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Cyclic Sulfoxides. I. Dihydrothiophene 1-Oxides

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Although there have been extensive investigations on cyclic sulfones, especially the unsaturated, 5-membered ring compounds (3), cyclic sulfoxides have received considerably less attention. In this report, we wish to present a synthesis of the previously unknown dihydrothiophene 1-oxide isomers and, also, some preliminary results regarding their chemical reactivity (4).

The isomeric sulfoxides, 2,5- and 2,3-dihydrothiophene 1-oxide (I and II, respectively) were each prepared by the oxidation of the corresponding sulfide. The sulfide precursors, 2,5- and 2,3-dihydrothiophene (III and IV, respectively) were obtained by two routes. To obtain III, the sodium-liquid ammonia-methanol reduction of thiophene was used to produce a mixture of III and IV (5). It was difficult to completely separate III and IV by distillation, however, and a chemical technique was developed. This technique, which involved contacting a mixture of the two sulfides with 30% sulfuric acid, rapidly polymerized IV without appreciable loss (< 1%) of III. Based on the starting thiophene, this procedure yielded up to 20% of III. For IV, the method reported by Sosnovsky (6) was employed.

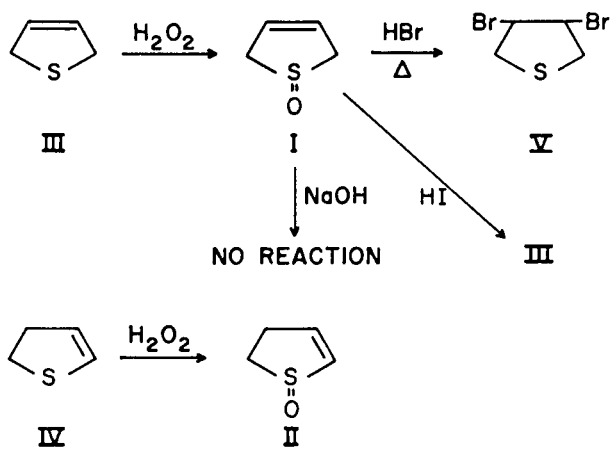
Careful oxidation of III and IV with hydrogen peroxide gave I and II as colorless oils whose structures were conveniently established by oxidation to the solid sulfones (7). A derivative of I, its *p*-tolyl sulfilimine, was useful for characterization. Infrared data are given in the Experimental section.

Hydrogen bromide in carbon tetrachloride reacted rapidly with I to form 3,4-dibromotetrahydrothiophene (V). Formation of V apparently occurs via the oxidation of hydrogen bromide by the sulfoxide group to produce bromine and III. The latter substances react to form 1,3,4-tribromotetrahydrothiophenonium bromide which, upon distillation, loses bromine to form V. A similar result was found when hydrobromic acid was substituted for hydrogen bromide. When I was treated with bromine in carbon tetrachloride, V was again isolated as the primary product. In acetic acid, however, bromine and I produced the above-mentioned, unstable, tetrabromo compound as an isolable solid.

With hydriodic acid, I was rapidly reduced to III with formation of iodine. This reaction represents a little-used, but efficient, method for the reduction of sulfoxides free of side reactions (8). Hydrochloric acid, on the other hand, gave only tars from which no organic product could be isolated.

Early work on the sulfone analog of I (2,5-dihydrothiophene 1,1-dioxide) established that a sulfone of this type is readily isomerized by base to its position isomer (9). A determination of the behavior of sulfoxide I under alkaline conditions was thus undertaken to evaluate the potential effect of such reaction media upon I. After 96 hours at room temperature, however, 0.5 *N* sodium hydroxide did not isomerize I to II.

The results discussed above are outlined in the following chart:



EXPERIMENTAL (10)

2,5-Dihydrothiophene (III).

The sodium-liquid ammonia methanol reduction of 15 moles of thiophene (in 5-mole portions) gave a mixture of unreacted thiophene, III, and IV (5). This mixture was distilled under nitrogen through a vacuum-jacketed, silvered column; 63 cm. x 2 cm. I.D., packed with glass helices and the fraction boiling at 100-117.8°/721 mm. collected. This mixture, which was largely III and IV, was diluted with twice its volume of isopentane and stirred at room temperature for 4 hours with 30% sulfuric acid. This treatment resulted in the selective removal of IV from the mixture. The isopentane layer was washed with water, dried, and distilled under nitrogen to give III, b.p. 116-119°/711 mm., n_D^{20} 1.5300, 140 g. (13% yield). The mercurichloride derivative from III showed m.p. 129.5-130.5°, lit. (5), m.p. 130-131°.

2,5-Dihydrothiophene 1-Oxide (I).

