with diazomethane.

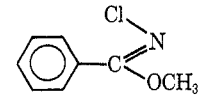
The N-haloimidates prepared were not well characterized structurally by present-day standards and their chemistry was not widely studied. The early workers devoted their efforts to a study of *syn–anti* isomerization of the N-haloimino group of these compounds.[2,3] Russian workers found that N-dialkoxyphosphinylimidates[8,9] could be prepared from the reaction of N-chlorobenzimidates with trialkyl phosphites while the use of triaryl phosphites and triaryl phosphines in place of the alkyl derivative gave instead, N-acyl phosphorimides.[10-15] More recently, α-aminocarboxylic esters were produced from base-catalyzed rearrangement of N-chlorimidates containing α hydrogen.[6] This paper describes the condensation of sulfides and mercaptans with N-chlorobenzimidates.

Methyl N-chlorobenzimidate (1) and methyl N-chloro-*p*-methoxybenzimidate (2) were most conveniently prepared by the sodium hypochloride procedure of Stieglitz[1] from their corresponding benzimidate hydrochloride salts in 80 and 70% yield, respectively.

Because compounds of type **1** and **2** were poorly identified by the early workers, some effort was devoted to establish further their structural identity. Both N-chloro compounds (**1** and **2**) were shown by nmr spectroscopy to be a mixture of isomers in which the OCH_3 and the Cl groups on an imine double bond are in *syn* and *anti* configuration. Assignments were made based on extension of the generalization for ethylenes (C=C) where it is known that protons *cis* (*syn*) to an electronegative group appear further downfield than *trans*(*anti*). Compound **1** was a 9:1 mixture of *syn* (δ 3.85 ppm) and *anti* (δ 3.65 ppm) isomers. Heating **1**



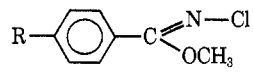
1 (*syn*)



1 (*anti*)

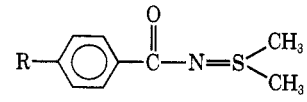
for 40 min at 100° produced an equilibrium mixture at 7.5:2.5 of *syn* to *anti* isomers, respectively. Compound **2** was a 8.7:1.3 mixture of *syn* (δ 3.87 ppm) and *anti* (δ 3.72 ppm), isomers, respectively. In the present work no separation of the isomeric products was attempted. Further analytical data supporting the assigned structures are presented in the Experimental Section.

Methyl N-chlorobenzimidate (**1**) reacted readily with methyl sulfide giving S,S-dimethyl-N-benzoylsulfilimine, **3** (72%), and methyl chloride and thus furnishing a fifth general route to dialkylsulfilimines.[16]



+ $(CH_3)_2S$ ⟶

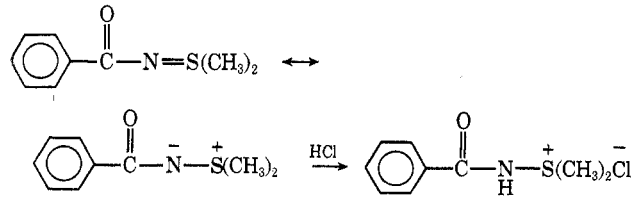
1, R = H
2, R = CH_3O



+ CH_3Cl

3, R = H
4, R = CH_3O

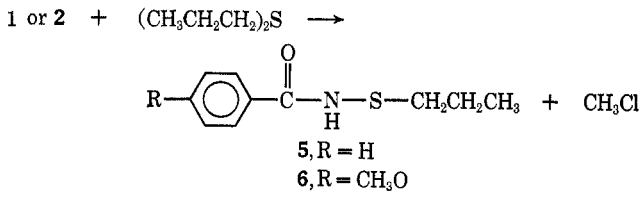
Similarly compound **2** gave S,S-dimethyl-N-(*p*-methoxybenzoyl)sulfilimine (**4**) in 65% yield. The reactions were exothermic when the starting materials were mixed at room temperature and methyl chloride was liberated. The extent of reaction was followed by methyl chloride evolution as the mixtures were finally heated to complete the reaction. The sulfilimine products were water soluble, colorless solids and insensitive to hydrolysis at room temperature. Boiling water caused partial hydrolysis to the benzamide. Assignment of structures was based on elemental analysis and infrared and nmr spectral data. The structure of **3** was further characterized by the formation and analysis of its hydrochloride salt.



