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[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

d-Orbital Resonance. I. The Acidity of Bridgehead α-Hydrogen in a Bicyclic Trisulfone[1]

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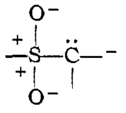
In the hope of gaining further information on the nature of the acidifying effect of the sulfone group on adjacent carbon–hydrogen bonds, the bicyclic trisulfones, 4-methyl-(I)- and 1,4-dimethyl-(II)-2,6,7-trithiabicyclo[2.2.2]-octane-2,2,6,6,7,7-hexaoxide, have been synthesized. The neutral character of II leaves no doubt that the acidic hydrogen (pK_a 3.3) of I is the bridgehead hydrogen atom. Although no theoretically unique conclusion can be drawn from the fact that I is a weaker acid than the acyclic trisulfone, tris-ethylsulfonylmethane, the involvement of d-orbital resonance is indicated.

It has been recognized that the interaction of a sulfone group with an adjacent function is responsible for the occurrence of a large number of reactions. Two explanations of the nature of the interaction have been proposed. The one involves solely electrostatic interaction of two positive charges on sulfur with the adjacent function; the other superimposes resonance interaction of a d-orbital of sulfur with an adjacent orbital and involves expansion of the octet of sulfur. This research attempts to uncover a geometrical factor in the interaction of the sulfone group and an adjacent carbanion and thereby attempts to distinguish between the alternate hypotheses.

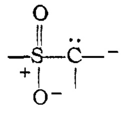
In addition to the examples of sulfone interaction referred to by Connor,[3] there may be cited several examples of activations of α-hydrogen,[4] an example of increased acidity of enols[5] and increased stabilization of a radical,[6] examples of the influence of a sulfone substituent on the reactivity of various aromatic compounds,[7] illustrations of the effect of the sulfone group on the ultraviolet spectra of aromatic compounds[7f,8] and a demonstration of hydrogen bonding in sulfones.[9,10]

Of the two current theories, the inductive or electrostatic is based on the non-expansion of the sulfur valence octet, whereas the resonance is based on the possibility of using d-orbitals with ten or more electrons about sulfur. In explaining the stabilizing effect of a sulfone on an adjacent carbanion, the first considers a single electronic structure for the sulfone grouping (a) wherein sulfur bears two positive charges. Stabilization is ascribed to coulombic attraction of the negative carbanion by the



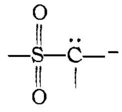
$-\overset{\overset{O^-}{|}}{\underset{\underset{O^-}{|}}{S^{+}_{+}}}-\ddot{C}^{-}$

a



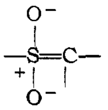
$-\overset{\overset{O}{\|}}{\underset{\underset{O^-}{|}}{S_{+}}}-\ddot{C}^{-}$

b



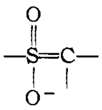
$-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-\ddot{C}^{-}$

c



$-\overset{\overset{O^-}{|}}{\underset{\underset{O^-}{|}}{S_{+}}}=C-$

d



$-\overset{\overset{O}{\|}}{\underset{\underset{O^-}{|}}{S}}=C-$

e

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[2] Sterling Chemistry Laboratory, Yale University, New Haven, Connecticut.

[3] R. Connor, "Organic Chemistry," 2nd ed., Vol. I, edited by H. Gilman, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 879–885.

[4] (a) J. Hochberg and K. F. Bonhoeffer, *Z. physik. Chem.*, **184**, 419 (1939); (b) E. Fromm, *Ann.*, **253**, 135 (1889); (c) H. Böhme and R. Marx, *Ber.*, **74**, 1667 (1941); (d) L. Ramberg and I. Hedlund, *Arkiv Kemi, Mineral. Geol.*, **11B**, No. 55 (1934); (e) E. Samén, *ibid.*, **12B**, No. 51 (1938); **14B**, No. 28 (1941); **15B**, No. 15 (1942); **24B**, No. 6 (1947); (f) E. A. Fehnel, THIS JOURNAL, **74**, 1569 (1952).

[5] R. H. Eastman and R. M. Wagner, *ibid.*, **71**, 4089 (1949).

[6] (a) H. Heymann, *ibid.*, **71**, 260 (1949); (b) E. A. Fehnel, *ibid.*, **71**, 1063 (1949).

[7] (a) F. G. Bordwell and G. D. Cooper, *ibid.*, **74**, 1058 (1952); (b) C. C. Price and J. J. Hydock, *ibid.*, **74**, 1943 (1952); (c) F. G. Bordwell and H. M. Anderson, *ibid.*, **75**, 6019 (1953); (d) A. Kotch, L. H. Krol, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.*, **71**, 108 (1952); (e) H. Kloosterziel and H. J. Backer, *ibid.*, **72**, 185 (1953); (f) **72**, 655 (1953).

