[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Preparation and Properties of 3-Benzothiepin 3-Dioxide

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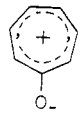
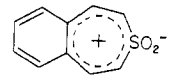
RECEIVED APRIL 15, 1955

3-Benzothiepin 3-dioxide is prepared from S-(β-phenylethyl)-mercaptoacetyl chloride. The non-aromatic character of 3-benzothiepin 3-dioxide is established by its susceptibility toward reactions of addition, its thermal instability and the difficulty of forming it by a dehydrogenation process.

Aromatic properties are generally associated with conjugated unsaturated systems having six π-electrons.[1a] Classical examples of such systems are benzene and thiophene. Of more recent vintage are such related systems as tropone for which the following molecular model (I)[2] has been suggested in view of its aromatic-type properties



I

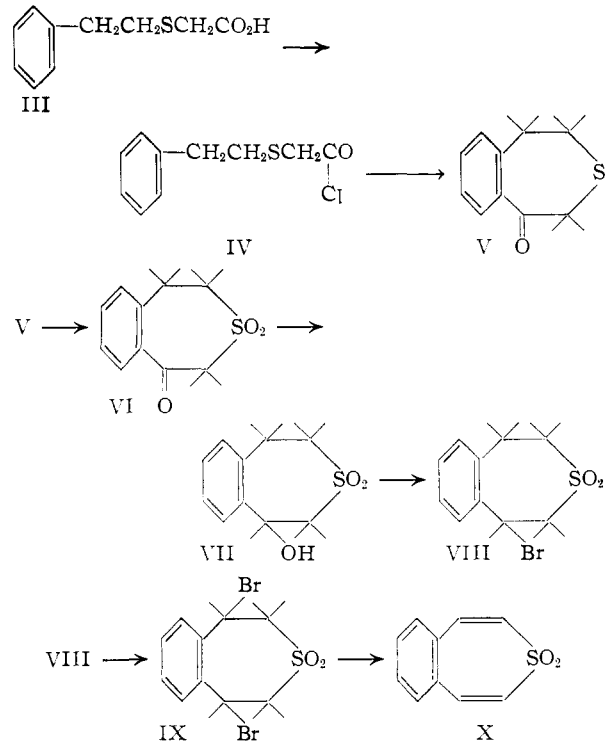


II

Since the sulfone grouping, like the carbonyl group, is capable of conjugation by electron attraction,[3] a similar model would be expected of the compound 3-benzothiepin 3-dioxide (II).

A second requirement for such systems to be appreciably resonance stabilized is a planar configuration. This apparently is achieved in the tropone system with some help from the trigonal configuration of a carbonyl group with a resultant increase in the carbon bond angles, which in turn would tend to decrease the strain inherent in a seven-membered planar carbocycle.[4] Whether an analogous coplanar state could be achieved nearly as readily by the sulfone analog is problematical.

Several approaches to the synthesis of 3-benzothiepin 3-dioxide (X) were considered. One of these paralleled the series of reactions used to prepare benzotropone[5] and benzotropolone.[6] Attempts to condense bis-(carbethoxymethyl) sulfone with *o*-phthalaldehyde in the presence of diethylamine, sodium hydroxide or sodium ethoxide were unsuccessful. Likewise unsuccessful were attempts to prepare 3-benzothiepin 3-dioxide (X) or its derivatives by condensing (1) *o*-phthalaldehyde with bis-(carbethoxymethyl) sulfide followed by oxidation and decarboxylation, and (2) *o*-phthalaldehyde and diethyl phthalate with dibenzyl sulfone, diphenacyl sulfone and dimethyl sulfone. Furthermore, 3-benzothiepin could not be prepared by treating the sodium salt of *o*-bis-(carboxymethyl)-benzene with phosphorus pentasulfide, a method used to prepare thiophenes from sodium succinates.[7] The synthesis of 3-benzothiepin 3-dioxide (X) was finally achieved by the following series of reactions