When *n*-propyl sulfide was employed in place of methyl sulfide, under identical reaction conditions, the

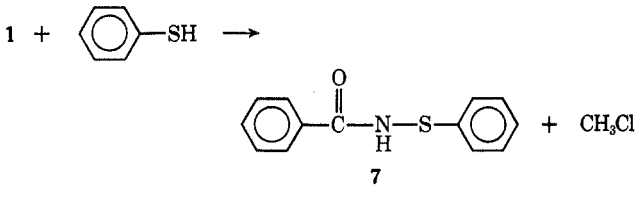
(1) J. Stieglitz, *Amer. Chem. J.*, **18**, 751 (1896).
(2) J. Stieglitz and R. B. Earle, *ibid.*, **30**, 399 (1903).
(3) W. S. Hilpert, *ibid.*, **40**, 150 (1908).
(4) J. Houben and E. Schmidt, *Ber.*, **46**, 3616 (1913).
(5) H. S. Wheeler and P. T. Walden, *Amer. Chem. J.*, **19**, 129 (1897).
(6) H. E. Baumgarten, H. E. Dirks, J. M. Petersen, and R. L. Zey, *J. Org. Chem.*, **31**, 3708 (1966).
(7) J. Stieglitz and E. E. Slosson, *Ber.*, 1613 (1901).
(8) G. I. Derkach, A. M. Lepesa, and A. V. Kirsanov, *J. Gen. Chem. USSR*, **32**, 167 (1962).
(9) K. A. Petrov, A. A. Neimysheva, M. G. Fomenko, L. M. Chemushevich, and A. D. Kuntsevich, *ibid.*, **31**, 516 (1961).
(10) G. I. Derkach, E. S. Gubnitskaya, V. A. Shokol, and A. V. Kirsanov, *ibid.*, **32**, 1201 (1962).
(11) G. I. Derkach, E. S. Gubnitskaya, V. A. Shokol, and A. V. Kirsanov, *ibid.*, **32**, 1874 (1962).
(12) G. I. Derkach, E. S. Gubnitskaya, L. J. Samarai, and V. A. Shokol, *ibid.*, **33**, 557 (1963).
(13) G. I. Derkach, G. K. Fedorova, and E. S. Gubnitskaya, *ibid.*, **33**, 1017 (1963).
(14) G. I. Derkach and L. J. Samarai, *ibid.*, **34**, 1161 (1964).
(15) G. I. Derkach and E. S. Gubnitskaya, *ibid.*, **35**, 1009 (1965).
(16) Synthesis of sulfilimines are described in the following references: (a) C. R. Johnson and J. J. Rigau, *J. Org. Chem.*, **33**, 4340 (1968); (b) L. Horner and A. Christmann, *Chem. Ber.*, **96**, 388 (1963); (c) C. King, *J. Org. Chem.*, **25**, 352 (1960); (d) D. S. Tarbell and C. Weaver, *J. Amer. Chem. Soc.*, **63**, 2939 (1941); (e) F. G. Mann and W. J. Pope. *J. Chem. Soc.*, **121**, 1052 (1922); (f) F. G. Mann, *ibid.*, 958 (1932).

sulfilimines were not obtained. Instead C–S bond cleavage resulted to give sulfenamides **5** and **6** and methyl chloride in quantitative yield. The structure of solid sulfenamides was confirmed by elemental analysis and infrared and nmr spectral data.