[8] (a) H. P. Koch, *J. Chem. Soc.*, 387, 394, 408 (1949); (b) E. A. Fehnel and M. Carmack, THIS JOURNAL, **71**, 84, 231, 2889 (1949); (c) **72**, 1292 (1950).

[9] D. Barnard, J. M. Fabian and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).

[10] E. D. Amstutz, I. M. Hunsberger and J. J. Chessick, THIS JOURNAL, **73**, 1220 (1951).

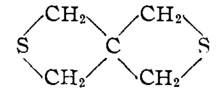
two positive charges. The second theory considers the sulfone group to be a resonance hybrid of a, b (two) and c, and therefore relies on the resonance energy (in addition to coulombic attraction) from structures d and e (two) for stabilization of the carbanion. This overlap of 3d-orbitals with 2p-orbitals has received extensive theoretical treatment.[11–13]

Among the many examples of interaction referred to above, some can be explained in either way, whereas others, notably the radical stabilization,[6] the effect on ultraviolet absorption spectra,[7f,8] and the effect of the methylsulfone group on reactivity and position of equilibria[7] are better accommodated by invoking expansion of the octet. Resolution of the question also has been attempted by studying the physical properties of sulfones and related compounds. Sugden, *et al.*,[14] compared the parachor of the sulfur–oxygen bond in sulfones with that of other double bonds and concluded the bond was semipolar. This conclusion has been questioned by Vogel.[15] Pauling and Brockway[16] recognized that the bond distances in phosphate, sulfate and perchlorate ions were slightly shorter than the sum of the (calculated) double bond radii and much shorter than the sum of the single bond radii in contrast to the bond distances in the nitrogen–oxygen and boron–oxygen bonds which were of normal single bond length. They concluded that the oxygen bond to the three second-row elements was double involving d-orbitals. Phillips, Hunter and Sutton[17] examined the dipole moment vectors of the oxygen, nitrogen, sulfur and phosphorus bonds with boron trichloride, and vectors of the nitrogen, sulfur and phosphorus oxide bonds. Finding that the sulfur and phosphorus oxide bonds had abnormally low dipole moment vectors, they concluded that these bonds had considerable double-bond character. From an examination of molar refractivities Strecker and Spitaler[18] concluded that the sulfur–oxygen bond in sulfoxides and sulfones was doubly covalent. The validity of this conclusion also has been questioned by Vogel, *et al.*[19]

This work reports the preparation of the bicyclic trisulfones, 4-methyl-(I) and 1,4-dimethyl-(II)-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,7,7-hexaoxide and a comparison of their acidities with that of the open chain trisulfone, trisethylsulfonylmethane (III). The conceptual inspiration lies in the paper by Bartlett and Woods,[20] whose elucidation of the non-acidic character of 2,6-diketobicyclo[2.2.2]-octane constitutes one of the most convincing experimental supports of the resonance theory of carbanion stabilization by a carbonyl group. If d-orbital resonance in α-sulfonyl carbanions had the same geometrical requirement as that demonstrated by Bartlett and Woods for p-orbital resonance in α-carbonyl carbanions (a supposition contrary to the theoretical results of Kimball[11]), it was reasoned that the bicyclic acid I would be much less acidic than the open chain analog III.

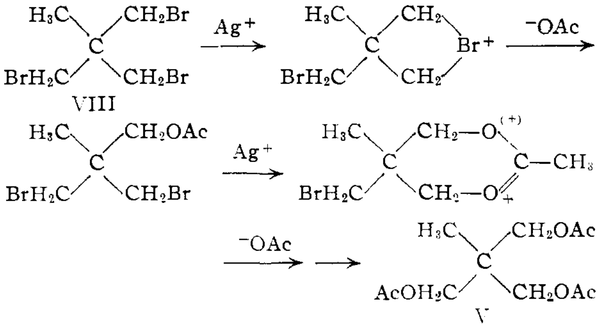
The starting material, 1,1,1-trishydroxymethylethane (IV, pentaglycerine), which was characterized as the triacetate V, the tribenzoate VI and the bicyclic orthoformate, 4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (VII), reacted with phosphorus tribromide to give 1,1,1-trisbromomethylethane (VIII, pentaglyceryl tribromide). This reaction also occurs with pentaerythritol[21] and 2,2-dimethylpropandiol-1,3.[22] Although VIII was not hydrolyzed by hydroxide ion at 140°, it was converted to V by silver acetate at 175°.

