[Contribution from Chandler Laboratory, Columbia University]

d-Orbital Resonance. II. Comparative Reactivity of Vinyldimethylsulfonium and Vinyltrimethylammonium Ions[1]

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Vinyldimethylsulfonium (I) ion has been prepared by very rapid elimination of hydrogen bromide from 2-bromoethyldimethylsulfonium (VI) ion with hydroxide ion. This reaction occurs much more rapidly than the reaction of 2-bromoethyltrimethylammonium ion with hydroxide which, by contrast, leads to normal displacement. Vinyldimethylsulfonium ion reacts very rapidly with a variety of bases by addition to give 2-substituted ethyldimethylsulfonium ions, the structures of which have been established by synthesis. By comparison it has been impossible to add bases to vinyltrimethylammonium ion. These differences in the activating effect of sulfonium and ammonium are quite striking and find reasonable explanation in the hypothesis that resonance structures involving a 3d-orbital (expansion of the octet to a decet) contribute significantly to the transition states in the sulfur compounds.

The preceding paper[3] outlined briefly the extensive efforts in the literature directed at unequivocal demonstration of the involvement of 3d-orbitals in the chemistry of sulfones. The success of many of these efforts was inherently limited by the lack of a reliable non-resonating standard with which the behavior of sulfones could be compared. The apposite oxygen analogs being obviously incapable of existence, use was made in some instances of amine oxides.[4,5] It was the general purpose of this research to explore further the rôle of the 3d-orbitals of sulfur in examples where reasonably valid standards of comparison were available.

Specifically the unknown reactions of dimethylvinylsulfonium (I) and trimethylvinylammonium (II) ions with nucleophilic reagents were chosen for study, II serving as non-resonating standard in lieu of dimethylvinyloxonium ion (III). These hypothetical reactions should involve transition states (or intermediates) in which a partial negative charge is placed on the carbon atom adjacent to the positively charged atom. Differences in the magnitude of interaction of these charges should then be reflected in the relative rates of reaction of I and II on the reasonable assumption that a difference in rates will parallel a difference in energies of activation. Assuming that electrostatic interaction alone would operate in the transition state Ia from the vinylammonium ion and that no greater electrostatic interaction would operate in the vinylsulfonium analog IIa, significant enhancement of reaction of the vinylsulfonium ion could reasonably be ascribed to resonance IIb.

$$(CH_3)_3\overset{+}{N}{-}CH{=}CH_2 + B^{-}: \longrightarrow$$

I

$$(CH_3)_3\overset{+}{N}{-}\underset{\cdot\cdot}{\overset{-}{C}}H{-}CH_2B \qquad (CH_3)_2\overset{+}{O}{-}CH{=}CH_2$$

Ia III

$$(CH_3)_2\underset{\cdot\cdot}{\overset{+}{S}}{-}CH{=}CH_2 + B^{-}: \longrightarrow$$

II

$$[(CH_3)_2\underset{\cdot\cdot}{\overset{+}{S}}{-}\underset{\cdot\cdot}{\overset{-}{C}}H{-}CH_2B \longleftrightarrow (CH_3)_2\overset{\cdot\cdot}{S}{=}CH{-}CH_2B]$$

IIa IIb

The available related facts are insufficient to allow reliable prediction of the probability of realizing the projected reactions. The addition of bases to unactivated olefins fails to occur except where the adding base is exceedingly strong.[6] The activated olefins which undergo Michael additions provide a large amount of resonance stabilization in the transition state. This stabilization is reflected in a marked acidifying effect on adjacent carbon–hydrogen bonds by the same activating groups. Although it can be estimated from the work of Wittig and Wetterling[7a] and Schlenk and Holtz[7b] that the acidity of the tetramethylammonium ion lies between that of benzene and toluene, the relative acidifying effect of positively charged sulfur in the trimethylsulfonium ion is not known.