To 200 ml. of redistilled acetone was added 58.9 g. (0.690 mole) of III and the solution, cooled to 4° in an ice bath with rapid stirring, was treated dropwise, with 96.3 g. of 30% hydrogen peroxide (28.9 g., 0.850 mole hydrogen peroxide) during 4 hours while maintaining the reaction mixture at 4-6°. The resulting solution was allowed to warm to room temperature and to stand 68 hours. The volatile material

was flash distilled and the residue was treated with 100 ml. of chloroform. The water layer was separated and extracted with three 50 ml. portions of chloroform. The united organic layers were dried over anhydrous magnesium sulfate. After flash distillation of the solvent, the residue was vacuum distilled to yield 33.8 g. (48%) of I, b.p. 82-84° (1.1-1.3 mm.), n_D^{20} 1.5361, d_{20}^{20} 1.2408; ν (10% C_6H_6), 2941, 1634, 1404, 1340, 1242, 1114, 1044, 962, 891, 638 cm^{-1}.

Anal. Calcd. for C_4H_6OS: C, 47.03; H, 5.92; S, 31.39. Found: C, 46.98; H, 6.05; S, 31.16.

In 25 ml. of redistilled acetone, 2.2 g. (0.022 mole) of I was treated with 3.4 g. of 30% hydrogen peroxide and the mixture was heated to reflux for 1 hour. Volatile matter was removed on the steam bath at *ca.* 25 mm. and the residue was dissolved in hot benzene. Petroleum ether (b.p. 30-60°) was added until the solution became cloudy. The mixture was chilled to yield 1.8 g. (73%) of crude 2,5-dihydrothiophene 1,1-dioxide. Recrystallization from methyl alcohol gave white plates, m.p. 63-64°. A mixture melting point of this material with an authentic specimen (7) showed no depression.

Sulfilimine from I.

A solution of 2.04 g. (0.020 mole) of I in 15 ml. of acetic anhydride was treated with 3.42 g. (0.020 mole) of *p*-toluenesulfonamide and heated on the steam bath for 45 minutes. After standing at room temperature for 2 hours, the solution was made barely basic with 2 *N* sodium hydroxide. A pasty solid was collected and recrystallized from acetone-benzene, 1.9 g., 37% crude yield. Recrystallization from benzene gave colorless platelets, m.p. 169.0-170.5°.

Anal. Calcd. for $C_{11}H_{13}NO_2S_2$: C, 51.74; H, 5.13; N, 5.49. Found: C, 51.50; H, 5.02; N, 5.36.

2,3-Dihydrothiophene 1-Oxide (II).

A solution of 20.0 g. (0.23 mole) of IV, prepared according to the method of Sosnovsky (6), in 100 ml. of redistilled acetone was cooled to 4° in an ice bath. While maintaining the temperature at 4-8°, 34.0 g. of 30% hydrogen peroxide (10.2 g., 0.30 mole hydrogen peroxide) was slowly added during 1.5 hour. The resulting solution was allowed to warm naturally and to stand at room temperature for 50 hours. The acetone was then removed by flash distillation and the residue was treated with 50 ml. of chloroform. The aqueous layer was separated and extracted with three 50 ml. portions of chloroform. The united chloroform layers were dried over anhydrous magnesium sulfate. The solvent was flash distilled and the residue was vacuum distilled to yield 11.2 g. (48%) of II, b.p. 78-80° (1.6 mm.), n_D^{20} 1.5321, d_{20}^{20} 1.2200; ν (10% C_6H_6), 2882, 1616, 1471, 1393, 1330, 1318, 1235, 1127, 1041, 885, 851, 769 cm^{-1}.

Anal. Calcd. for C_4H_6OS: C, 47.03; H, 5.92; S, 31.39. Found: C, 47.04; H, 6.08; S, 31.50.

The sulfone was prepared from II using the procedure previously described. Recrystallization of the crude product from benzene-petroleum ether gave 71% of 2,3-dihydrothiophene 1,1-dioxide m.p. 48-49°. A mixture melting point with an authentic sample (7) showed no depression.

3,4-Dibromotetrahydrothiophene (V).

This compound was prepared by the thermal decomposition of 1,3,4-tribromotetrahydrothiophenonium bromide which appeared to be the initial product formed upon the reaction of I with hydrogen bromide, hydrobromic acid, or bromine under the various conditions given below.

(a) Hydrogen Bromide in Carbon Tetrachloride.

A 250 ml. pear-shaped flask was equipped with a nitrogen inlet, a condenser, a magnetic stirrer, and a cylindrical fritted glass dispersion tube which extended to within 2 cm. of the bottom of the flask. A solution of 4.2 g. (0.040 mole) of I in 15 ml. of carbon tetrachloride was placed in the flask and the system was flushed with nitrogen. A vigorous stream of anhydrous hydrogen bromide was introduced through the dispersion tube for 0.5 hour. The exothermic reaction was accompanied by the formation of an insoluble red oil. The mixture was cooled and the solvent was removed under vacuum with evolution of bromine. The residue was then vacuum distilled to yield 57% of crude V, b.p. 78-81.5° (0.70-0.88 mm.). This material was redistilled for analysis, b.p. 85.0-85.7° (0.57 mm.): ν (10% in C_6H_6), 2941, 1429, 1290, 1227, 1163, 1111, 962, 885, 781 cm^{-1}.