This replacement proceeding without rearrangement is to be contrasted with the reaction of neopentyl iodide which gives only rearranged *t*-amyl acetate and trimethylethylene under the same conditions.[23] The present observation is, however, not unique, Franke[22] having discovered that 2,2-bisbromomethylpropane reacts with silver acetate to give unrearranged 2,2-bisacetoxymethylpropane. A clue to understanding the absence of rearrangement appears to lie in the work of Backer and Keuning[24] who found that the product of treating pentaerythrityl tetrabromide with sodium sulfide is dithiaspiroheptane (IX), of which the corresponding disulfoxide was resolved.



IX

A four-membered ring being the stable product here, it is reasonable to extrapolate and hypothesize that transient, intermediate, four-membered rings may also be formed with bases other than thiols, as has been abundantly demonstrated by Winstein for the interaction of adjacent substituents.[25] Such intermediate, four-membered interaction, illustrated by the reaction of silver acetate with a dibromide, would lower the electron-deficiency on carbon and thereby decrease the chance



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[11] G. E. Kimball, *J. Chem. Phys.*, **8**, 188 (1940).

[12] (a) W. E. Moffitt, *Proc. Roy. Soc.* (*London*), **A200**, 409 (1950); (b) H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951).

[13] D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel and L. E. Sutton, *J. Chem. Soc.*, 332 (1954).

[14] S. Sugden, J. B. Reed and H. Wilkins, *ibid.*, **127**, 1525 (1925).

[15] A. I. Vogel, *ibid.*, 1820, 1833 (1948).

[16] L. Pauling and L. O. Brockway, This Journal, **59**, 13 (1937).

[17] G. M. Phillips, J. S. Hunter and L. E. Sutton, *J. Chem. Soc.*, 146 (1945).

[18] W. Strecker and R. Spitaler, *Ber.*, **59**, 1754 (1926).

[19] A. I. Vogel, W. T. Cresswell, G. H. Jeffery and J. Leicester, *J. Chem. Soc.*, 514 (1952).

[20] P. D. Bartlett and G. F. Woods, This Journal, **62**, 2933 (1940).

[21] G. Gustavson, *J. prakt. Chem.*, [2] **54**, 98 (1896).

[22] A. Franke, *Monatsh.*, **34**, 1893 (1913).

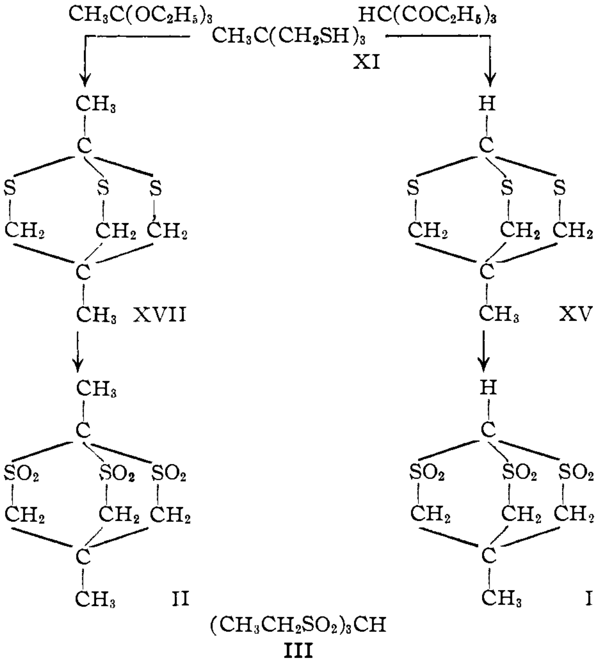
[23] F. C. Whitmore and C. H. Fleming, *J. Chem. Soc.*, 1269 (1934).

[24] H. J. Backer and K. J. Keuning, *Rec. trav. chim.*, **52**, 499 (1933); **53**, 798 (1934).

[25] Reviewed by E. A. Braude, *Ann. Rep. Prog. Chem.*, **46**, 122 (1949).

of rearrangement and increase the ease of replacement in comparison to the behavior of monosubstituted neopentane types.

1,1,1-Trisiodomethylethane (X, pentaglyceryl triiodide), prepared from the tribromide by displacement with potassium iodide in boiling butanone, reacted with silver acetate similarly to give pentaglyceryl triacetate, identified by ethanolysis to pentaglycerine. By the excellent method of Backer, *et al.*,[26] it was possible, where other conventional methods failed, to convert 1,1,1-trisbromomethylethane (VIII) to 1,1,1-trismercaptomethylethane (XI, trithiopentaglycerine) by treatment with sodium polysulfide followed by reduction of the resulting polymeric polysulfide with sodium in liquid ammonia. The tribenzoate XII, the tri-*p*-nitrobenzoate XIII and 1,1,1-tris-(methylsulfonylmethyl)-ethane (XIV) were prepared as derivatives.



