[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Ring Contraction by Rearrangement of a β-Chloro Sulfide

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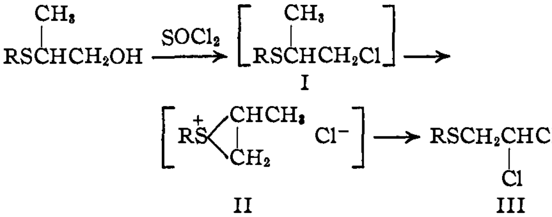
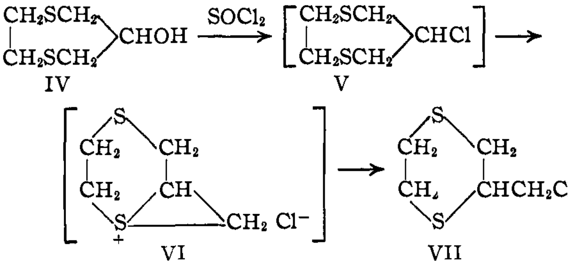
Treatment of certain β-hydroxyisopropyl sulfides with thionyl chloride or hydrochloric acid has been shown to yield not the expected 2-chloroisopropyl sulfides (I) but the corresponding 2-chloro-*n*-propyl sulfides (III).[2] It has been postulated that the rearrangement involves a cyclic sulfonium intermediate (II); the 2-chloroisopropyl sulfides, if formed at all, are likewise intermediates.



Certain 1,2-dialkylaminochloropropanes, nitrogen analogs of the sulfur compounds, have been observed to undergo a similar rearrangement involving the intermediate formation of ethyleneimonium compounds.[3]

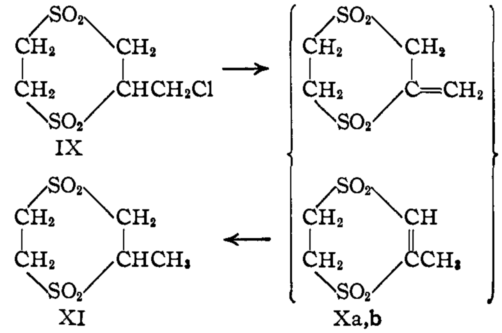
In the nitrogen series it has been possible also to effect ring enlargement by use of this type of rearrangement, 1-ethyl-2-chloromethylpyrrolidine having been found to isomerize to 1-ethyl-3-chloropiperidine.[4]

An attempt has been made to realize such a ring expansion in the sulfur series. It has been found, however, that in the one example so far examined ring contraction occurs instead of ring enlargement.



Treatment of 6-hydroxy-1,4-dithiacycloheptane (IV) with thionyl chloride in chloroform produced 2-chloromethyl-1,4-dithiane (VII). It is believed that the 6-chloro-1,4-dithiacycloheptane (V), if formed, rearranges to give the cyclic sulfonium ion intermediate (VI). The isomerization of the *n*-propyl structure to the isopropyl has also been observed in the reactions of 1-dialkylamino-2-chloropropanes.[3a,b,d]

The sulfones prepared from the crude and distilled chloro sulfide (VII) had identical melting points. A mixture of the two showed no depression in melting point indicating that rearrangement had occurred during the treatment with thionyl chloride and not during the distillation.



The dehydrochlorination of 2-chloromethyl-1,4-dithiane tetroxide (IX) was effected with triethylamine in anhydrous chloroform. Extraction of the product with boiling ethanol led to the isolation of two unsaturated compounds; m.p. 250–251° (Xa) and 233–234° (Xb), analytical values being in accord with those calculated values for the expected unsaturated compound. The infra-red absorption spectra were identical for the two compounds in major respects with the lower melting compound showing a few extra absorption bands. However, when hydrogenated with 10% palladium chloride on carbon, the two compounds gave the same product (XI), which was shown to be identical with an authentic sample of 2-methyl-1,4-dithiane tetroxide,[5] prepared from the previously known 2-methyl-1,4-dithiane.[6] It may well be that under the conditions of extraction with boiling ethanol a shift of the double bond occurred and that the structure of the two unsaturated sulfones may be represented by formulas Xa and Xb.