5, R = H
6, R = CH_3O

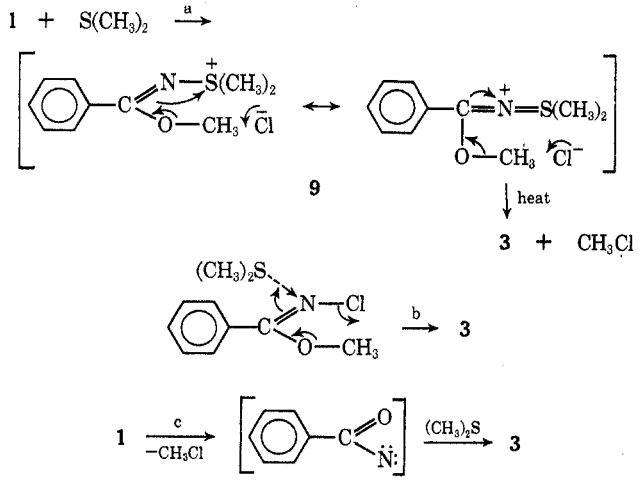
An attempt to prepare authentic **5** from the reaction of *n*-propyl mercaptan and **1** gave, instead, the oxidation product, *n*-propyl disulfide, and by-product methyl benzimidate hydrochloride as the only identified products, each in about 55% yield. On the other hand, a rapid and exothermic reaction occurred when phenyl mercaptan was used in place of the alkyl mercaptan. Thus, N-benzoylbenzenesulfenamide (**7**) was obtained in 60% yield.



7

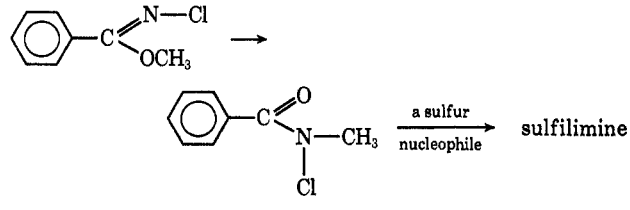
Attempts to employ an aromatic sulfide in place of the alkyl sulfides in reactions leading to products similar to **3** and **4** were unsuccessful. Instead, reaction of **1** with diphenyl sulfide at temperatures up to 193° gave N-benzoyl-N′-phenylurea as the only isolable product in very low yield while at room temperature only methyl benzimidate hydrochloride was identified. *n*-Propyl disulfide reacted with **1** with explosive violence. Heating a mixture of **1** and elemental sulfur also caused a sudden uncontrollable violent reaction. Both of these reactions gave product mixtures which were not completely separated and identified.

Detailed mechanisms for the formation of sulfilimines are not clear. One can postulate (a) an initial salt formation (**9**) which then loses methyl chloride to give product or (b) a concerted process involving product formation with simultaneous loss of methyl chloride and (c) formation of a nitrene intermediate.



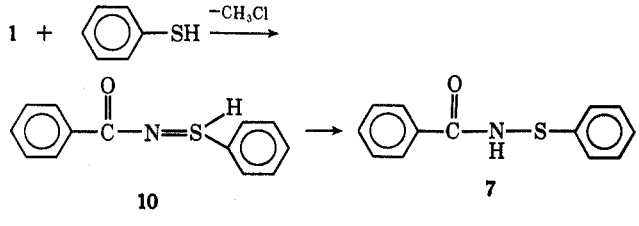
Although nitrene intermediates cannot be entirely excluded, the probability of their involvement is not favorable since reaction products of these species were not found by either thermolysis of **1** and **2** in cyclohexene[17–19] or treatment of mixtures of **1** and **2** in cyclohexene with dimethyl sulfide. Between the two remaining pathways (a and b), there is no absolute way of distinguishing one over the other. It is of interest that the reaction mixtures exhibited an increase in viscosity immediately after mixing the sulfide and N-chlorobenzimidates and that the sulfides were not boiled out of the reaction mixtures during heating.

A mechanism involving prior formation of a N-chlorobenzamide from the N-chlorobenzimidate in a Chapman-type rearrangement with subsequent α-elimination processes appears unlikely in view of the



overall low temperatures of the reactions described here and the stability of the N-chlorobenzimidates toward high temperatures as seen in the nmr study.