The trimercaptan XI reacted smoothly with ethyl orthoformate to give 4-methyl-2,6,7-trithiabicyclo[2.2,2]octane (XV). The structure rests on the method of preparation and the fact that reduction with Raney nickel, according to Bougault, Cattelain and Chabrier,[27] leads to neopentane.

On oxidation with hydrogen peroxide in acetic acid, XV is converted to 4-methyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,7,7-hexaoxide (I). This trisulfone is soluble in sodium bicarbonate and can be brominated either in that solution or in water to 1-bromo-4-methyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,7,7-hexaoxide (XVI).

At the suggestion of Professor P. D. Bartlett, Harvard University, whose interest we acknowledge with much thanks, 1,4-dimethyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,7,7-hexaoxide (II) was prepared to determine whether the acidity of I might be due to one of the methylene hydrogens rather than to the bridgehead hydrogen. The reaction of XI with ethyl orthoacetate produced 1,4-dimethyl-2,6,7-trithiabicyclo[2.2.2]octane (XVII), oxidation of which afforded the trisulfone II. In contrast to I, II was insoluble in both sodium bicarbonate and sodium hydroxide. There is, therefore, no reasonable doubt that the acidic hydrogen in I is at the bridgehead carbon atom (C_1).

The attempted preparation of another member of the series, 2,6,7-trithiabicyclo[2.2.1]heptane-2,2,6,6,7,7-hexaoxide (XVIII), in which attainment of coplanarity of the bridgehead carbon atom and the sulfur atoms is inhibited, failed. 1,2,3-Trimercaptopropane (XIX, trithioglycerine), prepared conveniently by the sodium polysulfide method, reacted with ethyl orthoformate to give almost entirely polymeric material. Sublimation of this polymer at 160° produced small amounts of 2,6,7-trithiabicyclo[2.2.1]heptane (XX), apparently by depolymerization. XX polymerized at an appreciable rate during recrystallization. Apparently the strain in the smaller bicyclic system leads to a position of equilibrium unfavorable for the bicyclic compound. Oxidation gave an unstable material containing four instead of six atoms of oxygen.

I is not quite as acidic as the acyclic trisulfone, trisethylsulfonylmethane (III), for which Samén[4e] reports an acidity indistinguishable from hydrogen chloride in water. Potentiometric titration in aqueous solution showed a pK_a of 3.30 ± 0.03 for I but for III no constant value could be obtained. III is definitely a stronger acid, but how much stronger cannot be said.

No strong theoretical conclusion is justified on the basis of the roughly equal acidity of I and III. The electrostatic, inductive explanation of the acidity involves no angular requirement and, therefore, predicts no difference between I and III. Similarly, the resonance hypothesis could operate in both I and III if one accepts the theoretical result that there is no strict angular requirement for d-p overlap[11,12] as there is for p-p overlap. Resonance in the carbanion does require coplanarity of the sulfur atoms and the bridgehead carbon atom (sp^2 bonding orbitals) and to the extent that there is any strain involved in satisfying this requirement in the bicyclic system, I would be less acidic than III. The actual difference between I and III is in the expected direction and constitutes an indication for asserting that the carbanion has a planar arrangement and is therefore stabilized by resonance.

Experimental[28]

1,1,1-Trishydroxymethylethane (IV).—The preparation is a modification of the method of Hosaeus.[29] Following the addition over 1/2 hr. of 525.5 g. of crystalline barium hydroxide to a stirred mixture of 145.2 g. of freshly distilled propionaldehyde and 337.5 g. of paraformaldehyde in 3 l. of water, the reaction was heated at 70° until the appearance of a yellow color, whereupon the heating was stopped and the stirring was continued for 2 hr. The mixture was neutralized with oxalic acid, filtered from precipitated salts, treated with Norit and concentrated *in vacuo* to an incompletely crystalline residue, which was extracted with acetone. Crystalline material which deposited slowly from the cooled sirup remaining after removal of the acetone was recrystallized several times from acetone to give 145 g. of

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[26] H. J. Backer and N. Evenhuis, *Rec. trav. chim.*, **56**, 174 (1937); H. J. Backer and A. F. Tamsma, *ibid.*, **57**, 1183 (1938).

[27] J. Bougault, E. Cattelain and P. Chabrier, *Bull. soc. chim.*, [5] **7**, 781 (1940).

[28] Melting points are corrected.

[29] H. Hosaeus, *Ann.*, **276**, 75 (1893).

colorless prisms of pentaglycerine (IV), m.p. 202–203° (reported m.p. 199°,[29,30] 201°,[31] 198–198.2°[32]). Distillation of the sirup and concentrated mother liquor at 0.25 mm. in a bath at 180° followed by recrystallization afforded an additional 31 g. of IV, m.p. 202–203°, making the total yield 59% of theory.