Hydrolysis of distilled 2-chloromethyl-1,4-dithiane (VII), afforded a 41% yield of the corresponding hydroxy sulfide (VIII), no other product being isolated. Even the crude chloro sulfide (VII) appeared to contain none of the isomer (V) since certain derivatives prepared from it were identical with those made from the purified material.

However, derivatives of both hydroxy compounds (IV and VIII) were obtained from the undistilled hydrolysis product of the crude chloro sulfide (VII).

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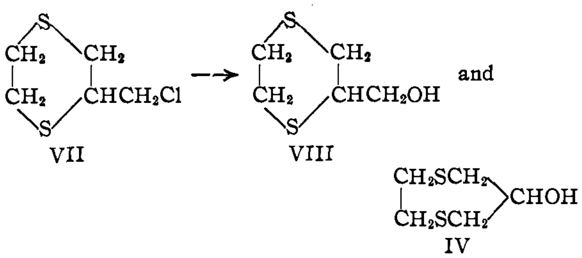
(2) Fuson, Price and Burness, *J. Org. Chem.*, **11**, 475 (1946).

(3) (a) Schultz, Robb and Sprague, THIS JOURNAL, **69**, 188, 2454 (1947); (b) Brode and Hill, *ibid.*, **69**, 724 (1947); (c) Kerwin, Ullyot, Fuson and Zirkle, *ibid.*, **69**, 2961 (1947); (d) Ross, *ibid.*, **69**, 2982 (1947); (e) Schultz and Sprague, *ibid.*, **70**, 48 (1948).

(4) Fuson and Zirkle, *ibid.*, **70**, 2760 (1948).

(5) Fuson and Speziale, *ibid.*, **70**, 823 (1948).

(6) Tucker and Reid, *ibid.*, **55**, 775 (1933).



Since only the six-membered carbinol (VIII) was isolated from the hydrolysis product of the purified chloro sulfide (VII) the origin of the seven-membered carbinol (IV) by hydrolysis of the crude sulfide (VII) is in doubt. It may have been produced by a rearrangement occurring during the hydrolysis or, conceivably, may have persisted unchanged during the treatment with thionyl chloride. If it represents a rearrangement product of the hydrolysis its absence from the hydrolysis product of the distilled chloro sulfide could possibly be due to mechanical loss. This carbinol (IV), if present, would be expected to be small in amount. Moreover, the hydrolysate in this case was subjected to distillation whereas that from the undistilled chloro sulfide was not.

Experimental

6-Hydroxy-1,4-dithiacycloheptane (IV).—The preparation and proof of structure of this compound have been given[5]; m. p. 64.5–65.5°. Its **benzoate** (m. p. 75–76°), **sulfone benzoate** (m. p. 229–230°) and **sulfone** (m. p. 233–234°) have also been reported.[5]

The **p-nitrobenzoate** was prepared by heating a mixture of 0.2 g. of IV, 2 ml. of dry pyridine and 0.4 g. of p-nitrobenzoyl chloride. After recrystallization from ethanol, the ester melted at 134–134.5°; yield 0.36 g. (90%).

Anal. Calcd. $C_{12}H_{13}NO_4S_2$: C, 48.14; H, 4.38. Found: C, 48.38; H, 4.59.

