The results for other amides are summarized graphically in Figures 1, 2, and 3.

Procedure for Product Analysis.—For analyzing reduction products separate experiments on a 20-mmol scale were carried out. The yields were determined by titration with 1.0 *N* HCl, isolation as the picrate, or by glpc analysis on a 10% Porimene JM-T on Fluoropak. Reduction of *N,N*-diisopropylbenzamide to *N,N*-diisopropylbenzylamine is representative. The experimental setup is as in the previous experiment. A typical reaction setup was assembled. Then 33.3 mmol of borane solution (20 ml of a 1.67 *M* solution in THF) was placed in the reaction flask maintained at *ca.* 25°. To this 4.1 g (20 mmol) of *N,N*-diisopropylbenzamide in 20 ml of THF was added and the mixture was stirred well. The resulting mixture was refluxed for 1 hr. The flask was allowed to cool to room temperature and 8 ml of 6 *M* HCl was added. The tetrahydrofuran was removed by distillation at atmospheric pressure as hydrogen was evolved (1.5 l., 60 mmol) from hydrolysis of excess borane. Sodium hydroxide pellets were added to saturate the aqueous phase and the latter was extracted three times with a total of 25 ml of ether. Titration of a known aliquot of this reaction mixture with a standardized HCl solution revealed the presence of amine in 98% yield.

To 2.5 ml (1 mmol) of the ether extract of the amine, a saturated solution of picric acid in 95% ethanol was added and heated. Water was added drop by drop until the solution turned slightly milky. After cooling, yellow needles of picrate crystallized out in 98% yield, mp 134–135°. *Anal.* Calcd for $C_{19}H_{24}N_4O_7$: C, 54.27; H, 5.75; N, 13.32. Found: C, 54.42; H, 5.82; N, 13.32.

General Preparative Procedure for the Reduction of Amides to Amines.—The following general procedure illustrated for the reduction of *N,N*-dimethylpivalamide to dimethylpivalamine is suggested for the reduction of amides. (Depending upon the nature of the amide and the substituents present, the hydride to compound ratio and the time required may require an increase or decrease.)

To a solution of 200 ml (334 mmol) of 1.67 *M* borane in THF in a 500-ml flask equipped with a reflux condenser, dropping funnel, and a magnetic stirring bar maintained under nitrogen was added 25.8 g (200 mmol) of *N,N*-dimethylpivalamide in 100 ml of THF over 15 min. The temperature was maintained approximately at 0° during the addition. The colorless solution was then brought to reflux and maintained there for 1 hr. The flask was permitted to cool to room temperature and 50 ml of 6 *M* hydrochloric acid was added slowly through a dropping funnel. The THF was removed by distillation at atmospheric pressure as hydrogen was evolved (15.5 l., 0.6 mol) from the hydrolysis of the amine–borane complex. Sodium hydroxide pellets were added to saturate the aqueous phase and the latter was extracted three times with a total of 100 ml of ether. After drying with sodium sulfate, distillation yielded 18.2 g (79% yield) of dimethylneopentylamine, bp 95–96°, $n^{20}D$ 1.3982.

Similarly, *N,N*-diethylpivalamide was converted into isolated diethylneopentylamine in an isolated yield of 81%.

Selective Reduction of *N,N*-Dimethyl-*p*-nitrobenzamide to Dimethyl-*p*-nitrobenzylamine.—To a solution of 50 ml (83.3 mmol) of a 1.67 *M* solution of borane in THF in a 200-ml flask maintained at 0° under nitrogen was added 9.76 g (50 mmol) of *N,N*-dimethyl-*p*-nitrobenzamide in 4.0 ml of THF over a period of 10 min. After the addition was completed, the resulting mixture was refluxed for 1 hr. After the reaction flask was cooled, the reaction mixture was worked up as in the previous experiment and the combined ether extracts were dried over sodium sulfate. Distillation yielded 7.6 g (84%) of dimethyl-*p*-nitrobenzylamine, bp 96–98° (1.5 mm), $n^{20}D$ 1.5421.

Registry No.—Diborane, 19287-45-7.

Formation of Mercaptomethylamine as an Intermediate[1]

KENNETH R. HENERY-LOGAN* AND SABET ABDOU-SABET[2]

Department of Chemistry, University of Maryland, College Park, Maryland 20742

Received November 20, 1972

Bis(aminomethyl) disulfide dihydrochloride (**2**) was hydrogenated to yield bis(aminomethyl) sulfide dihydrochloride (**3**) and hydrogen sulfide. Similarly, reaction of phthalimidomethyl aminomethyl disulfide hydrochloride (**4**) with hydrogen and palladium gave *N*-(mercaptomethyl)phthalimide (**5**), **3**, and hydrogen sulfide. These reactions indicate the formation of mercaptomethylamine hydrochloride (**1**) as an intermediate which undergoes self-condensation to yield **3** and hydrogen sulfide. Compounds **2** and **4** were prepared by the acid hydrolysis of bis(*o*-carboxybenzoylaminomethyl) disulfide (**8**), which was obtained by partial alkaline hydrolysis of bis(phthalimidomethyl) disulfide (**7**). Hydrazinolysis of **7** in liquid ammonia gave **2** directly in low yield. The sulfide **3** was independently synthesized from bis(phthalimidomethyl) sulfide (**10**) by saponification to bis(*o*-carboxybenzoylaminomethyl) sulfide (**11**) followed by acid hydrolysis. Treatment of β-mercaptoethylamine hydrochloride (**12**) with sulfur trioxide–pyridine afforded *S*-2-aminoethanethiosulfuric acid (**13**).