1,1,1-Trisacetoxymethylethane (V) was prepared in 97% yield according to Hosaeus[29] as a colorless oil; b.p. 102–103° at 0.45 mm., $n^{25}_{\rm D}$ 1.4342, d^{25}_{4} 1.1062, *MD* calcd. 58.0 (found 58.0).

Anal. Calcd. for $C_{11}H_{18}O_6$: C, 53.7; H, 7.4. Found: C, 53.5; H, 7.4.

Pentaglyceryl tribenzoate (VI) was prepared from 3.6 g. of IV and 8 cc. of benzoyl chloride by heating, continuously during the initial vigorous evolution of hydrogen chloride and then at reflux for 15 min. The viscous oil was warmed with alcohol and then recrystallized several times to give 0.6 g. of VI as colorless needles, m.p. 80.5–81.5°.

Anal. Calcd. for $C_{26}H_{24}O_6$: C, 72.2; H, 5.6. Found: C, 72.1; H, 5.7.

4-Methyl-2,6,7-trioxabicyclo[2.2.2]octane (VII).—When 12 g. of IV and 15 g. of ethyl orthoformate was heated at 140° in a flask surmounted by a small column, and condenser, the theoretical amount of ethanol distilled in 24 hr. leaving a residue which was sublimed. The partially crystalline sublimate was leached with hot hexane to remove the crystalline product. Recrystallization from hexane and two sublimations at 20 mm. and room temperature afforded 1.0 g. of VII, m.p. 105.5–106°.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.4; H, 7.8. Found: C, 55.6; H, 8.1.

VII smells sweet, sublimes at atmospheric pressure and room temperature and becomes sticky in air. On warming a suspension in water at 100° for 30 min. and evaporating to dryness, authentic IV, m.p. 202–203°, was recovered.

1,1,1-Trisbromoethylethane (VIII).—A mixture of 60 g. of pentaglycerine (IV) and 203.6 g. of phosphorus tribromide which had been added over 2 hr. while heating on the steam-bath, was heated 30 min. longer at 100° and then for 24 hr. at 170–180°. The reaction mixture was decomposed with 500 cc. of water, filtered and extracted with benzene. The benzene solution was washed with sodium bicarbonate solution and then with water, dried over calcium chloride, and concentrated *in vacuo*. Distillation afforded 100 g. (65%) of VIII; b.p. 127° at 17 mm., $n^{25}_{\rm D}$ 1.5560, d^{25}_{4} 2.0867, *MD* calcd. 48.6 (found 47.6) (reported[32] b.p. 108° at 6 mm., $n^{20}_{\rm D}$ 1.5593, d^{20}_{4} 2.0917).

Anal. Calcd. for $C_5H_9Br_3$: Br, 77.6. Found: Br, 77.6.

An attempt to hydrolyze VIII by heating 9 g. of the tribromide with 33 cc. of 20% aqueous potassium hydroxide in a sealed tube at 140° for 24 hr. resulted in the recovery after distillation of 7.8 g. of the tribromide.

A mixture of 6 g. of VIII, 10 g. of silver acetate and 20 cc. of glacial acetic acid was heated in a sealed tube at 175° for 24 hr. The filtered, concentrated reaction product was dissolved in ether, washed with aqueous sodium bicarbonate and water, dried with anhydrous potassium carbonate, and distilled. The pentaglyceryl triacetate (V), b.p. 164–166° at 18 mm., was hydrolyzed by treating with 1 cc. of saturated ethanolic hydrogen chloride in 25 cc. of methanol for 48 hr. at room temperature. Concentration and recrystallization afforded pentaglycerine, m.p. 202–203° alone and mixed with authentic IV.

1,1,1-Trisiodomethylethane (X).—A mixture of 57.3 g. of 1,1,1-trisbromomethylethane (VIII), 119.9 g. of dry sodium iodide and 550 cc. of butanone was refluxed for 48 hr., freed of solvent by distillation and diluted with 300 cc. of water. The heavy oil was separated from the aqueous phase and united with the benzene extract thereof. The benzene solution was washed with aqueous sodium bisulfite and water, dried with calcium chloride and concentrated *in vacuo*. Distillation of the residue afforded 68 g. (82%) of X, b.p. 118–120° at 0.1 mm. colored by free iodine. After several redistillations, the triiodide was obtained colorless; $n^{25}_{\rm D}$ 1.6798, d^{25}_{4} 2.6847, *MD* calcd. 63.7 (found 63.3).

Anal. Calcd. for $C_5H_9I_3$: I, 84.6. Found: I, 84.9.

Heating X with silver acetate in acetic acid in a sealed tube at 165–170° for 25 hr. followed by ethanolysis of the crude triacetate V, produced pentaglycerine (IV), m.p. 202–203°.

