

## Dithioheterocycles from Ethane-1,2-Disulfonyl Chloride

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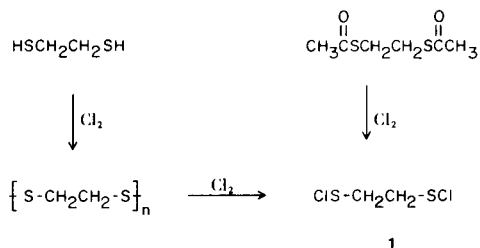
A convenient route to 1,4-dithianes from ethane-1,2-disulfonyl chloride and acetylenes is presented. The reaction of this new sulfonyl halide with primary and secondary amines is also discussed.

The chemistry of sulfonyl halides and their reactions with unsaturates has been a vigorously investigated field (1). Relatively ignored, however, is the chemistry of simple bis-disulfonyl chlorides. The simplest homologs, methanedisulfonyl chloride (2) and its dichloromethane (3) analog, have only recently been reported. We were prompted in this study to obtain the next homolog, ethane-1,2-disulfonyl chloride, particularly in view of its promise of forming five- and six-membered heterocycles by addition with appropriate molecules.

Also previously reported has been the preparation of *n*-propyl-1,3-disulfonyl chloride and *n*-butyl-1,4-disulfonyl chloride *via* chlorination of cyclic disulfides (4).

## RESULTS AND DISCUSSION

Ethane-1,2-disulfonyl chloride (1) can be afforded in good yield *via* the general route (5,6) of chlorinolysis of the corresponding dithiol or dithioacetate.

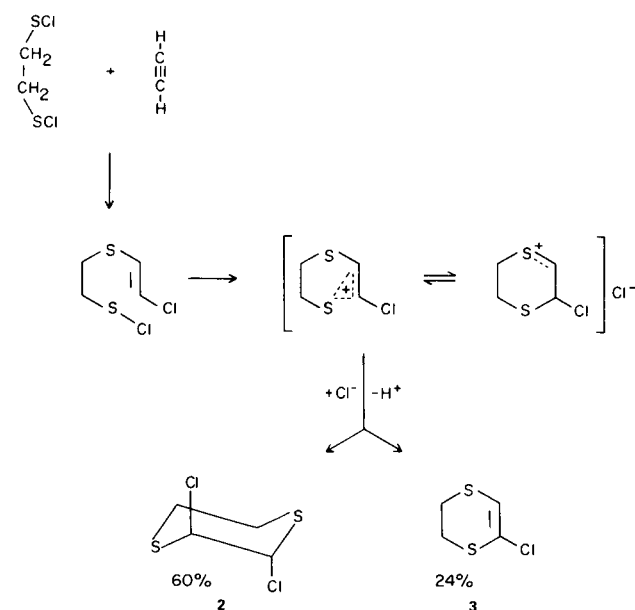


When the dithiol was starting material, the transient formation of insoluble polydisulfides was observed. In both cases, a convenient chlorinating agent was found to be sulfonyl chloride. The product, **1**, was a low melting solid of limited stability at ambient temperature. Indefinite storage was, however, possible at  $-20^\circ$ . Spectral data coupled with the formation of the expected diadduct with ethylene substantiated the structure of **1**.

The reaction of **1** with acetylenes (employing high dilution techniques) led to satisfactory yields of 1,4-dithianes as hoped. As expected, the reactivity of the acetylene was found to increase with its nucleophilicity

when a relatively non-polar solvent such as methylene chloride was employed. In ethyl or methyl acetate, however, reaction even with acetylene was essentially instantaneous at room temperature. The product in this case was composed of two compounds in a ratio of 7:3.

The composition as well as the structural assignments of the product was determined by nmr. Both compounds were subsequently isolated in 60% and 24% yields, respectively. Compound **2** proved to be the previously reported *trans*-1,2-dichloro-1,4-dithiane whose conformational assignment was verified by X-ray data (7).