Chemical protection of mammals against ionizing radiation was demonstrated in 1949.[3] It was soon established that compounds showing radiation protection possessed both the amino and mercapto groups,[4] and β-mercaptoethylamine (MEA) is one of the most active of the more than 3000 compounds tested.[5]

The protective action of aminothiols has been shown to decrease with increasing separation of the functional groups.[5,6] We were therefore led to examine the synthesis and properties of the hydrochloride of mercaptomethylamine (**1**), the parent *N,S*-acetal of formaldehyde. Two *N,S*-hemiacetals of **1** containing tertiary nitrogens have been reported, 1-piperidinemethanethiol and 4-morpholinemethanethiol.[7]

In general, Bunte salts (*e.g.*, **13**) are less toxic than the corresponding thiols, and *S*-2-aminoethanethiosulfuric acid (**13**) and MEA (**12**) are equally protective at their maximum tolerated doses.[6] A new synthesis of **13** is reported and an attempt was made to extend the reaction to the preparation of *S*-aminomethanethiosulfuric acid (**14**).

Results and Discussion

Hydrogenation of Disulfides 2 and 4.—This communication reports evidence for the formation of mercaptomethylamine hydrochloride (**1**) as an inter-

(1) Presented in part at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, Abstracts, I23.

(2) Taken in part from the dissertation submitted by S. Abdou-Sabet in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Maryland, 1966; *Diss. Abstr. B*, **27**, 3028 (1967).

(3) (a) A. Herve and Z. M. Bacq, *C. R. Soc. Biol.*, **143**, 881 (1949); (b) H. M. Patt, E. B. Tyree, R. L. Straube, and D. E. Smith, *Science*, **110**, 213 (1949).

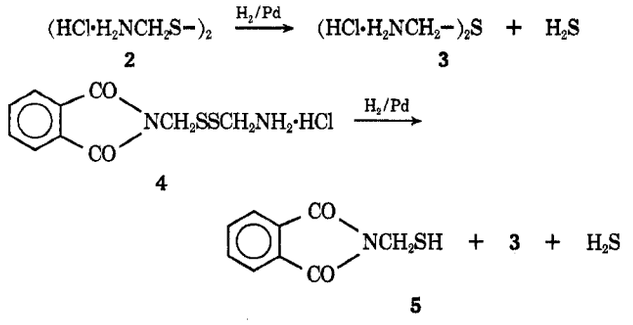
(4) Z. M. Bacq and A. Herve, *Schweiz. Med. Wochenschr.*, **82**, 1018 (1952).

(5) Z. M. Bacq, "Chemical Protection against Ionizing Radiation," Charles C Thomas, Springfield, Ill., 1965, p 12.

(6) D. L. Klayman, M. M. Grenan, and D. P. Jacobus, *J. Med. Chem.*, **12**, 510 (1969).

(7) A. Binz and L. H. Pence, *J. Amer. Chem. Soc.*, **61**, 3134 (1939).

mediate in two related reactions. The reaction of bis(aminomethyl) disulfide dihydrochloride (2) with

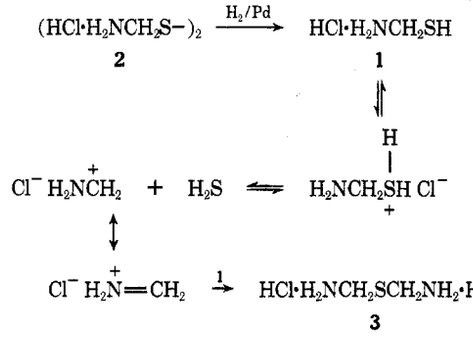


hydrogen in the presence of palladium black afforded crystalline bis(aminomethyl) sulfide dihydrochloride (3) and hydrogen sulfide. In a similar reaction, hydrogenation of phthalimidomethyl aminomethyl disulfide hydrochloride (4) gave *N*-(mercaptomethyl)phthalimide (5), 3, and hydrogen sulfide.

Catalytic reduction of disulfides is known to produce mercaptans,[8] and the primary products from the hydrogenation of the disulfides 2 and 4 were very likely the corresponding mercaptans 1 and 5. The mercaptan 5 was isolated and its structuree was confirmed by an independent synthesis. Two molecules of mercaptan 1 are considered to have undergone condensation with elimination of hydrogen sulfide and formation of the sulfide dihydrochloride 3. The mechanism proposed in Scheme I suggests the forma-