1,1,1-Trismercaptomethylethane (XI).—A solution of 0.8 mole of sodium tetrasulfide in aqueous alcohol, prepared by the method of Backer and co-workers,[26] to which 123.6 g. of 1,1,1-trisbromomethylethane (VIII) in 800 cc. of alcohol had been added with stirring, was refluxed 4 hr. and then concentrated *in vacuo* removing 700 cc. of alcohol. Addition of 50 cc. of water precipitated a tar which was separated by decantation and dissolved in the benzene extract of the aqueous phase. The mixture was distilled to dryness *in vacuo*, resuspended in benzene and concentrated again to remove water. The polysulfide was cooled in a Dry Ice-bath, covered with 700 cc. of liquid ammonia, and reduced by adding sodium in small strips with stirring until permanently blue. Following the decomposition of unreacted sodium by adding 25 cc. of ethanol slowly, the ammonia was evaporated leaving a residue which was dissolved in 400 cc. of cold water, washed with benzene and then acidified with 20% sulfuric acid with stirring and cooling. The benzene extract of the mixture was washed with aqueous sodium bicarbonate, dried with anhydrous sodium sulfate, concentrated and distilled *in vacuo* under nitrogen to give 67 g. (63%) of stinking liquid, b.p. 141–144° at 18 mm. Redistilled XI was a pale yellow oil; b.p. 142° at 18 mm., $n^{25}_{\rm D}$ 1.5769, d^{25}_{4} 1.1625; *MD* calcd. 48.4 (found 48.0).

Anal. Calcd. for $C_5H_{12}S_3$: C, 35.7; H, 7.2; S, 57.1. Found: C, 35.9; H, 7.1; S, 57.3.

A mixture of 0.2 g. of XI and 1 cc. of benzoyl chloride was refluxed for a few minutes, poured into 5 cc. of water, warmed on the steam-bath and extracted with ether. The ether extract was washed with 5% sodium carbonate solution and saturated sodium chloride, treated with Norit and concentrated. The residue oil was leached with pentane several times. Evaporation of the pentane left an oil which crystallized. Six recrystallizations from pentane afforded **1,1,1-trisbenzoylthiomethylethane** (XII, trithiopentaglyceryl tribenzoate) as colorless needles, m.p. 42.5–43.5°.

Anal. Calcd. for $C_{26}H_{24}O_3S_3$: C, 65.0; H, 5.0; S, 20.0. Found: C, 65.1; H, 5.1; S, 19.5.

Refluxed in 25 cc. of xylene for 2 hr., a mixture of 0.33 g. of XI and 1.5 g. of *p*-nitrobenzoyl chloride was freed of xylene *in vacuo*, diluted with 10 cc. of water and extracted with benzene. The benzene solution was washed with 5% aqueous sodium carbonate and with saturated sodium chloride, dried with sodium sulfate, brought to 40 cc. volume, diluted with 10 cc. of pentane and chromatographed on Brockmann alumina. Concentration of the development fractions afforded semicrystalline material which gave **1,1,1-tris-(*p*-nitrobenzoylthiomethyl)-ethane** (XIII, trithiopentaglyceryl tri-*p*-nitrobenzoate), m.p. 150.5–151.5°, after recrystallization from benzene–hexane.

Anal. Calcd. for $C_{26}H_{21}N_3S_3O_9$: C, 50.7; H, 3.4; S, 15.6. Found: C, 51.2; H, 3.5; S, 15.7.

A mixture of 0.84 g. of trithiopentaglycerine (XI), 6 cc. of methyl iodide and 30 cc. of 10% aqueous sodium hydroxide was shaken for 2 hr., freed of excess methyl iodide by evaporation and extracted with benzene. The residue from concentration of the benzene was dissolved in 15 cc. of glacial acetic acid, cooled in ice and treated with 5 cc. of 30% aqueous hydrogen peroxide. After 30 min. at 0°, the mixture was warmed to 95–100° over a 30 min. period and maintained there for 30 min. more. Concentration, precipitation by adding 2 cc. of water and scratching gave 0.08 g. of **1,1,1-tris-(methylsulfonylmethyl)-ethane (XIV)**, m.p. 153.5–154.5° after recrystallization from water. The trisulfone is no more soluble in 10% aqueous sodium hydroxide than it is in water.

Anal. Calcd. for $C_8H_{18}O_6S_3$: C, 31.4; H, 5.9. Found: C, 31.1; H, 5.8.