Anal. Calcd. for $C_4H_6Br_2S$: C, 19.53; H, 2.46; S, 13.04. Found: C, 19.77; H, 2.36; S, 13.16.

To 0.70 g. (0.0028 mole) of V in 1.5 ml. of glacial acetic acid was added 1.0 g. of 30% hydrogen peroxide. The mixture was stirred at room temperature for 17.5 hours. It was then heated to reflux for 2.5 hours, cooled, and the volatile matter was removed under vacuum on the steam bath. The solid which formed was collected and recrystallized from 2.5 ml. of 95% ethyl alcohol as fine, white needles of 3,4-dibromotetrahydrothiophene 1,1-dioxide, m.p. 143-145°, 0.80 g. (99%), (lit. (11), m.p. 141-142°). A mixture melting point of this material with an authentic specimen showed no depression, and the infrared spectra of the two samples were identical.

(b) Hydrobromic Acid.

At room temperature, 2.04 g. (0.020 mole) of I was treated with 6.73 g. of 48% hydrobromic acid (3.24 g., 0.040 mole hydrogen bromide). The mixture was stirred at room temperature for 48 hours and then extracted with two 2.5 ml. portions of chloroform. The combined chloroform layers were dried over anhydrous magnesium sulfate and the chloroform was evaporated on the steam bath. The residue was vacuum distilled to yield 1.4 g. (28%) of V, b.p. 84-86° (0.45 mm.).

(c) Bromine in Carbon Tetrachloride.

A solution of 5.1 g. (0.050 mole) of I in 15 ml. of carbon tetrachloride was placed in a 100 ml. three-necked flask equipped with a magnetic stirrer, a condenser, and a pressure equilibrated dropping funnel. During 45 minutes a solution of 8.0 g. (0.050 mole) of bromine in 10 ml. of carbon tetrachloride was added to the contents of the flask, and an insoluble red oil settled to the bottom. After stirring 6 hours at room temperature, the red oil was allowed to settle and the solvent was decanted. The oil was distilled to yield 4.2 g. (34%) of V, b.p. 86-89° (0.58-0.65 mm.).

(d) Bromine in Acetic Acid.

To a solution of 2.04 g. (0.20 mole) of I in 2 ml. of glacial acetic acid was slowly added 8 g. (0.050 mole) of bromine in 5 ml. of glacial acetic acid. The exothermic reaction was accompanied by the formation of an orange solid. After standing for 18 hours at room temperature, the solid was collected as 4.3 g. (50%) of crude, 1,3,4-tribromotetrahydrothiophenonium bromide which evolved bromine upon exposure to the atmosphere. This material was carefully recrystallized from warm carbon tetrachloride as irregular plates, m.p. 100-102° (dec.), lit. (7), m.p. 101-102° (dec.).

Reduction of 2,5-Dihydrothiophene 1-Oxide by Hydriodic Acid.

A solution of 2.04 g. (0.020 mole) of I in 3 ml. of carbon tetrachloride was treated with 11.4 g. of 48% hydriodic acid (5.12 g., 0.040 mole hydrogen iodide) in a 50 ml. flask equipped with a magnetic stirrer and a reflux condenser. Iodine formed immediately and the mixture was stirred 0.5 hours and allowed to cool to room temperature. The mixture was then extracted with a single 10 ml. portion of ethyl ether and the extract was analyzed by gas chromatography. The chromatogram showed only one component, 2,5-dihydrothiophene, in addition to the solvents.

Attempted Base-Catalyzed Isomerization of 2,5-Dihydrothiophene 1-Oxide.

In 50 ml. of 0.5 *N* potassium hydroxide, 1.02 g. (0.010 mole) of I was stirred for 96 hours at room temperature. The solution was then extracted with three 25 ml. portions of chloroform and the combined chloroform layers were dried over anhydrous magnesium sulfate. The chloroform was flash distilled and the residue was dissolved in 10 ml. of water. With cooling, 5.33 g. of 48% hydriodic acid was added dropwise. The resulting solution was stirred 1 hour and then extracted with three 5 ml. portions of ethyl ether. The combined extracts were dried over anhydrous magnesium sulfate and analyzed by gas chromatography. The extract contained III, but no IV.

REFERENCES

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(2a) Taken from a portion of the Ph.D. dissertation of D. E. Boswell, Virginia Polytechnic Institute, November 1963; Allied Chemical Corporation Fellow, 1962-1963; present address: Mobil Oil Corporation, P. O. Box 1025, Princeton, New Jersey 08540. (b) Author to whom inquiries should be addressed.

(3) See, for example, R. C. Krug and T. F. Yen, *J. Org. Chem.*, 21, 1082, 1441 (1956); R. C. Krug and J. A. Rigney, *ibid.*, 23, 1697 (1958); R. L. Krug and D. E. Boswell, *ibid.*, 27, 95 (1962).

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