SCHEME I

PROPOSED MECHANISM FOR CONVERSION OF DISULFIDE 2 INTO SULFIDE 3



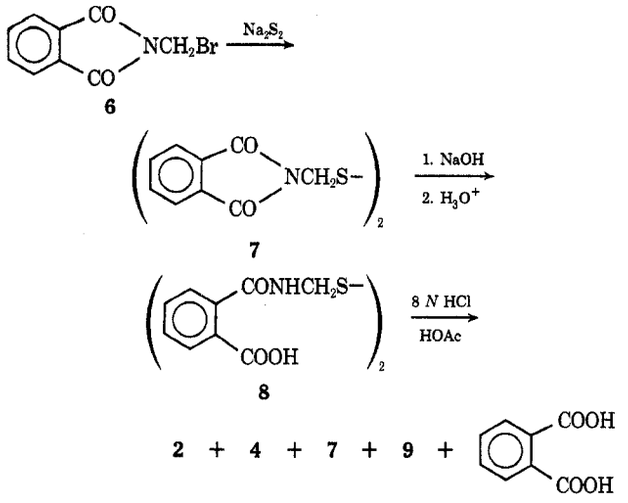
tion of protonated methyleneimine[9] as an intermediate. A similar intermediate, *N*,*N*-dimethylbenzaliminium ion, has been presented to explain the kinetics observed in the SN1 cleavage of alkyl α-dimethylaminobenzyl sulfides in aqueous acidic media.[10]

Synthesis of Disulfides 2 and 4.—The route leading to the disulfides 2 and 4 is outlined in Scheme II. Utilization of a thiol ester as a single protective group was not attempted, since α-aminothio esters were prepared successfully only with tertiary amino groups.[11] The synthesis of monoalkylaminomethanethiol esters is not practical (3% yield) owing to the predominance of polymer formation.[11]

(8) C. Berse, R. Boucher, and L. Piche, *J. Org. Chem.*, **22**, 805 (1957).
(9) F. Cacace and A. P. Wolf, *J. Amer. Chem. Soc.*, **87**, 5301 (1965).
(10) W. M. Schubert and Y. Motoyama, *ibid.*, **87**, 5507 (1965).
(11) S. Searles, Jr., S. Nukina, and E. R. Magnuson, *J. Org. Chem.*, **30**, 1920 (1965).

SCHEME II

SYNTHESIS OF DISULFIDES 2 AND 4



The synthesis of the known *N*-(bromomethyl)phthalimide (6) from *N*-(hydroxymethyl)phthalimide was carried out by a modification of the literature procedure.[12] A purer and more stable product was obtained in higher yield (85%) by substitution of 62% for 48% hydrobromic acid and by the use of glacial acetic acid as the solvent in place of concentrated sulfuric acid.

The reaction of 6 with sodium disulfide in 0.1 *M* quantities following the general literature procedure[13] gave variable and low yields (1–29%) of bis(phthalimidomethyl) disulfide (7). No product, however, was isolated with larger scale reactions. With acetone–water as the solvent system and using freshly prepared sodium disulfide, compound 7 was reproducibly obtained in 70–80% yield.

Cleavage of the phthalimido group of 7 with hydrazine in dioxane–water, methyl alcohol, carbon tetrachloride, chloroform, or benzene gave phthalhydrazide but 2 could not be isolated; however, it was later found that a very low yield of the disulfide 2 could be obtained using liquid ammonia as the solvent. An improved method was the two-step hydrolysis which afforded 2 and 4 simultaneously. Treatment of 7 with 2 equiv of sodium hydroxide followed by acidification with hydrochloric acid gave analytically pure bis(*o*-carboxybenzoylaminomethyl) disulfide (8) in 80% yield. Hydrolysis of 8 was effected using 8 *N* hydrochloric acid in acetic acid at room temperature to give five products, 2 (13–20%), 4 (41%), 7 (39%), phthalic acid, and a small amount of compound 9 whose structure was not determined. Attempted hydrolysis of 8 using 12 *N* hydrochloric acid in acetic acid resulted in dehydration and cyclization of the phthalamic acid to 7, whereas 4 *N* hydrochloric acid in acetic acid gave phthalic acid, ammonium chloride, and uncharacterized polymers, possibly derived from thioformaldehyde. The disulfide dihydrochloride 2 is unstable in moist air and when dissolved in water it decomposes with the evolution of hydrogen sulfide and formation of a white polymeric precipitate.

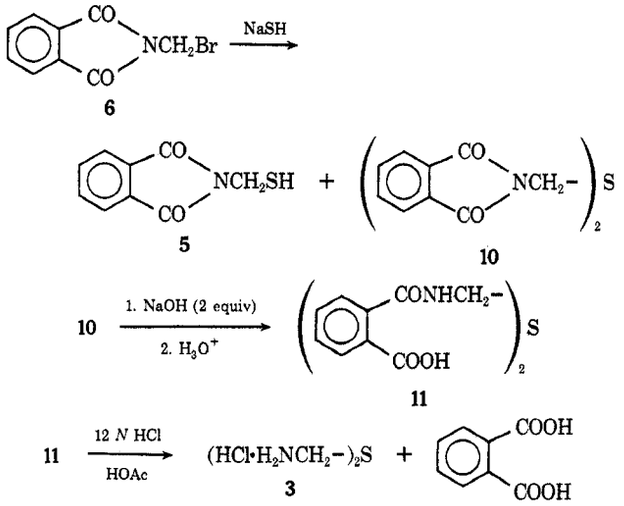
Syntheses of Bis(aminomethyl) Sulfide Dihydro-