4-Methyl-2,6,7-trithiabicyclo[2.2.2]octane (XV).—A solution of 0.42 g. of trithiopentaglycerine (XI) and 0.37 g. of ethyl orthoformate in 10 cc. of benzene was added slowly to a refluxing solution of a few crystals of *p*-toluenesulfonic acid in benzene. After refluxing 3 hr., the solution was washed with 5% aqueous sodium carbonate, dried with sodium sulfate, brought to 25 cc., diluted with 25 cc. of

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pentane and chromatographed with Brockmann alumina. The crystalline eluates were recrystallized from hexane to give 0.30 g. (67%) of XV as colorless needles, m.p. 130.5–131°. In larger runs, using crude XI, b.p. 141–144° at 18 mm., the yield was reduced to 40% of theory.

Anal. Calcd. for $C_6H_{10}S_3$: C, 40.4; H, 5.7. Found: C, 40.5; H, 5.4.

A mixture of 2 g. of XV, 50–55 g. of Raney nickel, 20 cc. of ethanol and 50 cc. of water was heated 6 hr. on the steam-bath under reflux, the effluent vapors being condensed in a trap cooled in trichloroethylene and Dry Ice. The trap was then warmed, its contents distilling into another, similarly cooled trap. The distillate was apparently neopentane, b.p. 10° and m.p. −20° (reported b.p. 10° and m.p. −20°[33]; b.p. 9.5° and m.p. −20°[34]).

4-Methyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,7,7-hexaoxide (I).—A solution prepared by adding 10.2 g. of 30% hydrogen peroxide to 1.78 g. of XV in 75 cc. of glacial acetic acid at 0–10° was maintained 15 min. at that temperature, warmed gradually for 15 min., and finally heated on the steam-bath for 30 min. The crude sulfone which crystallized during the reaction and that obtained by concentration of the reaction filtrate weighed 2.34 g. (85%). The trisulfone I, insoluble in the common organic solvents, can be purified by dissolving in 5% aqueous sodium bicarbonate and precipitating with acid or by recrystallization from a large volume of acetonitrile or water. Introduced in a m.p. block at 351° and heated 4° per min., the trisulfone darkened at 357–360°.

Anal. Calcd. for $C_6H_{10}O_6S_3$: C, 26.3; H, 3.7; S, 35.1. Found: C, 26.4; H, 3.5; S, 35.1.

1-Bromo-4-methyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,-6,6,7,7-hexaoxide (XVI).—I in aqueous suspension was dissolved by adding aqueous sodium hydroxide dropwise and then treated with bromine dropwise. The precipitated XVI, recrystallized from much water, darkened from 269–273° when introduced in a block preheated to 265°. XVI also could be prepared by bromination of an aqueous solution of I.

Anal. Calcd. for $C_6H_9BrO_6S_3$: C, 20.4; H, 2.6; Br, 22.6. Found: C, 20.2; H, 2.9; Br, 23.1.

1,4-Dimethyl-2,6,7-trithiabicyclo[2.2.2]octane (XVII).—The mixture of 1.68 g. of XI and 1.63 g. of ethyl orthoacetate in 45 cc. of absolute ethanol to which 1 cc. of ethanolic hydrogen chloride had been added was kept at 4° for 2 days. The residue from evaporation of the alcohol was dissolved in benzene. This solution was washed with aqueous sodium bicarbonate and saturated sodium chloride solution, dried with sodium sulfate, brought to a volume of 75 cc., diluted with 50 cc. of pentane and filtered through a column of Brockmann alumina. The concentrated filtrates were evaporatively distilled at 20 mm. and 130° giving partially crystalline material from which 0.58 g. (30%) of XVII as colorless needles was obtained by crystallization from benzene–hexane; m.p. 133–135°. Mixed with XV, m.p. 130.5–131°, XVII melted at 84–95°.

Anal. Calcd. for $C_7H_{12}S_3$: C, 43.7; H, 6.3; S, 50.0. Found: C, 43.7; H, 6.4; S, 49.9.

1,4-Dimethyl-2,6,7-trithiabicyclo[2.2.2]octane-2,2,6,6,-7,7-hexaoxide (II).—XVII (0.0841 g.) reacted with 5 cc. of peracetic acid in glacial acetic acid (1.5 *N*) for 15 min., at room temperature, then gradually at higher temperatures and finally on the steam-bath for 30 min. The residue from evaporation of the acetic acid was recrystallized from water to give II as fine needles (0.0594 g., 47%). The sulfone did not decompose up to 370°. It is not soluble in 10% aqueous sodium hydroxide.

Anal. Calcd. for $C_7H_{12}O_6S_3$: C, 29.2; H, 4.2; S, 33.4. Found: C, 29.3; H, 4.2; S, 33.2.