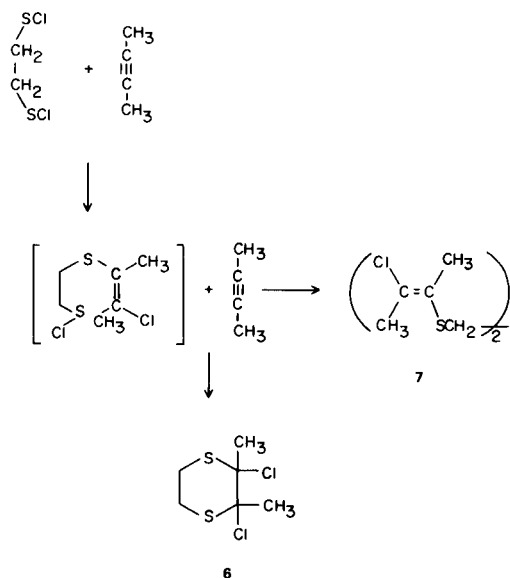
The first step in the cycloaddition, the reaction of the sulfonyl chloride with acetylene, generally occurs with formation of a *trans* adduct (8). Cyclization then may involve an episulfonium ion (9) or a carbonium ion as shown (10). The less strained carbonium ion seems more likely, particularly since the observed *trans* stereochemistry of product **2** does not require the intermediacy of an episulfonium ion. (Free-radical chlorination of 1,4-dithiane formerly afforded the diaxial *trans* product (7).

Furthermore, the formation of dithiene **3** presumably by expulsion of a proton is more consistent with an intermediate approaching a carbonium ion than with a relatively symmetrical episulfonium ion (10). The possibility of **3** being formed *via* dehydrohalogenation of **2** can be excluded under the reaction conditions employed (11).

Since methylacetylene is considerably more reactive than acetylene toward sulfenyl chlorides, the cycloaddition of ethane-1,2-disulfenyl chloride was carried out in methylene chloride. The 2-chloro-3-methyl-1,4-dithiene (**4**) was isolated in 81% yield together with a small amount of polymeric material. There was no evidence for the dichloride **5** as the possible precursor of **4**. Thus compound **4** appears to be directly formed *via* proton expulsion of the carbonium ion intermediate as it has been postulated above for product **3**.



2-Butyne and ethane-1,2-disulfenyl chloride afforded 2,3-dichloro-2,3-dimethyl-1,4-dithiane (**6**) together with the open chain adduct **7** in a ratio of 9:2. Cyclization was maximized by adding 2-butyne to a highly dilute solution (<1%) of the sulfenyl chloride in methyl acetate. Simultaneous introduction of the acetylene and the sulfenyl chloride into methylene chloride favors product **7** and only 31% of the cyclic adduct **6** was obtained. Apparently, open chain product formation becomes competitive when internal acetylenic bonds are involved. This

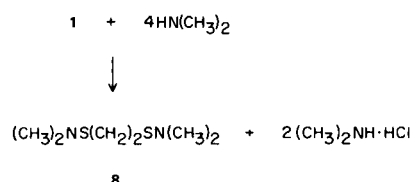


is in accord with the observed greater tendency of internal acetylenes *vs.* terminal acetylenes to add sulfenyl chlorides (12), or it may simply result from unfavorable steric interactions in the cyclization pathway.

The dichloride **6** is air sensitive and decomposes slowly at ambient temperature. It can be stored indefinitely at  $-20^{\circ}$  under pentane. The stereochemistry of **6** is not known; however, its relatively narrow melting range,  $87-89^{\circ}$ , together with the appearance of one narrow singlet for all methyl protons suggests only one isomer is present. The *trans* stereochemistry assigned to **7** is based on the generally assumed *trans*-addition to acetylenic bonds (8).

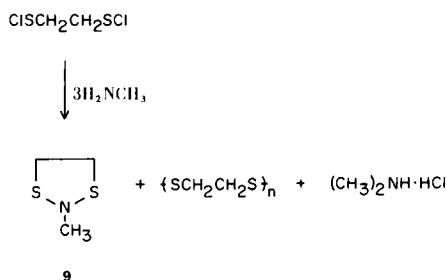
#### Reactions with Amines.