(12) G. W. Pucher and T. B. Johnson, *J. Amer. Chem. Soc.*, **44**, 820 (1922).
(13) F. I. Rachinskii, N. M. Slavacheskaia, and D. V. Iofee, *Zh. Obshch. Khim.*, **28**, 2998, 3027 (1958).

chloride (3) and Phthalimidomethyl Mercaptan (5).—The structures of **3** and **5** were confirmed by independent syntheses, as shown in Scheme III. The

SCHEME III

SYNTHESIS OF SULFIDE 3 AND MERCAPTAN 5



reaction of sodium hydrosulfide with **6** at 0° in a tetrahydrofuran–water medium gave mainly the mercaptan **5** and very little **10**; at room temperature, however, the predominant product was the sulfide **10**. The phthaloyl protecting group of **10** was removed in two steps. The initial saponification gave the phthalamic acid **11** in good yield. The subsequent hydrolysis of **11** using 12 *N* hydrochloric acid in glacial acetic acid afforded the sulfide dihydrochloride **3** in moderate (41%) yield.

***S*-2-Aminoethanethiosulfuric Acid (13).**—Aminoalkanethiosulfuric acids, an important class of zwitterionic Bunte salts, are usually prepared by the reaction of the corresponding bromoalkylamine hydrobromide with sodium thiosulfate.[6] Thiophenols react with sulfur trioxide–pyridine to give the corresponding phenylthiosulfuric acids,[14] and later workers[15] have prepared aliphatic and aromatic thiosulfuric acids by reaction of the corresponding mercaptan with sulfur trioxide. This reaction was extended to an aminoalkanethiol; the reaction of β-mercaptoethylamine hydrochloride (**12**) with sulfur trioxide–pyridine afforded a new route to **13**.

$$\underset{\mathbf{12}}{HCl\cdot H_2NCH_2CH_2SH} + SO_3\text{–}Py \xrightarrow{DMF} \underset{\mathbf{13}}{H_2NCH_2CH_2S_2O_3H} + Py\cdot HCl$$

An unsuccessful attempt was made to trap **1** as a Bunte salt by hydrogenation of **2** in the presence of

$$\underset{\mathbf{2}}{(HCl\cdot H_2NCH_2S)_2} \xrightarrow[SO_3\text{–}Py]{H_2/Pd} \underset{\mathbf{14}}{H_2NCH_2S_2O_3H}$$

sulfur trioxide–pyridine. The reaction mixture turned black immediately and no pure products could be isolated.

(14) P. Baumgarten, *Ber.*, **63**, 1330 (1930).
(15) M. Schmidt and G. Talsky, *Chem. Ber.*, **94**, 1352 (1961).

Experimental Section[16]

***N*-(Bromomethyl)phthalimide (6).**—Major modifications were made in the Pucher and Johnson[12] procedure. To a mixture of 17.7 g (0.1 mol) of *N*-(hydroxymethyl)phthalimide[12] in 35 ml of glacial acetic acid was added, with stirring, 27.5 ml of 62% hydrobromic acid (Michigan Chemical Co., New York, N. Y.). The mixture was heated and kept at 48–52° for 20 hr. After cooling overnight at 0–5°, the colorless solid was collected by filtration and washed with water, then with dilute ammonium hydroxide solution, and again with water. The dry solid (22.1 g) was crystallized from benzene and gave 18.5 g (85%) of **6**, mp 152° (lit. mp 148°,[12] 150°[17]).

Anal. Calcd for $C_9H_6BrNO_2$: C, 45.03; H, 2.51; N, 5.84; Br, 33.29. Found: C, 44.94; H, 2.51; N, 5.98; Br, 33.11.

Bis(phthalimidomethyl) Disulfide (7).—This compound was prepared using a modification of the general literature procedure.[12] A 2-g portion (0.0625 mol) of sublimed sulfur was dissolved in a solution of 15 g (0.0625 mol) of $Na_2S\cdot 9H_2O$ in 20 ml of water with heating; then an additional 30 ml of water was added. After cooling to room temperature, the Na_2S_2 solution was added to a solution of 24 g (0.1 mol) of **6** in 200 ml of acetone with vigorous stirring and ice-bath cooling over a period of 2 min. The suspension was stirred for an additional 5 min, then 200 ml of water was added, the mixture was cooled, and 16.5 g of crude product was collected by filtration. Crystallization from chloroform–*n*-hexane afforded 14.65 g (76%) of the analytically pure disulfide **7**: mp 194°; ir 5.63 and 5.85 (phthalimido carbonyls), 6.23, 6.83, 7.10, 7.15, 7.30, 7.70, 7.88, 8.40, 8.55, 9.25, 10.95, 12.40, 12.65, 13.50, and 14.80 μ.

Anal. Calcd for $C_{18}H_{12}N_2O_4S_2$: C, 56.23; H, 3.15; N, 7.29; S, 16.68. Found: C, 56.43; H, 3.29; N, 7.08; S, 16.63.