1-Oxo-1,2,4,5-tetrahydro-3-benzothiepin (V)[8] had been prepared in 17% yield by cyclizing S-(β-phenylethyl)-mercaptoacetyl chloride (IV) with aluminum chloride. Attempts to prepare the keto sulfide V and the corresponding sulfone VI by cyclizing S-(β-phenylethyl)-mercaptoacetic acid and S-(6-phenylethyl)-sulfonylacetic acid with polyphosphoric acid[9] gave tars and recovered starting material, respectively. In addition stannic chloride failed to cyclize S-(β-phenylethyl)-mercaptoacetyl chloride. However, the yield obtained in the condensation of IV to V was finally increased to 80% by utilizing tetrachloroethane as a solvent in a high dilution procedure. 1-Oxo-1,2,4,5-tetrahydro-3-benzothiepin (V) was oxidized to 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VI) with 30% hydrogen peroxide in glacial acetic acid. The Wolff–Kishner reduction of 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VI) yielded an acidic material instead of the expected 1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (XI). The failure of the Wolff–Kishner reduction is no doubt due to an accompanying β-elimination, similar to that observed by Leonard, *et al.*,[10] for such reactions.

(1) Purdue Research Foundation Fellow, 1953-1954.

(1a) E. Hückel, *Z. Elektrochem.*, **43**, 752 (1937).

(2) W. von E. Doering and L. H. Knox, THIS JOURNAL, **74**, 5683 (1952).

(3) F. G. Bordwell and H. M. Andersen, *ibid.*, **75**, 6019 (1953).

(4) S. B. Maerov, Ph.D. Dissertation, University of Washington, 1954.

(5) J. Thiele and J. Schneider, *Ann.*, **369**, 288 (1904).

(6) D. S. Tarbell and J. C. Bill, THIS JOURNAL, **74**, 1237 (1952).

(7) J. Volhard and H. Erdmann, *Ber.*, **18**, 454 (1885).

(8) J. von Braun and K. Weissbach, *ibid.*, **62**, 2416 (1929).

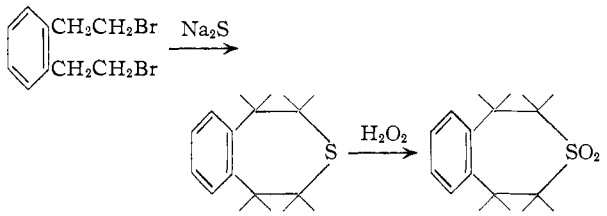
(9) H. R. Snyder and F. X. Werber, THIS JOURNAL, **72**, 2965 (1950).

(10) N. J. Leonard and R. C. Sentz, *ibid.*, **74**, 1705 (1952).

1-Oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VI) was hydrogenated over Raney nickel to 1-hydroxy-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VII) which with phosphorus tribromide gave 1-bromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VIII). Compound VIII reacted with free bromine to give a poor yield of impure dibromosulfone IX. Attempts to improve the yield of 1,5-dibromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (IX) by varying reaction time, light source, solvent, reaction temperature and brominating agent were unsuccessful.

In the bromination experiments with free bromine the major part of the reaction mixture consisted of a brominated red oil which contained no sulfur and analyzed closely for a tribromodiethylbenzene; furthermore, sulfur dioxide was present in the gases evolved during bromination. Presumably a major portion of the 1-bromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (VIII) underwent brominolysis at the sulfone linkage to give sulfur dioxide and α,β,β-tribromo-*o*-diethylbenzene.

Dehydrohalogenation of 1,5-dibromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (IX) with triethylamine yielded 90% of the theoretical amount of triethylamine hydrobromide. The structure of the resulting 3-benzothiepin 3-dioxide (X) was established by reducing it to 1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (XII) which was identical with the material prepared by



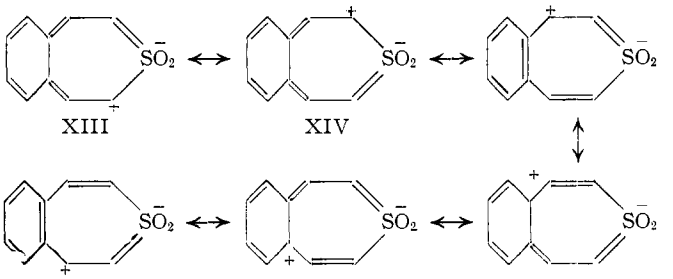
The isolation of naphthalene in good yield from the pyrolysis of 3-benzothiepin 3-dioxide (X) further substantiated its structure. Likewise, Scott[11] found that 3-benzothiepin-2,4-dicarboxylic acid decomposed to 2,3-naphthalenedicarboxylic acid.