2-Chloromethyl-1,4-dithiane (VII).—The procedure of Fuson, Price and Burness[2] was followed. To a solution of 16.6 g. of purified thionyl chloride in 75 ml. of dry chloroform, 18.0 g. of 6-hydroxy-1,4-dithiacycloheptane in 150 ml. of dry chloroform was added dropwise at temperatures below 25°, stirring being continued for twenty-two hours at room temperature. Removal of the solvent *in vacuo* left a slightly turbid oil which was dissolved in ether. The solution was washed twice with water and dried over anhydrous magnesium sulfate. After evaporation of the ether, the residue was fractionated through a 10-cm. vacuum-jacketed Vigreux column; b. p. 81–86° (0.2 mm.). Refractionation yielded 15.0 g. (75%) of 2-chloromethyl-1,4-dithiane; b. p. 80–82° (0.3 mm.); n^{20}_{D} 1.5884; d^{20}_{20} 1.315; MR_{D} 43.18; calcd. for $C_5H_9ClS_2$: MR_{D} 43.89.

The material designated as crude or undistilled 2-chloromethyl-1,4-dithiane is the dried, unfractionated residue remaining after evaporation of the ether.

The **p-toluenesulfilimine** was prepared by the method of Mann and Pope.[7] To 2 g. of the crude chloro sulfide, 6.8 g. of Chloramine-T in 50 ml. of water was added. The mixture was shaken vigorously for ten minutes, heated on a steam-bath for an additional ten minutes and allowed to stand in the ice-box overnight. The white crystals were removed and dissolved in boiling methylcellosolve. After the solution had stood two days in the ice-box, the sulfilimine settled out; m. p. 153.5–154.5°.

Anal. Calcd. for $C_{19}H_{23}ClN_2O_4S_4$: C, 44.98; H, 4.57. Found: C, 44.56; H, 4.65.

2-Chloromethyl-1,4-dithiane Tetroxide (IX).—To a solution of 5.6 g. of undistilled chloro sulfide (VII) in 50 ml. of glacial acetic acid, 2.2 g. of hydrogen peroxide (30%) was added slowly. Then an additional 4.4 g. of hydrogen peroxide was added rapidly. The reaction mixture was stirred for one-half hour at room temperature and for eighteen hours at 60°. The sulfone was collected on a filter, washed well with cold water and dried for several days over potassium hydroxide; m. p. 245–249° (dec.); yield 6.6 g. (85%). It melted at 253–255° with decomposition after recrystallization from ethanol.

Anal. Calcd. for $C_5H_9ClO_4S_2$; C, 25.80; H, 3.89. Found: C, 26.11; H, 3.95.

When the distilled chloro sulfide was substituted for the crude chloro sulfide, a 91% yield of 2-chloromethyl-1,4-dithiane tetroxide was obtained; m. p. 255–256°. A mixture melting point with the above chloro sulfone showed no depression; m. p. 255–256° (dec.).

Dehydrochlorination of 2-Chloromethyl-1,4-dithiane Tetroxide.—To a suspension of 5.4 g. of the chloro sulfone (IX) in 250 ml. of anhydrous dioxane at 60°, 2.4 g. of anhydrous triethylamine was added with stirring. The temperature was maintained at 60° for five and one-half hours, during which time the appearance of the solid in the reaction vessel changed appreciably. The amine hydrochloride was removed by filtration and the dioxane solution reduced in volume under diminished pressure to about 25 ml. The crude sulfone was collected on a filter, washed several times with cold water and dried; it weighed 3.5 g. (77%). A portion was decolorized with Darco in hot dioxane, the solvent being removed *in vacuo*. Several recrystallizations of the unsaturated sulfone (Xa) from ethanol gave a product melting at 250–251° (dec.). An aqueous solution of permanganate was instantly decolorized by a dioxane solution of the sulfone.

Anal. Calcd. for $C_5H_8O_4S_2$: C, 30.60; H, 4.11. Found: C, 30.88; H, 4.28.

The crude unsaturated sulfone (3.62 g.) as prepared above was extracted with three 200-ml. portions of boiling ethanol. The first extract, when cooled, yielded 2.12 g. of crystals (Xb) which, after crystallization from ethanol, melted at 233–234° (dec.). The second and third extracts, when cooled, did not yield any solid material. Removal of the solvent left solids which melted at 244–246° and 244–249°, respectively. They were combined (Xa) and recrystallized from ethanol; m. p. 250–251° (dec.), (0.87 g.). A mixture of Xa and Xb melted at 241–242° (dec.). Analysis of the lower melting compound gave the following results.