Bis(*o*-carboxybenzoylaminomethyl) Disulfide (8).—To a suspension of 7.68 g (0.02 mol) of **7** in 600 ml of 95% ethyl alcohol at 42–45° was added 40 ml (0.02 mol) of 1.00 *N* NaOH dropwise over a period of 30 min to give a homogeneous solution which was evaporated *in vacuo* at 35°. Crystallization of the residue from water–ethanol gave 8.5 g of crystalline solid, mp 143°, which on recrystallization afforded 7.52 g (81%) of needle-shaped crystals of the hydrate of the disodium salt of **8**: mp 175° dec; ir 3.00 (NH), 6.06 (sh), 6.17 (sh), 6.35, 6.95, 7.30, 7.52, 7.90, 8.60, 9.15, 9.65, 10.60, 11.85, and 13.70 μ.

Anal. Calcd for $C_{18}H_{14}O_6N_2S_2Na_2\cdot H_2O$: C, 44.82; H, 3.34; N, 5.81; S, 13.29. Found: C, 44.76, 45.30; H, 3.30, 3.52; N, 5.93; S, 13.53.

To a solution of 5.36 g (0.0115 mol) of the disodium salt hydrate of **8** in 50 ml of water was added 23 ml of 1.0 *N* HCl dropwise with stirring and ice bath cooling. After cooling at 0° for 2 hr, 4.20 g (80% based on **7**) of analytically pure **8** was collected by filtration: mp 142° dec; ir 3.00, 3.35, 3.40, 5.90 (COOH), 6.08 (CONH), 6.20, 6.30, 6.50, 6.60, 6.80, 7.30, 7.60, 7.95, 8.20, 8.75, and 9.25 μ.

Anal. Calcd for $C_{18}H_{16}O_6N_2S_2$: C, 51.44; H, 3.84; N, 6.66; S, 15.22. Found: C, 51.40; H, 4.05; N, 6.62; S, 15.27.

Hydrolysis of 8.—A suspension of 5.3 g (0.0125 mol) of **8** in 150 ml of glacial acetic acid and 6.25 ml of 8 *N* HCl was stirred for 24 hr. The suspension was lyophilized and the dry white solid residue was extracted with a 100-ml portion of refluxing $CHCl_3$ and washed with four 25-ml portions of hot $CHCl_3$. The combined chloroform extract was concentrated to give a white solid (0.2 g) that was crystallized three times from chloroform–ether to afford compound **9**: mp 163–165°; ir 2.95, 5.65, 5.82, 5.88 6.20, 7.05, 7.20, 7.62, 7.72, 9.05, 9.35, 10.35, 10.80, 12.50, 13.65, and 13.90 μ.

Anal. Found: C, 44.66; H, 4.50; Cl, 15.22; N, 11.53; S, 12.30. Compound **9** was not characterized further.

The chloroform filtrate was evaporated to dryness and the residue was crystallized from chloroform–*n*-hexane to afford 1.9 g (39%) of disulfide **7**, mp 194°; the infrared spectrum was identical with that of an authentic sample.

The solid insoluble in the original chloroform extract was extracted in a Soxhlet apparatus with anhydrous ether for 12 hr. The ether extract afforded 2.1 g (51%) of phthalic acid, mp 191–192° dec.

(16) All melting points are uncorrected. Infrared spectra were determined in KBr on a Beckman IR-5 instrument (reported in μ) or on a Perkin-Elmer Model 337 spectrophotometer (reported in cm^{-1}). Elemental analyses were performed by Dr. Franz J. Kasler.
(17) O. Mancera and O. Lemberger, *J. Org. Chem.*, **15**, 1253 (1950).

The residue remaining after the ether extraction was digested with 60 ml of anhydrous dimethylformamide–ether (5:1) mixture. The extract was evaporated at low pressure to give 1.5 g (41%) of solid that was purified by crystallization from 12 ml of benzyl alcohol–ether (5:1) to afford pure disulfide hydrochloride **4**: mp 114°; ir 2.95, 3.90 (sh), 5.60, 5.80, and 6.30 μ.

Anal. Calcd for $C_{10}H_{11}ClN_2O_2S_2$: C, 41.26; H, 3.81; N, 9.65. Found: C, 41.48; H, 4.03; N, 9.70.

The residue remaining after the dimethylformamide–ether extraction, 0.52 g, showed no absorption for the carbonyls of the phthalimido in the ir spectrum. The solid was dissolved in 15–20 ml of glacial acetic acid by heating and adding concentrated HCl dropwise. Cooling afforded 0.34 g (14%) of crystalline, analytically pure disulfide dihydrochloride **2**: shrinking at 145°, obvious decomposition at 210°, and extensive decomposition with strong, unpleasant odor above 235°; ir 2.94 (m), 3.36 (vs), 3.42 (vs), 3.51 (vs), 3.91 (m), 6.28 (m), 6.32 (m), 6.67 (s), 7.05 (m), 7.60 (w), 8.92 (vw), 9.25 (w), 10.24 (m), 11.85 (m), and 14.6–15.0 μ (broad and weak).

Anal. Calcd for $C_2H_{10}Cl_2N_2S_2$: C, 12.18; H, 5.07; Cl, 35.99; N, 14.21; S, 32.55. Found: C, 12.29; H, 5.30; Cl, 36.23; N, 14.11; S, 32.35.