Formation of the sulfenamide from phenyl mercaptan and **1** could have involved rearrangement of the unusual sulfilimine (**10**). This compound is representative of an unknown class of compounds and it could well be postulated that in such structural circumstances a tendency toward molecular rearrangement for the sulfur atom to exist in its more stable divalent would prevail.



10 **7**

The mechanism of C–S bond cleavage when *n*-propyl sulfide was employed in the reaction is unclear, and the fate of the fragmented propyl group has not been established. However, propane and propylene derivatives were not found (by mass spectrometry) in the gaseous product.

Experimental Section

Methyl Benzimidate Hydrochloride.—The procedure employed was basically that of Pinner.[20,21] Extreme care was taken to maintain anhydrous conditions for the preparation and handling of this compound. Dry gaseous hydrogen chloride (58.5 g, 1.6 mol) was bubbled into a mixture of benzonitrile (154.5 g, 1.5 mol) and anhydrous methanol (57.7 g, 1.8 mol) during about 4 hr while the reaction temperature was maintaind at −5 to 0°. When the addition was complete, the reaction mixture was held at 0° for 3 days. The crystallized product was filtered quickly

(17) D. Saika and D. Swern, *J. Org. Chem.*, **33**, 4548 (1968).
(18) R. J. Cotter and W. F. Beach, *ibid.*, **29**, 751 (1964).
(19) D. S. Breslow, E. I. Edwards, R. Leone, and P. von E. Schleyer, *J. Amer. Chem. Soc.*, **90**, 7097 (1968).
(20) R. Roger and D. G. Neilson, *Chem. Rev.*, **61**, 179 (1961).
(21) A. Pinner, "Die Imidoather und ihre Derivate," Oppenheim, Berlin, 1892.

in a nitrogen atmosphere, washed thoroughly with ether, and dried in a vacuum desiccator over sodium hydroxide pellets to yield 163.5 g (64%) of pure salt, mp 103.5–104° (gas evolution) (lit.[22] mp 105°). Crystallization from chloroform–benzene did not change the melting point.

Methyl N-Chlorobenzimidate (1).—The chlorination procedure employed was a modification of that of Stieglitz.[1] To a freshly prepared solution of sodium hypochlorite [prepared by adding gaseous chlorine (218 g, 3.08 mol) to a solution of sodium hydroxide (176 g, 4.4 mol) in 1055 g of water at 0°] was added 300 ml of 1,1,2-trichloro-1,2,2-trifluoroethane (UCON-113). To the resulting mixture was added portionwise 150 g (0.88 mol) of crude methyl benzimidate hydrochloride over 20 min while keeping the reaction temperature at 0–5°. When the addition was complete, the reaction mixture was stirred at 0–5° for 10 min, the layers were separated, and the aqueous layer was extracted three times with 50-ml portions of UCON-113. The combined UCON-113 extracts were dried over anhydrous $MgSO_4$ for 1 hr, filtered, and evaporated to give a colorless oil. Distillation afforded 121 g (81%) of colorless product 1, bp 118–120° (15.0 mm).

Anal. Calcd for C_8H_8ClNO: C, 56.65; H, 4.75; Cl, 20.90; N, 8.26. Found: C, 56.70; H, 4.64; Cl, 21.90; N, 8.25.

The infrared absorption spectrum revealed bands at 6.15 (C=N) and 9.68 μ (O–CH_3). The nmr spectrum ($CDCl_3$) exhibited two singlets in a 9:1 ratio at δ 3.85 and 3.65 ppm, respectively, attributed to the methyl protons, and a multiplet centered at δ 7.34 ppm for the phenyl ring protons. Raising the temperature from 25 to 70° altered the methyl proton ratio of the low-field to high-field singlets to 8.5:1.5, respectively. A 7.5:2.5 equilibrium mixture of the 3.85 to 3.65 ppm singlets, respectively, was obtained after 40 min at 100°.