The reaction of ethane-1,2-disulfenyl chloride with dimethylamine followed the expected course leading to the corresponding bis-disulfenamide **8**, in good yield and high purity. Compound **8** is stable and can be vacuum distilled, and its nmr spectrum is in accord with the structure indicated.



A similar reaction of bis-sulfenyl chlorides with primary amines was expected to provide a simple synthetic route to new heterocycles, particularly since a normal reaction course between primary amines and sulfenyl chlorides appeared to be generally accepted (13). Introduction of one equivalent of ethane-1,2-disulfenyl chloride into a highly dilute ethereal solution of three equivalents of methylamine at  $-20^{\circ}$ , however, afforded the heterocycle **9** in only 5% yield. Compound **9** is a white crystalline solid melting at  $28-29^{\circ}$ . In addition, high molecular weight disulfides (77%) and dimethylamine hydrochloride (88%) were isolated. The fate of the third equivalent of amine could not be traced, although it has most likely supplied the hydrogen for the formation of the hydrogen chloride which was isolated as amine hydrochloride. The observed stability of the heterocyclic material **9** seems to preclude it as a labile intermediate which then decomposes to form the disulfides.

A preliminary examination of the reaction of methane- and benzenesulfenyl chloride with various primary amines revealed that the anomalous reaction course is not unique to bis-sulfenyl chlorides. Complex product mixtures containing the corresponding disulfides were again obtained.



## EXPERIMENTAL

## Methods of Analysis.

Nmr spectra were recorded on a Varian Model A-60 resonance spectrometer using tetramethylsilane as an internal standard.

Gas liquid chromatography was performed on a Aerograph 1520 programmed temperature gas chromatograph with a 5 ft. x 0.125 in. o.d. column. The packing consisted of 3% Dowfax 9N40 (an ethylene oxide-*p*-nonylphenol polyether of a 40:1 molar ratio) on 60-80 mesh Gas Chrom W. Operating conditions were as follows: detector, 270°; injector, 190°; flow rate, 50 cc/min.; column heating rate, 4°/min.; starting temperature, 50°, final temperature 200°.

## Starting Materials.

Ethane-1,2-dithiol was obtained from Wateree Chemical Co. The acetylene and methylacetylene are Matheson Co. products. 2-Butyne was obtained from Columbia Organic Chemicals Co. Ethane-1,2-bis-thioacetate was prepared *via* a reported procedure (14).

## Ethane-1,2-Disulfenyl Chloride (1) (15).

Sulfuryl chloride (54 g., 0.4 mole) was added dropwise to a solution of 35.6 g. (0.2 mole) of ethane-1,2-bisthioacetate in 200 ml. of methylene chloride at ambient temperature. The reaction was slightly exothermic. After stirring the reaction mixture for 45 minutes at room temperature, nmr analysis indicated completion of the reaction. The mixture was cooled to 0° and the solvent and by-products were removed at 2 mm. pressure giving 32 g. (98%) of the pale yellow solid **1**, m.p. 30-35° (dec.); nmr (deuteriochloroform)  $\delta$  3.57 (s).

Similar chlorinolysis of ethane-1,2-dithiol resulted initially in a white precipitate which slowly disappeared during the addition of the sulfuryl chloride. After completion of the addition (*ca.* 15 minutes) the mixture was stirred for an additional 30 minutes. Removal of the volatiles afforded pure ethane-1,2-disulfenyl chloride in quantitative yield.

## Ethylene Adduct.

Ethylene was slowly introduced into a solution of 32.6 g. (0.2 mole) of the sulfenyl chloride **1** in 250 ml. of methylene chloride at -20°. The reaction was exothermic and its termination was marked by the disappearance of the yellow-orange color and subsidence of the exothermicity. Distillation of the solvent at 10° (2 mm.) resulted in a white solid. Recrystallization from ether-pentane afforded 33.1 g. (76%) of the pure (glc) adduct, m.p. 55-57°; nmr (deuteriochloroform)  $\delta$  2.79 (s, 4, SCH<sub>2</sub>CH<sub>2</sub>S), 2.9 (m, 4, ClCH<sub>2</sub>CH<sub>2</sub>S), 3.7 (m, 4, ClCH<sub>2</sub>).