Preparation of Bis(aminomethyl) Disulfide Dihydrochloride (2) by the Hydrazinolysis of Bis(phthalimidomethyl) Disulfide (7).—To about 250 ml of liquid ammonia, 5.51 g (0.01435 mol) of **7** and 1.0 ml of 97+% anhydrous hydrazine were added. The mixture was stirred at −36° for 25 hr. The ammonia was then allowed to evaporate under anhydrous conditions to give a yellow solid, which was dissolved in 50 ml of glacial acetic acid, followed by the addition of 10 ml of 36% hydrochloric acid during which H_2S gas was evolved and a white solid precipitated. The mixture was digested for 2 hr, heated to 50–60°, and then filtered to give 2.0 g (86%) of phthalhydrazide. The filtrate upon standing afforded a crystalline solid, 1.1 g, which was collected by filtration. This solid was then extracted with dimethylformamide to afford 0.7 g of white solid that was suspended in 17 ml of glacial acetic acid and 3 ml of concentrated hydrochloric acid, heated to 70°, and filtered hot; the residue was found to be ammonium chloride, mp 330° dec. The filtrate upon cooling in the ice box afforded a crystalline solid that was recrystallized from acetic acid–concentrated hydrochloric acid to give 0.2 g (7%) of pure **2**. The melting point, the infrared spectrum, and the chemical analyses were identical with those obtained for an authentic sample prepared by the two-step hydrolysis.

Hydrogenation of Bis(aminomethyl) Disulfide Dihydrochloride (2).—Hydrogen gas was bubbled for 5 hr at room temperature through a solution of 0.148 g (0.75 mmol) of **2** in 75 ml of glacial acetic acid–concentrated hydrochloric acid (2:1) to which had been added 0.452 g of purified palladium black (Fisher Scientific); the exiting gas had the odor of H_2S and when bubbled through a 10% lead acetate solution a black precipitate of lead sulfide was obtained. After the catalyst was removed by filtration, the filtrate was lyophilized to give a white solid, which was dissolved in about 20 ml of glacial acetic acid containing a few drops of concentrated hydrochloric acid by heating to 70–80°. The solution was cooled to 30°, then ethyl ether was added, and on further cooling to 5° crystallization occurred. Collection of the crystals by filtration afforded 0.105 g (85%) of analytically pure bis(aminomethyl) sulfide dihydrochloride (**3**): the melting point and mixture melting point were identical with the melting point of an authentic sample of **3**, prepared by an independent route (*vide infra*), and the infrared spectrum was identical with that of the authentic sample.

Anal. Calcd for $C_2H_{10}Cl_2N_2S$: C, 14.55; H, 6.10; Cl, 42.95; N, 16.97; S, 19.42. Found: C, 14.98; H, 6.14; Cl, 43.73; N, 16.58; S, 19.72.

Hydrogenation of Phthalimidomethyl Aminomethyl Disulfide Hydrochloride (4).—Hydrogen gas was bubbled for a period of 5 hr at room temperature through a solution of 0.1 g (0.346 mmol) of **4** in 50 ml of glacial acetic acid–concentrated hydrochloric acid (9:1), containing 0.3 g of purified palladium black; H_2S was detected in the exiting gases. After the catalyst was removed by filtration, the filtrate was lyophilized to a white solid which was extracted with ethyl acetate. The residue, 0.056 g (85%), was crystallized and the needle-shaped crystals obtained were found to be identical with an authentic sample of **3**. The ethyl acetate extract was concentrated to a white solid, which was crystallized from ethyl acetate–*n*-hexane to afford 0.06 g (90%) of *N*-(mercaptomethyl)phthalimide (**5**), mp 135–137°, identical with an authentic sample (*vide infra*) by melting point, mixture melting point, and comparison of infrared spectra.

***N*-(Mercaptomethyl)phthalimide (5) and Bis(phthalimidomethyl) Sulfide (10).**—To a cooled (0°) solution of 12 g (0.05 mol) of pure *N*-(bromomethyl)phthalimide (**6**) in 100 ml of reagent-grade tetrahydrofuran was added, over a period of 1–2 min with vigorous stirring and ice-bath cooling, a cooled (0°) solution of 2.8 g (0.05 mol) of NaSH[18] in 15 ml of water; the stirring was continued for an additional 5–10 min. The two liquid phases were separated and the organic layer was evaporated *in vacuo* to give an amorphous solid that was extracted with a 50-ml portion of refluxing ethyl acetate. Cooling the filtrate afforded crystalline mercaptan which on recrystallization gave 6.7 g (79%) of analytically pure **5**: mp 138–139°; ir 3.40, 3.95 (SH), 5.68 and 5.87 (C=O), 6.25, 6.89, 7.10, 7.30, 7.60, 7.74, 7.85, 8.45, 9.00, 9.40, 10.15, 10.38, 11.00, 11.45, 12.55, and 13.90 μ.

Anal. Calcd for $C_9H_7NO_2S$: C, 55.96; H, 3.65; N, 7.25; S, 16.60. Found: C, 55.98; H, 3.64; N, 7.45; S, 16.32.

The ethyl acetate insoluble solid was crystallized from 99% ethanol and gave 0.9 g (10%) of the sulfide **10**: mp 241–242°; the ir spectrum was very similar to that of the disulfide **7** except for the appearance of doublets at 9.08 and 9.32 and at 10.80 and 10.92 instead of singlets in **7** at 9.28 and 10.92 μ.