In contrast to the resistance of tropolone toward hydrogenation under similar conditions, 3-benzothiepin 3-dioxide was readily reduced at atmospheric pressure with palladium and hydrogen. Cook, *et al.*,[12] found that tropolone could not be reduced with a palladium catalyst. This would seem to indicate that 3-benzothiepin 3-dioxide (X) does not possess as much aromatic character as tropolone. However, this evidence is not conclusive since Cook, *et al.*, did not indicate the type of palladium catalyst used. More conclusive evidence was obtained from a study on the ease of reduction of ω-styryl methyl sulfone, 1,2-dihydro-3-benzothiepin 3-dioxide and 3-benzothiepin 3-dioxide. These compounds absorbed hydrogen under the catalytic influence of palladium with the same ease, thus indicating that 3-benzothiepin 3-dioxide (X) possesses little, if any, more resonance energy than does ω-styryl methyl sulfone or 1,2-dihydro-3-benzothiepin 3-dioxide. Furthermore, 3-benzothiepin 3-dioxide (X) decolorized an acetone solution of potassium permanganate and a solution of bromine in chloroform in the presence of light. Also, selenium dioxide, which has been used to dehydrogenate certain compounds[13] to resonance-stabilized systems, failed to react with 1,2-dihydro-3-benzothiepin-3-dioxide even in boiling nitrobenzene.

3-Benzothiepin 3-dioxide (X) was nitrated with fuming nitric acid presumably on the benzene ring. The product from this reaction took up 5 moles of hydrogen per molecule of nitro compound. The reduced compound was diazotized and coupled with β-naphthol to give an orange dye in 90% yield.

The ultraviolet spectrum of 3-benzothiepin 3-dioxide was determined in an attempt to learn more about the possible aromatic character of this compound. However, the results were inconclusive and no interpretation of the spectrum is included in this paper. The compound exhibited maxima at 232 mμ (log ϵ 4.5) and 268 mμ (log ϵ 3.9). Also inconclusive was the infrared spectrum of 3-benzothiepin 3-dioxide which was taken in nujol since the compound was insoluble in such solvents as carbon tetrachloride and carbon disulfide. This compound as well as 1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide showed strong absorption peaks at 7.80 and 8.95 μ indicating the presence of a sulfone grouping. Weaker peaks were also observed at 8.65, 10.97, 12.3 and 12.8 μ.

From the experimental evidence it appears that 3-benzothiepin 3-dioxide has little aromatic character. A Fisher-Hirschfelder model of this structure shows the heterocyclic ring to be distinctly puckered. Furthermore, it is highly unlikely that forms XIII and XIV would contribute appreciably, since these forms would involve the high energy orthoquinoid system.[6] Therefore, this factor should also restrict the degree of resonance stabilization.



Experimental

1-Oxo-1,2,4,5-tetrahydro-3-benzothiepin (V).—To a stirred mixture of 158 g. (1.18 moles) of aluminum chloride and 200 ml. of tetrachloroethane cooled in an ice-bath was added dropwise to a solution of 120 g. (0.567 mole) of S-(β-phenylethyl)-mercaptoacetyl chloride in 160 ml. of tetrachloroethane. After stirring the reaction mixture for an additional 8 hours it was allowed to stand 12 hours at room temperature and then poured on ice. Hydrolysis was completed by warming to 60°. The resulting material was filtered through glass wool and the organic layer was distilled to give 81 g. (80% yield) of impure 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin, which melted at 51–53° after recrystallization from ethanol; its oxime melted at 150.5–152° (lit.[8] 151–152°).

(11) G. P. Scott, THIS JOURNAL, **75**, 6332 (1953).