Methyl *p*-Methoxybenzimidate Hydrochloride.—The preparation of this hydrochloride was carried out by the same procedure as described for the preparation of methyl benzimidate hydrochloride. From 199.7 g (1.5 mol) of anisonitrile, 57.7 g (1.8 mol) of anhydrous methanol, and 58.5 g (1.6 mol) of hydrogen chloride there was obtained 263 g (87%) of crude, dried white crystalline product. This material was used without purification in the subsequent chlorinations.

Methyl N-Chloro-*p*-methoxybenzimidate (2).—To a 2.8 to 3.0 *M* solution of sodium hypochlorite [prepared by adding 70 g (2.0 mol) of chlorine to a solution of 80 g (2 mol) of sodium hydroxide in 250 g of water while keeping the temperature at 0–5°] was added 300 ml of UCON-113, and gradually 263 g (1.30 mol) of crude methyl *p*-methoxybenzimidate hydrochloride during 15 min while maintaining the temperature at 0–5°. The resulting mixture was stirred for 30 min after the addition of the salt was complete, the layers were separated, and the aqueous layer was extracted with three 50-ml portions of UCON-113. The combined UCON-113 extracts were dried over anhydrous $MgSO_4$ for 1 hr, filtered, and evaporated to give a crude colorles oil. Distillation gave 178.5 g (69%) of product, bp 94.5–107° (0.025–0.050 mm). Redistillation afforded 137.2 g (53%) of pure product: bp 95.5–99° (0.18–0.20 mm); ir 6.18 (conjugated C=N) and 9.67 μ (O–CH_3); nmr ($CDCl_3$) δ 7.63 (m, 2 H, aromatic), 6.87 (m, 2 H, aromatic), 3.72 (s, 3 H, $CH_3OC_6H_4$), and two singlets at 3.87 and 3.72 ppm (3 H) from the *syn* and *anti* forms in an 87.4 to 12.6 ratio, respectively, at 25°.

Anal. Calcd for $C_9H_{10}ClNO_2$: C, 54.15; H, 5.05; Cl, 17.76; N, 7.02. Found: C, 54.44; H, 5.27; Cl, 17.57; N, 7.00.

S,S-Dimethyl-N-benzoylsulfilimine (3).—Methyl N-chlorobenzimidate (17.0 g, 0.1 mol) was added dropwise to a stirred solution of 6.21 g (0.1 mol) of methyl sulfide in 10 ml of benzene while keeping the temperature at 30–35°. When the addition was complete, the mixture was heated to 75° during 2 hr. The next day additional methyl sulfide (2.7 g, 0.044 mol) was added and the reaction mixture was heated at 55° for 1 hr. During this time 1520 ml (68%) of methyl chloride was collected and identified by mass spectrometry. The solvent and excess methyl sulfide were evaporated by means of a stream of nitrogen gas, the crude white product was washed successively with 20 ml of petroleum ether and 20 ml of benzene, and dried to yield 13.0 g (72%), mp 106.5–108.5°. Recrystallization from benzene raised the melting point to 107.5–108.5°; ir (KBr) 6.25, 6.67 (aromatic C=C), 6.44 (C=O), 7.50 (N=S), and 7.66 μ (S–CH_3); nmr ($CDCl_3$) δ 2.62 (s, 6 H, $(CH_3)_2S<$), 7.33 (m, 3 H, aromatic), and 8.06 ppm (m, 2 H, aromatic).

(22) M. J. Hunter and M. S. Ludwig, *J. Amer. Chem. Soc.*, **84**, 3491 (1962).

Anal. Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73; S, 17.69. Found: C, 60.37; H, 6.20; N, 7.77; S, 17.65.