There are some further examples in the literature reflecting the activating effect of positively charged nitrogen and sulfur atoms. 9-Fluorenyldimethylsulfonium and 9-fluorenyltrimethylammonium bromides have been converted to ylids, the former by treatment with sodium hydroxide[8] and the latter by reaction with phenyllithium.[9] Reactions which appear to depend on the activating effect include the rearrangement of benzylammonium salts[10] and the cyclization of dimethyl-(*o*-acetyl-*p*-tolyl)-sulfonium hydroxide to 3,5-dimethyl-3-methoxy-2,3-dihydrothionaphthene.[11] A greater activating effect by positively charged sulfur is strongly indicated in the hydroxide-catalyzed decomposition of (2-benzoyloxymethyl)-dimethylsulfonium iodide to acetylene when compared with the inertness of the corresponding ammonium salt.[12]

The preparation of vinyldimethylsulfonium ion

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

[3] W. von E. Doering and L. K. Levy, This Journal, **77**, 509 (1955).

[4] (a) L. Pauling and L. O. Brockway, *ibid.*, **59**, 13 (1937); (b) G. M. Phillips, J. S. Hunter and L. E. Sutton, *J. Chem. Soc.*, 146 (1945).

[5] Amine oxides have the obvious disadvantage of possessing only one of the two non-resonating positive charges required of a standard and even as standards for comparison with sulfoxides they lack the unshared pair of electrons of the latter.

[6] P. D. Bartlett, S. Friedman and M. Stiles, This Journal, **75**, 1771 (1953).

[7] (a) G. Wittig and M.-H. Wetterling, *Ann.*, **557**, 193 (1947); (b) W. Schlenk and J. Holtz, *Ber.*, **50**, 274 (1917).

[8] C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 713 (1930).

[9] G. Wittig and G. Felletschin, *Ann.*, **555**, 133 (1944).

[10] S. W. Kantor and C. R. Hauser, This Journal, **73**, 4122 (1951).

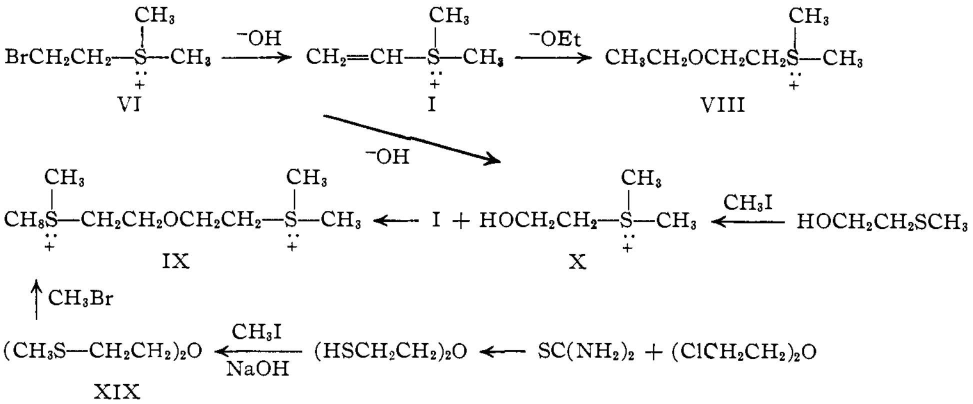
[11] F. Krollpfeifer, H. Hartmann and F. Schmidt, *Ann.*, **563**, 15 (1949).

[12] (a) C. W. Crane and H. N. Rydon, *J. Chem. Soc.*, 766 (1947); (b) P. Mamalis and H. N. Rydon, *Nature*, **166**, 404 (1950); (c) P. Mamalis and H. N. Rydon, *Chemistry & Industry*, 93 (1951).