Anal. Calcd for $C_{18}H_{12}N_2O_4S$: C, 61.37; H, 3.43; N, 7.95; S, 9.08. Found: C, 61.24; H, 3.45; N, 8.10; S, 9.30.

Bis(*o*-carboxybenzoylaminomethyl) Sulfide (11).—To a stirred suspension of 14.08 g (0.04 mol) of **10** in 800 ml of 95% ethanol was added dropwise a solution of 3.3 g (0.08 mol) of 97% NaOH in 200 ml of water while heating at 65–70°. The resulting clear solution was stirred for an additional 1 hr at 65–70°. The solution was concentrated *in vacuo* to a volume of 150 ml and then 6.7 ml of 36% HCl in 50 ml of water was added with stirring; an oil began to separate halfway through the addition and again near the end of the addition, and enough dioxane was added in each case to restore homogeneity. Upon standing, solid began to precipitate from the clear solution and after storage at 5° overnight, 14 g of colorless solid was collected by filtration, mp 110° dec. Crystallization from methanol–water gave 10 g (63%) of the crystalline monohydrate of **11**: mp 116° dec; the ir spectrum showed absence of the phthalimido carbonyls and the appearance of new carbonyl bands at 1700 and 1640 cm^{-1}.

Anal. Calcd for $C_{18}H_{16}N_2O_6S \cdot H_2O$: C, 53.21; H, 4.46; N, 6.89; S, 7.86. Found: C, 53.18; H, 4.28; N, 6.40; S, 7.98.

Bis(aminomethyl) Sulfide Dihydrochloride (3).—To a suspension of 2.1 g (5.2 mmol) o fthe hydrate of **11** in 50 ml of glacial acetic acid was added with stirring 2 ml of 36% HCl; the resulting clear solution was heated at 40° for 29 hr, during which time a precipitate formed. Lyophilization gave a solid which was extracted with a 50-ml portion of refluxing $CHCl_3$ and then washed with three 25-ml portions of hot $CHCl_3$. The residue was extracted in a Soxhlet apparatus with anhydrous ether for 12 hr. Concentration of the ether extract afforded 0.8 g (39%) of phthalic acid, mp 194–195°. The residue was digested with 25 ml of anhydrous benzyl alcohol–ether (4:1); a solid was collected by filtration and washed with 2 ml of benzyl alcohol and then with anhydrous ether. The dry solid was dissolved in acetic acid by adding a few drops of 36% HCl. After addition of ether and storage at 5°, 0.17 g (41%) of needles of pure **3** was obtained: slight yellowing at 175° and extensive decomposition at 225–230°; ir 3.33 (vs), 3.48 (vs), 3.88 (s), 6.23 (s), 6.32 (m), 6.70 (vs), 7.00 (m), 7.56 (s), 8.97 (m), 9.19 (m), 9.38 (m), 10.21 (s), 10.32 (s), 11.34 (s), 12.38 (m), 13.85 (w), and 14.85 μ (w).

Anal. Calcd for $C_2H_{10}Cl_2N_2S$: C, 14.55; H, 6.10; Cl, 42.95; N, 16.97. Found: C, 14.82; H, 6.23; Cl, 42.68; N, 17.26.

***S*-2-Aminoethanethiosulfuric Acid (13).**—To a solution of 2.26 g (0.02 mol) of dry β-mercaptoethylamine hydrochloride in 40 ml of anhydrous dimethylformamide in a nitrogen atmosphere was added with stirring 3.2 g (0.02 mol) of sulfur trioxide–pyridine,[19] and stirring was continued for 24 hr at room temperature. The dimethylformamide was removed *in vacuo* at room temperature and then a 50-ml portion of 95% EtOH was added and the mixture was stored at 5° overnight to afford 1.8 g (57%) of crystalline **13**: mp 185° dec (lit.[20] mp 183–185°); the mixture melting

(18) A. Rule, *J. Chem. Soc.*, **99**, 558 (1911).

(19) H. H. Sisler and L. F. Audrieth in "Inorganic Synthesis," Vol. II, W. C. Fernelius, Ed., McGraw-Hill, New York, N. Y., 1946, p 173.

(20) D. L. Klayman, W. F. Gilmore, and T. R. Sweeney, *Chem. Ind. (London)*, 1632 (1965).

point with an authentic sample was undepressed; the infrared spectrum was identical with that of an authentic sample. Conditions were not developed to obtain an optimum yield.

Registry No.—**1**, 16627-75-1; **2**, 37709-20-9; **3**, 37710-01-3; **4**, 37710-02-4; **5**, 32280-93-6; **6**, 5332-26-3; **7**, 37710-05-7; **8**, 37710-06-8; **8** disodium salt, 37710-07-9; **10**, 37710-08-0; **11**, 37710-09-1; **12**, 156-57-0; **13**, 2937-53-3; *N*-(hydroxymethyl)phthalimide, 118-29-6.

Acknowledgment.—We gratefully acknowledge support of this work by the U. S. Army Medical Research and Development Command (Contract DA-49-193-MD-2609).