1,2,3-Trimercaptopropane (XIX).—A solution of 56.2 g. of 1,2,3-tribromopropane in 350 cc. of alcohol was added slowly and with vigorous stirring to 0.4 mole of sodium tetrasulfide in aqueous alcohol at room temperature. After 90 minutes reflux, the precipitate was filtered, washed with water, alcohol and ether, dried *in vacuo*, suspended in 1200 cc. of liquid ammonia and reduced with small pieces of sodium (*ca.* 46 g.) until the blue color persisted. After 2 hours additional stirring, the excess sodium was decomposed by adding 35 cc. of absolute ethanol slowly. Removal of the ammonia left a salt which was dissolved in 500 cc. of ice-water and acidified with 20% sulfuric acid. The benzene extract of the separated oil was washed with 5% sodium carbonate, dried with sodium sulfate and concentrated *in vacuo*. The residue, twice distilled under nitrogen, yielded 18 g. (65%) of trithioglycerine (XIX); b.p. 111° at 11 mm., n^{25}_{D} 1.6082, d^{25}_{4} 1.2516, MD calcd. 39.1 (found 38.8).

A few drops of XIX was shaken 30 minutes with 2 cc. of methyl iodide and 10 cc. of 10% sodium hydroxide, the excess methyl iodide then being evaporated and the residue being extracted with benzene. Washing and concentrating the benzene extract left an oil which was oxidized in 5 cc. of glacial acetic acid with 2 cc. of 30% aqueous hydrogen peroxide. The residue from concentrating the mixture was twice recrystallized from water to give colorless needles of 1,2,3-trimethylsulfonylpropane, m.p. 205–206° (reported m.p. 206°[35]).

2,6,7-Trithiabicyclo[2.2.1]heptane (XX).—A mixture of 5.6 g. of 1,2,3-trimercaptopropane (XIX) and 5.93 g. of ethyl orthoformate was heated at 140° for 3 days, the ethanol being distilled as formed. Sublimation of the glassy product at 20 mm. and 160° gave 0.98 g. (16%) of sublimate partly soluble in hexane, from which it crystallized in feathery plates sintering at 145° and finally clearing at 198°. On each subsequent recrystallization, about half the material became amorphous and insoluble in hexane and benzene. Sublimation of the amorphous form at 130° and 30 mm. reproduced the crystalline form.

Anal. Calcd. for $C_4H_6S_3$: C, 32.0; H, 4.0; S, 64.0. Found: C, 31.8; H, 4.0; S, 64.3.

A suspension of 0.15 g. of freshly sublimed XX in 20 cc. of glacial acetic acid was oxidized with 30% aqueous hydrogen peroxide. Concentration, cooling and triturating with water induced crystallization. Recrystallization from water gave 0.118 g. (48%) of material which decomposed at 224–226° when placed in a preheated block. Recrystallization could be effected from glacial acetic acid. The substance dissolved very slowly in cold aqueous sodium carbonate and could not be recovered on acidification.

Anal. Calcd. for $C_4H_6O_6S_3$: C, 19.5; H, 2.5; S, 39.1. Calcd. for $C_4H_6O_4S_3$: C, 22.4; H, 2.8; S, 44.9. Found: C, 22.8, 22.3, 23.1; H,.3.0, 2.9, 3.2; S, 46.3, 45.1.

Trisethylsulfonylmethane (III).—A solution of peracetic acid (50% excess) in acetic acid was added dropwise with vigorous stirring to 4.91 g. of ethyl trithioörthoformate at 15–18°. The reaction proceeded 30 min. without cooling, 30 min. while being heated to 80° and 30 min. at 80–90°. On cooling, III separated. Recrystallization from water afforded 3.73 g. (51%) of III, m.p. 218–220° (reported m.p. 212°,[36] 216°[4c] and 218–220°[4e]). Tris-(ethylsulfonyl)-bromoethane, m.p. 133.5–134°, was prepared according to Samén[4e] who reported m.p. 134–135°.

Potentiometric Titration.—Homogeneous 0.001 *M* solutions of I and III were prepared by dissolving the salt in boiling water and diluting the cooled solution. Using a Beckman pH meter, 50 cc. of the sulfone solutions were titrated with 0.009911 *N* sodium hydroxide at 25 ± 0.5°. The values of pK_a at all points were calculated from the equation $pK_a = p\text{H} + \log[([\text{S}] - [\text{NaOH}] - [\text{H}^+])/([\text{NaOH}] + [\text{H}^+])]$ where [S] is the concentration of sulfone had no reaction, only dilution, occurred; [NaOH] is the concentration of sodium hydroxide had no reaction occurred; and $[\text{H}^+]$ is the measured hydrogen ion concentration. For I a constant value of $pK_a = 3.30 \pm 0.03$ was obtained; for III no constant value was obtainable and the acid appeared to be indistinguishable from aqueous hydrogen chloride.

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