(12) J. Cook, A. Gibb, R. Raphael and A. Somerville, *J. Chem. Soc.*, 503 (1951).

(13) N. Rabjohn, *Org. Reactions*, **5**, 331 (1949).

1-Oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-Dioxide (VI). Hydrogen peroxide (30%, 16 ml.) was slowly added to 10 g. (0.056 mole) of 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin in 20 ml. of glacial acetic acid cooled in an ice-bath. The solution was allowed to stand 24 hours at room temperature. After scratching the side of the container with a glass rod, 8.3 g. (70% of theory) of 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide crystallized, m.p. 133–134.5° after recrystallization from ethanol.

Anal. Calcd. for $C_{10}H_{10}SO_3$: C, 57.12; H, 4.71. Found: C, 57.17; H, 4.51.

1-Hydroxy-1,2,4,5-tetrahydro-3-benzothiepin 3-Dioxide (VII).—A mixture of 6 g. (0.0286 mole) of 1-oxo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide, 50 ml. of purified dioxane and 2 g. of Raney nickel was shaken under hydrogen at 40 p.s.i. until the theoretical amount of hydrogen was taken up. The Raney nickel was filtered and the dioxane evaporated to yield 6 g. (99% yield) of 1-hydroxy-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide, m.p. 185.5–187°.

Anal. Calcd. for $C_{10}H_{12}SO_3$: C, 56.57; H, 5.70. Found: C, 56.24; H, 5.66.

1-Bromo-1,2,4,5-tetrahydro-3-benzothiepin 3-Dioxide (VIII).—A mixture of 8.13 g. (0.03 mole) of phosphorus tribromide and 5 g. (0.0236 mole) of 1-hydroxy-1,2,4,5-tetrahydro-3-benzothiepin-3-dioxide was allowed to stand 14 hours at room temperature. The solution was heated on the steam-bath for 1 hour and then poured into a mixture of ice and water. The solid was removed by filtration and recrystallized from methanol to give 5.2 g. (80% yield) of 3-bromo-1,2,4,5-tetrahydro-3-benzothiepin-3-dioxide, m.p. 175–177°.

Anal. Calcd. for $C_{10}H_{11}SO_2Br$; C, 43.62; H, 4.03. Found: C, 43.80; H, 4.20.

1,5-Dibromo-1,2,4,5-tetrahydro-3-benzothiepin 3-Dioxide (IX).—To a refluxing solution of 100 ml. of carbon tetrachloride and 3 g. (0.0109 mole) of 1-bromo-1,2,4,5-tetrahydro-3-benzothiepin-3-dioxide illuminated with a No. 2 photoflood bulb was slowly added (over a 1.5-hour period) 4.3 g. (0.0269 mole) of bromine dissolved in 15 ml. of carbon tetrachloride. The carbon tetrachloride was evaporated with the aid of an air jet and the remaining material was extracted with ethyl ether. Evaporation of the ethyl ether yielded 3.2 g. of red oil. The solid remaining after the ether extraction was boiled with 100 ml. of methanol. The impure 1,5-dibromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide (0.7 g., 18% yield) which did not dissolve was filtered and melted at 188–194°. Evaporation of the methanol extract yielded 0.9 g. of solid melting at 148–155°.

3-Benzothiepin 3-Dioxide (X).—Triethylamine (1.0 g.) was added to 1.0 g. (0.0028 mole) of impure 1,5-dibromo-1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide dissolved in 100 ml. of boiling benzene. After heating the solution for 10 minutes, the triethylamine hydrobromide was filtered and the benzene was evaporated. The residue was washed with water, dried and recrystallized twice from methanol and once from petroleum ether to yield a solid melting at 161.5–163.5°, 0.33 g., 61% yield.

Anal. Calcd. for $C_{10}H_8SO_2$: C, 62.48; H, 4.19; mol. wt., 192. Found: C, 62.80; H, 4.16; mol. wt., 186.