*Anal.* Calcd. for C<sub>6</sub>H<sub>12</sub>Cl<sub>2</sub>S<sub>2</sub>: C, 32.87; H, 5.52; S, 29.26. Found: C, 33.16; H, 5.38; S, 29.65.

## Cycloadditions of Ethane-1,2-Disulfenyl Chloride (1) to Acetylenes.

## To Acetylene.

A solution of 65 g. (0.4 mole) of ethane-1,2-disulfenyl chloride in ~150 ml. of ethyl acetate and gaseous acetylene (4.8 liter/hour) were simultaneously introduced into 250 ml. of ethyl acetate at room temperature over a period of two hours. A cooled dropping funnel was used to minimize decomposition of the sulfenyl chloride. Removal of the solvent on the rotary evaporator after completion of the reaction afforded a waxy solid. Nmr analysis of this crude product indicated compounds **2** and **3** in a 7:3 ratio. This crude product mixture was redissolved in 1000 ml. of chloroform and small amounts of insoluble material were removed by filtration through a bed of filter aid. Concentration of the filtrate and addition of pentane afforded upon cooling, 45.6 g. (60.4%) of *trans*-2,3-dichloro-1,4-dithiane (**2**), m.p. 127-129°.

Its identity with an independently prepared authentic sample (**7**) was proven by nmr analysis and a mixed melting point.

The mother liquor was concentrated and the residual liquid distilled. This resulted in 14.5 g. (23.7%) of pure 2-chloro-1,4-dithiane (**3**), b.p. 82-85° (0.8 mm.); nmr (deuteriochloroform)  $\delta$  6.23 (s, 1), 3.28 (m, 4).

*Anal.* Calcd. for C<sub>4</sub>H<sub>5</sub>ClS<sub>2</sub>: C, 31.47; H, 3.30; S, 42.00. Found: C, 31.44; H, 3.43; S, 41.90.

## To Methylacetylene.

A solution of 32.5 g. (0.2 mole) of ethane-1,2-disulfenyl chloride in 150 ml. of methylene chloride and gaseous methylacetylene (4.8 liter/hour) were simultaneously introduced into 250 ml. of methylene chloride. Reaction conditions and workup as described above afforded ~35 g. of a tan liquid. Distillation yielded 27 g. (81%) of pure 2-chloro-3-methyl-1,4-dithiane (**4**), b.p. 83° (0.08 mm.); nmr (deuteriochloroform)  $\delta$  3.25 (s, 4) 2.00 (s, 3).

*Anal.* Calcd. for C<sub>5</sub>H<sub>7</sub>ClS<sub>2</sub>: C, 36.03; H, 4.23; S, 38.47. Found: C, 36.07; H, 4.38; S, 38.54.

## To 2-Butyne.

To a solution of 32.5 g. (0.2 mole) of ethane-1,2-disulfenyl chloride in 1700 ml. of ethyl acetate was added 12 g. (0.22 mole) of 2-butyne dissolved in 100 ml. ethyl acetate at ambient temperature over a period of three hours. The solution was then concentrated on a rotary evaporator and the residual semi-solid was dissolved in 800 ml. chloroform. Filtration through a bed of filter aid removed some insoluble material. Removal of the solvent afforded 57.4 g. of semi-solid, tan material. Nmr analysis of this crude product showed ~82% of the cyclic compound **6** and ~18% of unsaturated product **7**. Recrystallization twice from chloroform-pentane afforded 20 g. (47.4%) of the colorless, crystalline 2,3-dichloro-2,3-dimethyl-1,4-dithiane (**6**), m.p. 86-89° (dec.); nmr (deuteriochloroform)  $\delta$  3.18 (m, 4) 2.06 (s, 6).