Anal. Calcd. for $C_5H_8O_4S_2$: C, 30.60; H, 4.11. Found: C, 30.58; H, 4.36.

Infrared absorption curves of these unsaturated sulfones were identical in major respects, those of lower melting material (Xb) having a few bands not found in the other.

Hydrogenation of the Unsaturated Sulfones (Xa,b).—A solution of 0.4 g. of Xa in 75 ml. of anhydrous dioxane was added to 5 g. of 10% palladium chloride on carbon[8,9] in 100 ml. of anhydrous dioxane. The hydrogenation was completed in four hours at three atmospheres. The catalyst was removed by filtration and the solvent distilled *in vacuo*. The 2-methyl-1,4-dithiane tetroxide (XI) weighed 0.32 g. (79%) and melted at 303–304° (dec.) after recrystallization from ethanol. It did not decolorize a permanganate solution.

Anal. Calcd. for $C_5H_{10}O_4S_2$: C, 30.29; H, 5.08. Found: C, 30.43; H, 5.27.

Hydrogenation of 0.75 g. of Xb was accomplished exactly as in the preceding experiment. The saturated sulfone weighed 0.63 g. (83%) and melted at 300–301° (dec.). A mixture of these two products melted at 300–302° (dec.). Mixture melting points of either product with an authentic sample of 2-methyl-1,4-dithiane tetroxide[5] showed no depression; m. p. 303–304° (dec.).

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(7) Mann and Pope, *J. Chem. Soc.*, **121**, 1052 (1922).

(8) Mozingo, Harris, Wolf, Hoffhine, Easton and Folkers, THIS JOURNAL, **67**, 2092 (1945).

(9) Mozingo, *Org. Syn.*, **26**, 77 (1946).

Hydrolysis of 2-Chloromethyl-1,4-dithiane.—A mixture of 13.0 g. of distilled 2-chloromethyl-1,4-dithiane (VII) and 75 ml. of distilled water was stirred at room temperature for sixty hours. As the mixture became acid to congo red paper, it was neutralized by adding a few milliliters of 20% sodium carbonate solution. At the end of forty-eight hours, a negligible amount of chloro sulfide was left undissolved and at the end of sixty hours, the amount of insoluble liquid began to increase. Salt was added to the reaction mixture, and the carbinol (VIII) was extracted with 200 ml. of ether in small portions. The solution was dried overnight with anhydrous sodium sulfate. After removal of the solvent, fractionation of the residue through a 10-cm. vacuum-jacketed Vigreux column yielded 4.7 g. (41%) of product; b. p. 103–105° (0.4 mm.); $n^{20}D$ 1.5935; $n^{25}D$ 1.5910. The distillate partially crystallized in the condenser and completely solidified in the receiver, which had been immersed in an ice-bath.

The **p-nitrobenzoate**, prepared in the usual manner, was recrystallized from ethanol; m. p. 96–97°; yield 67%.

Anal. Calcd. for $C_{12}H_{13}NO_4S_2$: C, 48.14; H, 4.38; N, 4.68. Found: C, 47.96; H, 4.59; N, 4.68.

The **benzoate** of the undistilled 2-hydroxymethyl-1,4-dithiane, prepared in turn by the hydrolysis of undistilled 2-chloromethyl-1,4-dithiane, separated as an oil which resisted all attempts at crystallization. The oil was dissolved in ether and dried overnight over anhydrous magnesium sulfate. Evaporation of the solvent and distillation of the residue yielded the benzoate, which solidified in the condenser; b. p. 77° (0.5 mm.). Recrystallization of the ester from ethanol gave white crystals melting at 47.5–48.5°.

Anal. Calcd. for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 57.20; H, 5.61.