(I)[13] presented difficulties the resolutions of which were of significance to the main problem. Vinyl methyl sulfide (IV), prepared most conveniently from 2-bromoethyl methyl sulfide (V) and solid potassium hydroxide, reacts with methyl iodide or with methyl bromide to give trimethylsulfonium ion instead of I. The reaction of 2-bromoethyldimethylsulfonium (VI) ion with strong base was expected to lead to vinyldimethylsulfonium ion by analogy with the convenient preparation of vinyltrimethylammonium ion (II, neurine) from 2-bromoethyltrimethylammonium (VII, bromocholine bromide) ion with alcoholic potassium hydroxide.[14] Unexpectedly, the product was 2-ethoxyethyldimethylsulfonium ion (VIII). It was synthesized independently from 2-chloroethyl ethyl ether and sodium methyl mercaptide, followed by treatment with methyl iodide. A quantitative comparison of the reaction of VI and VII with hydroxide ion revealed a most striking difference: VI reacted at 0° with a second-order rate constant of roughly 100 l. mole^{-1} sec.$^{-1}$ whereas VII reacted much more slowly, the rate constant being 0.0361 l. mole^{-1} sec.$^{-1}$ at 25°. The product from VII, demonstrated not to have been formed by a secondary reaction of neurine with hydroxide ion, was the normal SN2 displacement product, choline bromide. Evaporation to dryness of the reaction mixture of VI and silver oxide gave oxyethylene-bis-(dimethylsulfonium) ion (IX). This material was synthesized independently from 2,2'-dichloroethyl ether and sodium methyl mercaptide, followed by treatment with methyl bromide. Two observations showed that IX was a secondary and not an initial product of the reaction of VI and silver oxide. When picrylsulfonic acid was added to the reaction mixture before evaporation a picrylsulfonate different from IX picrylsulfonate was isolated and when the reaction mixture was acidified with acetic acid after five minutes and then evaporated to dryness, the product was vinyldimethylsulfonium ion (I) and not IX.

It is striking that the structurally similar molecules VI and VII, both reacting with hydroxide ion with second-order kinetics, give different products: VI, by a bimolecular elimination (EN2), giving the olefin I, and VII, by a bimolecular displacement (SN2), giving choline. This difference, explicable by assuming much more facile removal of α-hydrogen in VI than in VII, indicates that the sulfonium salt is more effective (on the basis of this fact alone to an inestimable degree) than the ammonium ion in activating α-hydrogen, *i.e.*, in stabilizing the resulting anionic intermediate or transition state. Resonance stabilization involving a 3d-orbital of sulfur IIb appears on the basis of this observation of considerable energetic significance. Rydon, *et al.*,[12] have drawn the same conclusion from their observation of the remarkable ease of the decomposition of $\mathrm{XCH_2CH_2\overset{+}{S}(CH_3)_2}$ to acetylene[12a] in contrast to the inertness of the corresponding ammonium ions. They hypothesized, but failed to isolate, vinyldimethylsulfonium ion as an intermediate[12b] and attributed the ease of formation of this hypothetical intermediate to the formation of a preceding intermediate of neutral character in which sulfur has an electron decet.[12b,c]

The reaction of vinyldimethylsulfonium ion (I) with nucleophilic reagents is a base-catalyzed addition proceeding with remarkable rapidity. Ethanol, unreactive by itself, reacts in the presence of a drop of 5% aqueous sodium hydroxide in a few minutes at room temperature giving the 2-ethoxyethyldimethylsulfonium ion (VIII). It seems likely that the formation of this compound from 2-bromoethyldimethylsulfonium ion (VI) proceeded through the intermediate formation of I. Water, containing a little hydroxide, reacted to give oxyethylene-bis-(dimethylsulfonium) (IX) ion, presumably by the initial formation of 2-hydroxyethyldimethylsulfonium (X) ion. This latter compound is in fact produced from I and 0.1 *M* potassium hydroxide, and has been synthesized independently from 2-hydroxyethyl methyl sulfide. These reactions are formulated below.



2-Phenoxyethanol likewise adds rapidly to the β-carbon of I in the presence of hydroxide as catalyst. The product, 2-(2-phenoxyethoxy)-ethyldimethylsulfonium (XI) bromide, was synthesized independently from 2-bromoethyl methyl sulfide (V).