*Anal.* Calcd. for C<sub>6</sub>H<sub>10</sub>Cl<sub>2</sub>S<sub>2</sub>: C, 33.18; H, 4.64; S, 29.53. Found: C, 33.53; H, 4.77; S, 29.44.

Distillation of the mother liquor yielded 6 g. (13.6%) of product **7**, b.p. 119-120° (0.3 mm.); nmr (deuteriochloroform)  $\delta$  2.77 (s, 4), 2.48 (m, 3, C=C(Cl)-CH<sub>3</sub>) 2.13 (m, 3, C=C(CH<sub>3</sub>)-).

*Anal.* Calcd. for C<sub>10</sub>H<sub>16</sub>Cl<sub>2</sub>S<sub>2</sub>: C, 44.27; H, 5.96; S, 23.64. Found: C, 44.65; H, 6.12; S, 23.96.

## Reactions with Amines.

Ethane-1,2-Bis-*N,N*-Dimethyl Sulfenamide (**8**).

A cold solution (-20°) of 16.3 g. (0.1 mole) of ethane-1,2-disulfenyl chloride in 60 ml. ether was slowly added to 20 g. of dimethylamine in 50 ml. ether at -20°. The reaction was exothermic. After completion of the addition the mixture was allowed to warm to room temperature, the amine hydrochloride

was filtered off, and the ether was removed on the rotary evaporator giving 16.2 g. (90%) of the pale yellow sulfenamide (**8**), b.p. 40-43° (0.01 mm.); nmr (deuteriochloroform)  $\delta$  2.59 (s, 12, NCH<sub>3</sub>), 2.89 (s, 4, CH<sub>2</sub>S).

*Anal.* Calcd. for C<sub>6</sub>H<sub>16</sub>N<sub>2</sub>S<sub>2</sub>: C, 39.96; H, 8.94; S, 35.56. Found: C, 40.07; H, 9.03; S, 36.03.

Ethane-1,2-Disulphenyl Chloride (**1**) with Methyl Amine.

Methyl amine (18.6, 0.6 mole) was slowly added over a period of 10 hours to a solution of 32.6 g. (0.2 mole) of bis-sulphenyl chloride (**1**) at -20°. The reaction mixture was kept under a nitrogen atmosphere, was stirred overnight at room temperature, and the precipitate was filtered off (43 g.). The ethereal solution was then concentrated giving 10 g. of a dark red oil. Fractional distillation afforded 1.15 g. (~5%) of the colorless heterocyclic compound **9**, b.p. 48-50° (3 mm.), m.p. 27-29°; nmr (deuteriochloroform)  $\delta$  2.87 (s, 3, NCH<sub>3</sub>) 3.58 (s, 4, CH<sub>2</sub>-S).

*Anal.* Calcd. for C<sub>3</sub>H<sub>7</sub>NS<sub>2</sub>: C, 29.72; H, 5.82; S, 52.90. Found: C, 30.08; H, 6.08; S, 52.92.

The nmr spectrum of the semi-solid black distillation residue (7.25 g.) only showed broad peaks at 0.9 and 1.35 ppm.

The initially obtained solid (43 g.) was shaken in 100 ml. of water for 48 hours. The undissolved material was then separated and washed with tetrahydrofuran followed by ether. Drying afforded 14.2 g. (77%) of a virtually insoluble polyethanedisulfide, m.p. 85-90°, presumably contaminated with some methylamine hydrochloride (see N and Cl under *Anal.* Found).

*Anal.* Calcd. for C<sub>2</sub>H<sub>4</sub>S<sub>2</sub>: C, 26.06; H, 4.37; S, 69.57. Found: C, 26.37; H, 4.68; S, 64.85; N, 2.20; Cl, 2.90.

The aqueous extract yielded on concentration 23.5 g. (88%) of methylamine hydrochloride which was identified by comparison of its IR spectrum with that of an authentic sample.

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