The Reduction of 3-Benzothiepin 3-Dioxide.—A solution of 100 ml. of methanol, 1 g. (0.0052 mole) of 3-benzothiepin 3-dioxide and a catalytic amount of Raney nickel was shaken under hydrogen at 50 p.s.i. until the theoretical amount of hydrogen was taken up. The Raney nickel was filtered and the methanol evaporated to yield 0.8 g. (78%) of 1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide. This material melted at 154–156° after recrystallization from methanol and petroleum ether.

1,2,4,5-Tetrahydro-3-benzothiepin 3-Dioxide (XII).—To 100 ml. of ethanol was slowly added a mixture of 5.84 g. (0.02 mole) of *o*-bis-(β-bromoethyl)-benzene, 4.8 g. (0.0201 mole) of sodium sulfide nonahydrate and 300 ml. of ethanol. The addition was made over an 8-hour period and the solution was allowed to reflux for an additional 84 hours. The ethanol was removed by distillation and the remaining material was extracted with ethyl ether. Evaporation of the ether yielded 2 g. of a viscous liquid. To a solution of this liquid in 10 ml. of glacial acetic acid, 4.5 ml. of 30% hydrogen peroxide was added slowly. The reaction mixture was allowed to stand 24 hours at room temperature and was then poured on ice and water. The solid (2 g., 51% yield) was filtered and dried, m.p. 154–156° after recrystallization from methanol and petroleum ether (90–100°); it produced no melting point depression on admixture with the 1,2,4,5-tetrahydro-3-benzothiepin 3-dioxide prepared by the reduction of 3-benzothiepin 3-dioxide.

Nitro-3-benzothiepin 3-Dioxide.—A solution of 10 ml. of fuming nitric acid and 1.1 g. (0.00573 mole) of 3-benzothiepin 3-dioxide was allowed to react for 2 hours at 0° and 3 more hours at room temperature. The solution was poured into 150 ml. of a mixture of ice and water and the precipitate (1.3 g., 95%) was filtered, washed with water and recrystallized twice from methanol to yield a light yellow crystalline material melting at 173–176°.

Anal. Calcd. for $C_{10}H_7SO_4N$: C, 50.61; H, 2.98. Found: C, 50.73; H, 3.14.

LAFAYETTE, IND.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Heterocyclic Vinyl Ethers. XI. Electrophilic Substitution and Rearrangements of the 1,4-Dithiadiene Ring System[1]

BY WILLIAM E. PARHAM, ISADORE NICHOLSON[2] AND VINCENT J. TRAYNELIS

RECEIVED AUGUST 25, 1955

A study of the reaction of 2,5-diphenyl-1,4-dithiadiene with electrophilic reagents has shown that both mono- and disubstituted products can be obtained in high yield and that substitution occurs exclusively in the sulfur-containing ring. Reactions are discussed which involve the conversion of derivatives of dithiadiene into the corresponding derivatives of thiophene.

Reactions were described in previous communications[3,4] which constitute a new synthesis of thiophenes from[5] the readily available diaryl-1,4-dithiadienes. This paper describes work related to: (a) the orientation of electrophilic substitution of 2,5-diphenyl-1,4-dithiadiene (I), and (b) the structures of thiophenes derived from substituted dithiadienes.

The reaction of equivalent quantities of bromine and I, in acetic acid, afforded a 71% yield of a single monobromo derivative. This product was shown to be 2,5-diphenyl-3-bromo-1,4-dithiadiene (II) by its oxidation with potassium permanganate. A 64% yield of the theoretical amount of benzoic acid was obtained, and there was no evidence for the presence of bromobenzoic acid.

The conversion of II into derivatives of thiophene

(1) This work was supported by the Office of Ordnance Research, Contract No. D.A.-11-022-ORD-571. Work related to the substitution reactions of 2,5-diphenyl-1,4-dithiadiene was presented before the 126th Meeting of the American Chemical Society, New York, 1954.

(2) Du Pont Postdoctoral Instructorship, 1954–1955.

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(4) W. E. Parham and V. J. Traynelis, *ibid.*, **76**, 4960 (1954).

(5) R. H. Baker and C. Barkenbus, *ibid.*, **58**, 262 (1936).