Acid Decomposition of Tosylazocyclohex-1-ene and 3-Tosylazocholesta-3,5-diene

L. CAGLIOTI,* F. GASPARRINI, AND G. PAOLUCCI

Cattedra di Chimica Organica, Università di Roma, Italy

G. ROSINI

Istituto di Chimica Organica e Industriale, Università di Bologna, Italy

P. MASI

Laboratorio di Ricerche, Farmitalia-Milano, Italy

Received August 1, 1972

The decomposition in acetic acid of tosylazocyclohex-1-ene and 3-tosylazocholesta-3,5-diene is described. The first furnishes a mixture of 1,2-cyclohexanediol diacetate (**3**), 1-tosylcyclohex-2-ene (**4**), *cis*-2-tosylbicyclo[3.1.0]hexane (**5**), *trans*-2-tosyl-1-acetoxycyclohexane (**6**), (*Z*)-2-tosylcyclohexan-1-one tosylhydrazone (**7**), and (*E*)-2-tosylcyclohexan-1-one tosylhydrazone (**8**); the second furnishes practically the sole 3-acetoxy-6β-tosylcholest-4-ene (**9**).

The chemical properties of azoalkenes have been of interest to us recently. Tosylazoalkenes in particular showed dual behaviour in their transformations; either they kept the original sequence of CNS bonds during a reaction, or exhibited extensive rearrangement with loss of nitrogen.[1]

Some new reactions of tosylazocyclohex-1-ene (**1**)[2] and 3-tosylazocholesta-3,5-diene (**2**)[3] are reported.

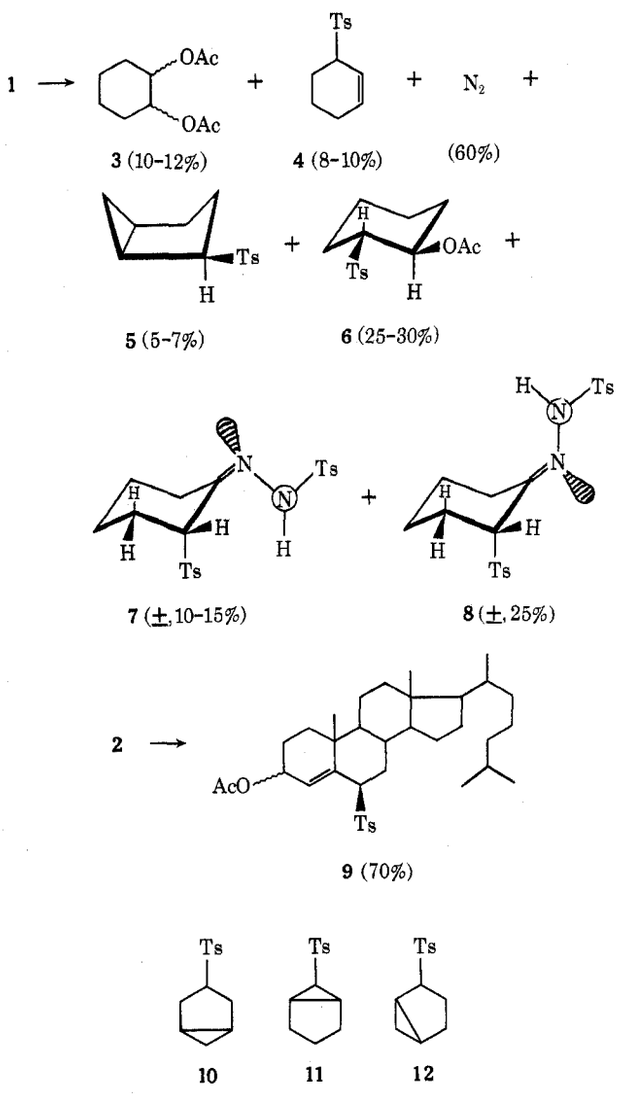
Results

Treatment of **1** and **2** with acetic acid in chloroform at room temperature resulted in the evolution of nitrogen accompanied by the disappearance of the yellow color of the solutions. By absorption chromatography, compounds **3**–**8** were isolated starting from **1** and compound **9** from **2**.

Structures **3** and **4** were determined by direct comparison with specimens prepared by independent routes (ir, pmr, mass spectra).[4] The ir spectrum of **5** revealed the presence of the sulfone function, para-substituted phenyl group, and aliphatic hydrogens. The analytical data indicated the molecular formula $C_{13}H_{16}SO_2$. Osmotic determination of the molecular weight (235.6) and the highest *m/e* peak in the mass spectrum (236) confirmed the monomeric nature of **5**.

The high-resolution pmr spectrum at 100 MHz of compound **5** is reported in Table I.

On the ground of the absence of vinyl hydrogens and as a tetrasubstituted ethane structure is impossible the bicyclic structures **10**, **11**, or **12** are proposed.



(1) L. Caglioti and G. Rosini, *Chem. Ind. (London)*, 1093 (1969).

(2) (a) L. Caglioti, P. Grasselli, F. Morlacchi, and G. Rosini, *ibid.*, 25 (1968); (b) A. Dondoni, G. Rosini, G. Mossa, and L. Caglioti, *J. Chem. Soc. B*, 1404 (1968).

(3) L. Caglioti, M. Poloni, and G. Rosini, *Chim. Ind. (Milan)*, 156 (1970).

(4) K. B. Wiberg and K. A. Saegebart, *J. Amer. Chem. Soc.*, **79**, 6256 (1957).