S,S-Dimethyl-N-benzoylsulfilimine Hydrochloride.—The hydrochloride was prepared by saturating a solution of 2.5 g (0.014 mol) of S,S-dimethyl-N-benzoylsulfilimine in 50 ml of benzene with hydrogen chloride gas at ambient temperature. The reaction mixture was allowed to stand for 2 hr and then filtered. The white product was washed with two 20-ml portions of ether and dried to yield 2.52 g (84%), mp 180–182°. Recrystallization from ethanol afforded 2.14 g (71%), mp 180–182°; ir 3.30–3.80 (salt), 5.88 (C=O), and 7.05 μ (N=S); nmr (D_2O) δ 3.50 (s, 6 H, $(CH_3)_2S<$), 4.85 (s, 1 H, $=N<_H$), and 7.83 ppm (m, 5 H, aromatic).

Anal. Calcd for $C_9H_{12}ClNOS$: C, 49.63; H, 5.55; Cl, 16.28; N, 6.43; S, 14.72. Found: C, 49.93; H, 5.57; Cl, 16.12; N, 6.53; S, 14.40.

Reaction of Methyl N-Chlorobenzimidate with *n*-Propyl Sulfide.—*n*-Propyl sulfide (11.8 g, 0.1 mol) was added to 17.0 g (0.1 mol) of methyl N-chlorobenzimidate over a period of 20 min while maintaining the temperature at 25–30°. There was a strong exotherm of reaction, and during this time methyl chloride (identified by mass spectrometry) commenced to be liberated and was collected over water. The mixture was stirred and gradually heated to 134° until (about 4 hr) 1 mol of methyl chloride per mol of starting N-chloro compound had been collected. After cooling the reaction mixture, the crude **N-benzoyl-1-propanesulfenamide (5**, 19.3 g, 100%) was extracted with four 500-ml portions of boiling petroleum ether (63–75°) to yield 6.0 g (36%). An analytical sample was prepared by crystallization from benzene–cyclohexane: mp 70–73°; ir 3.01 (N–H), 6.0 (C=O), and 7.9 μ (S–CH_2); nmr ($CDCl_3$) δ 0.98 (t, 2 H, SCH_2CH_2-), 1.63 (sextet, 2 H, $-CH_2CH_2CH_3$), 2.78 (t, 3 H, $-CH_2CH_3$), 7.39 (m, 3 H, aromatic), 7.60 (s, 1 H, –NH–), and 7.84 ppm (m, 2 H, aromatic).

Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.51; H, 6.71; N, 7.17. Found: C, 61.83; H, 6.61; N, 7.44.

Reaction of Diphenyl Sulfide with Methyl N-Chlorobenzimidate.—A mixture of 5.7 g (0.031 mol) of diphenyl sulfide and 8.45 g (0.05 mol) of methyl N-chlorobenzimidate was slowly heated to a maximum temperature of 193° during 7 hr. A total of 350 ml of methyl chloride was collected. The black tarry-appearing reaction mixture was filtered and a black solid was collected, washed with 20 ml of a 1:1 mixture of benzene–cyclohexane, and dried to yield 0.40 g (6.7%), mp 183–190° dec. The crude gray product was purified by two recrystallizations from benzene to yield 0.10 g (1.7%) of **N-benzoyl-N′-phenylurea**, mp 197–199° dec. The ir and nmr spectra were identical with that of an authentic sample of the urea product.

Reaction of Methyl N-Chlorobenzimidate with Benzenethiol.—Benzenethiol (5.51 g, 0.05 mol) was added dropwise to a solution of 8.45 g (0.05 mol) of methyl N-chlorobenzimidate in 5 ml of benzene during 1 hr with cooling to maintain the temperature at 25–30°. The resulting reaction mixture was then slowly heated to 81° in 3 hr. During this time 670 ml (60%) of methyl chloride was collected. The solid brown residue product was washed with three 15-ml portions of cold benzene and dried to yield 6.9 g (60%) of white **N-benzoylbenzenesulfenamide (7)**, mp 87–90°. An analytical sample was prepared by recrystallization from benzene to yield 5.5 g (48%), mp 95–97°: ir 3.05 (N–H), 6.00 (C=O), 6.74 (N–H), 9.10 (S–C_6H_5), and 9.67 μ (S–C_6H_5); nmr ($CDCl_3$) δ 8.06 (s, 1 H, –NH–), 7.86 (m, 2 H, aromatic), and 7.32 ppm (m, 8 H, aromatic).

Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.10; H, 4.84; N, 6.11; S, 13.98. Found: C, 68.35; H, 5.04; N, 6.41; S, 13.20.

S,S-Dimethyl-N-(*p*-Methoxybenzoyl)sulfilimine (4).—Methyl sulfide (6.83 g, 0.11 mol) was added dropwise to 20.0 g (0.10 mol) of methyl N-chloro-*p*-methoxybenzimidate with stirring. The addition was complete in 10 min and during this time the temperature rose from 25 to 35° and 60 ml of methyl chloride was collected. The mixture was slowly heated to 64° during 4.5 hr. After cooling, 10 ml of benzene and an additional 0.62 g (0.01 mol) of methyl sulfide was introduced, and the reaction mixture was heated for 4 hr at 85–88° until gas evolution was complete. The solid product was washed successively with 20 ml of petroleum ether (63–75°) and two 30-ml portions of diethyl ether and dried to yield 13.76 g (65%), mp 87–92°. Recrystallization from benzene gave 12.30 g (58%), mp 87.5–92°. An analytical sample was prepared by two recrystallizations from benzene, mp 95–99°: ir (KBr) 3.50 (O–CH_3), 6.23 (C=O), 6.30, 6.46, 6.54, 6.62, 6.75 (aromatic C=C), 7.50 (N=S),

8.04 (O-C_6H_4), 9.60, and 9.80 μ (O-CH_3); nmr ($CDCl_3$) δ 2.73 (s, 6 H, =S(CH_3)$_2$, 3.82 (s, 3 H, -OCH_3), 6.85 (d, 2 H, aromatic), and 8.03 ppm (d, 2 H, aromatic).

Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63; S, 15.18. Found: C, 56.54; H, 5.92; N, 6.70; S, 14.86.

N-(*p*-Methoxybenzoyl)-1-propanesulfenamide (6).—*n*-Propyl sulfide (5.91 g, 0.05 mol) was added to 10 g (0.05 mol) of methyl N-chloro-*p*-methoxybenzimidate during 10 min. There was only very slight exotherm of reaction (2° rise) and no gas evolved under these conditions. The resultant reaction mixture was slowly heated to 135° during 3.5 hr and maintained at 135–137° temperature for 2.0 hr. During this time the theoretical quantity (1120 ml) of methyl chloride (identified by mass spectrometry) had been collected. The reaction product was filtered to give a tacky, pale yellow solid which was washed with cyclohexane and dried to yield 11.30 g (100%). This product was extracted with five 400-ml portions of boiling petroleum ether (63–75°). The yellow insoluble amorphous residue was discarded and the extracts were allowed to stand for 2 days. The crystallized product was collected by filtration and dried to yield 3.45 g (31%), mp 86.5–89°. An analytical sample was prepared by recrystallization of 0.5 g from 200 ml of petroleum ether (63–75°): yield 0.43 g; mp 92–93.5°; ir (KBr) 3.05 (N-H), 3.52 (O-CH_3), 6.08 (amide C=O), 6.24, 6.36, and 6.66 μ (aromatic C=C); nmr ($CDCl_3$) δ 0.99 (t, 2 H, -SCH_2CH_2-), 1.64 (sextet, 2 H, -$CH_2CH_2CH_3$), 2.79 (t, 3 H, -CH_2CH_3), 3.82 (s, 3 H, CH_3-OC_6H_4-), 6.89 (m, 2 H, aromatic), 7.45 (s, 1 H, -NH-), and 7.82 ppm (m, 2 H, aromatic).

Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.62; H, 6.74; N, 6.42.