The *sulfone* prepared from the benzoate as previously described and recrystallized from an ethanol-water mixture, melted at 261–262° (dec.).

2-Hydroxymethyl-1,4-dithiane Tetroxide and 6-Hydroxy-1,4-dithiacycloheptane Tetroxide.—Two grams of the above crude 2-hydroxymethyl-1,4-dithiane was oxidized to the sulfone with 30% hydrogen peroxide in glacial acetic acid in the usual manner. After twenty-six and one-half hours at 60°, the solid sulfone was collected on a filter; m. p. 258° (dec.); yield 2.0 g. (70%). Repeated crystallizations of the product from water produced an amorphous-appearing compound (XII); m. p. 277–278°. This sulfone melts approximately forty degrees higher than the hydroxy sulfone prepared directly from 6-hydroxy-1,4-dithiacycloheptane (IV).

Anal. Calcd. for $C_5H_{10}O_5S_2$: C, 28.02; H, 4.70. Found: C, 28.14; H, 4.78.

Distillation of the acetic acid filtrate left another solid (XIII); m. p. 218°; yield 0.64 g. (22.5%). After repeated recrystallization from water this compound had a melting point of 223–224° (dec.). Its benzoate, prepared in the usual manner and recrystallized from ethanol, melted at 229–230°. A mixture melting point proved it to be identical with the sulfone benzoate made from 6-hydroxy-1,4-dithiacycloheptane.

In attempts to prepare the benzoate of XII, a compound was isolated, m. p. 265–266° (dec.), which may be the sulfone benzoate, but lack of material prevented identification.

The **acetate** was prepared by refluxing a solution of 0.5 g. of the hydroxy sulfone (XII) and 20 ml. of acetic anhydride for three and one-half hours. The reaction mixture was then poured on cracked ice and the resulting mixture heated on a steam-bath. Within two minutes, crystals appeared. After the addition of 150 ml. of water, heating was continued for one hour. The solution was filtered while hot and allowed to cool. The white crystals which formed were recrystallized once from acetone and three times from water; m. p. 256–257°; yield 0.41 g. (69.5%).

Anal. Calcd. for $C_7H_{12}O_6S_2$: C, 32.80; H, 4.71. Found: C, 32.82; H, 4.83.

Dehydration of 2-Hydroxymethyl-1,4-dithiane Tetroxide.—Five-tenths gram of XII was dissolved in 30 ml. of anhydrous pyridine with gentle warming. The clear solution was cooled to 45°, and 1 ml. of phosphorus oxychloride was added dropwise, the temperature being maintained at 50–55°. The reaction mixture was allowed to stand at room temperature for three hours and then stirred at 50–55° for one and one-half hours. The cooled mixture was poured on cracked ice and extracted with chloroform. The aqueous layer was again extracted with a chloroform–pyridine mixture (1:1). The extracts were combined and evaporated almost to dryness. The tetroxide (X), recrystallized five times from water, weighed 0.15 g. (33%); m. p. 247–248°. An aqueous solution of potassium permanganate was instantly decolorized by a dioxane solution of this compound.

Anal. Calcd. for $C_5H_8O_4S_2$: C, 30.60; H, 4.11. Found: C, 30.71; H, 4.34.

2-Methyl-1,4-dithiane Tetroxide (XI).—Hydrogenation of 0.08 g. of the above compound (X) was carried out as previously described with 10% palladium chloride on carbon. The reduction was completed after twelve hours at three atmospheres. After recrystallization from water, the saturated sulfone decomposed at 302–303°; yield 0.06 g. (74%). A mixture melting point with an authentic sample of 2-methyl-1,4-dithiane tetroxide[5] was not depressed; m. p. 302–303° (dec.).

Summary

Treatment of 6-hydroxy-1,4-dithiacycloheptane with thionyl chloride has been shown to bring about ring contraction with the formation of 2-chloromethyl-1,4-dithiane.

A mechanism involving a bicyclic sulfonium ion intermediate has been proposed to account for this transformation.

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