Registry No.—**1** *syn*, 23632-48-6; **1** *anti*, 23632-47-5; **2** *syn*, 24978-55-0; **2** *anti*, 25024-02-6; **3**, 19397-91-2; **3** (HCl), 24978-57-2; **4**, 25024-03-7; **5**, 24978-58-3; **6**, 24978-59-4; **7**, 23847-33-8.

Nucleophilic Scission of Disulfides by Selenolate. Synthesis and Some Properties of Acyclic Thiolselenenates[1,2]

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Received January 27, 1970

Various types of compounds possessing a sulfur–sulfur bond, *e.g.* diaryl disulfides (ArSSAr), dialkyl disulfides (RSSR), sulfenyl thiocyanates (RSSCN), sulfenyl sulfites ($RSSO_3^-$), and sulfenyl thiosulfates ($RSS_2O_3^-$), are susceptible to nucleophilic attack.[3] The ionic scission of sulfur–sulfur bonds by nucleophilic agents has been repeatedly investigated and, on the basis of kinetic studies, appears to involve an S_N2 mechanism.[4]

This paper describes the scission of disulfides by selenolate. As an *a priori* consideration, this type of reaction would be expected to proceed readily. On the one hand the valence shell electrons of selenium are highly polarizable,[5] resulting in highly nucleophilic species;[6,7] on the other hand sulfur in a disulfide bridge is capable of using the empty 3d orbitals in the transition state, facilitating nucleophilic scission of S–S bonds.[4] Added interest in this type of reaction stemmed from a possible general application of this method for the synthesis of thiolselenenates, particularly those which are aliphatic and acyclic in nature; it appears that the first compound of this type, *viz.* 1-amino-3-selena-4-thiatetradecane, was prepared only recently.[8]

In this study 2-naphthylsulfenylthiocyanate (**2**),[9] a relatively stable compound among the labile sulfenylthiocyanates, was allowed to react with the selenolate of N-carbobenzoxy-L-selenocysteine diphenylmethyl ester (**1**);[10] the thiolselenenate (**3**) was isolated in moderate yield following chromatographic separation from the diselenide (**4**) and disulfide (**5**) (Scheme I). In independent experiments it was noticed that **2** is rather labile in an alkaline medium giving rise to the disulfide **5**; since it was felt that the moderate yield of **3** may have been associated with the lability of the substrate **2**, experiments were repeated using increasing amounts of **2** (up to 3 mol equiv). The fact that neither the yield of **3** nor the ratio of **3** to **4** were changed indicated that the moderate yield of product could be due to an intrinsic instability of **3**, a possibility in line with earlier observations with thiolselenenates.[8,11]

In order to eliminate definitively possible interference by a base-labile substrate, **2** was replaced with the more stable sulfenyl sulfite (Bunte salt); pure unsymmetrical disulfides have been prepared in weakly alkaline reaction media using sulfenyl sulfites.[12] However, when the anion **1** treated with sodium S-benzylthiosulfate (**6**)[13] the desired thiolselenenate (**7**) was isolated only in somewhat higher yield (Scheme II). This again pointed to an instability of the thiolselenenate.

Further semiquantitative studies with **3** and **7** involving solvent variation *per se* showed that disproportionation takes place, the rate depending in first approximation on the polarity of the solvent. Essentially, instantaneous disproportionation of **3** and **7** occurs in basic media and a rapid disproportionation also takes place in acidic media as illustrated by the attempt to decarbobenzoxylate **3** which resulted in L-selenocystine. From these and other findings[8,11] it appears that aliphatic acyclic thiolselenenates are exceedingly reactive molecules, while cyclic thiolselenenates are generally more stable,[14–16] although excep-

(1) This work was supported by U. S. Publich Health Service Grants AM-10080, AM-13567 of the National Institute of Arthritis and Metabolic Diseases and by the U. S. Atomic Energy Commission.

(2) The following abbreviations have been adopted: Z = $C_6H_5CH_2OCO$, DMF = N,N-dimethylformamide, AcOH = acetic acid, EtOH = ethanol, MeOH = methanol, Et_2O = diethyl ether, EtOAc = ethyl acetate.

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