With the carbanionic bases derived from diethyl malonate and methyl acetoacetate, I reacted vigorously at room temperature in the presence of a small amount of hydroxide ion, giving a good yield of the addition products, 3,3-dicarbethoxypropyldi-

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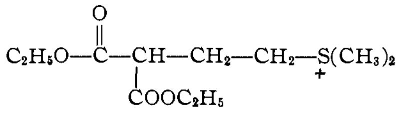
(13) Vinyldimethylsulfonium perchlorate has been claimed as a by-product from the reaction of ethylene chlorohydrin, dimethyl sulfide and mercuric chloride at 80° for 100 hr. but the assignment of structure rests only on an unsatisfactory analysis [K. A. Hofmann, K. Höbold and F. Quoos, *Ann.*, **386**, 304 (1911)]. The preparation of bis-(β-chloroethyl)-vinylsulfonium, trivinylsulfonium and vinyl-1,4-dithianesulfonium salts and their reactions by addition with thiosulfate and pyridine have been reported [M. A. Stahmann, J. S. Fruton and M. Bergmann, *J. Org. Chem.*, **11**, 704 (1946)].

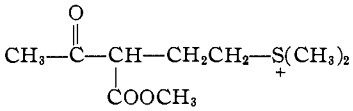
(14) R. R. Renshaw and J. C. Ware, THIS JOURNAL, **47**, 2989 (1925).

methylsulfonium (XII) ion and 3-acetyl-3-carbomethoxypropyldimethylsulfonium (XIII) ion. The latter molecule was synthesized independently,



$C_2H_5O-\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle COOC_2H_5}{|}}{CH}-CH_2-CH_2-\underset{+}{S}(CH_3)_2$

XII



$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle COOCH_3}{|}}{CH}-CH_2CH_2-\underset{+}{S}(CH_3)_2$

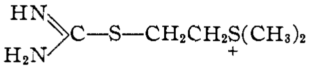
XIII

starting with 2-bromoethyl methyl sulfide (V) and sodio methyl acetoacetate followed by methylation with methyl bromide.

Sodium methyl mercaptide in water adds rapidly, giving 2-methylmercaptoethyldimethylsulfonium (XIV) ion. XIV was synthesized independently from 1,2-bis-(methylmercapto)-ethane and methyl bromide. Similarly, 2-mercaptoethanol and I, unreactive alone, react very rapidly with evolution of heat on adding a small amount of hydroxide ion to produce 2-(2-hydroxyethylmercapto)-ethyldimethylsulfonium (XV) ion, synthesized from 2-bromoethyl methyl sulfide (V) and mercaptoethanol by methylation of the resulting 2-hydroxy-2'-methylmercaptodiethyl sulfide (XVI). Concentrated aqueous thiourea reacts with I without catalyst giving 2-isothiouroniumethyldimethylsulfonium (XVII) isolated as the bromide hydrobromide which was synthesized from thiourea and 2-bromoethyl methyl sulfide (V) and is assigned the iso-structure on the basis of the formation of isothiouronium salts in displacement reactions with thiourea.

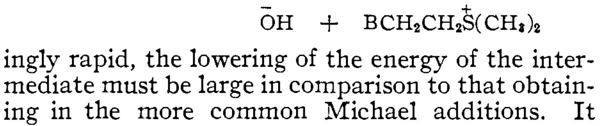
$CH_3SCH_2CH_2\underset{+}{S}(CH_3)_2$ XIV

$HOCH_2CH_2SCH_2CH_2\underset{+}{S}(CH_3)_2$ XV



XVII

The addition reaction of nucleophilic reagents to vinyldimethylsulfonium (I) ion and, presumably to vinylsulfonium salts in general, is now established as a facile, convenient reaction with preparative possibilities. The reaction is base-catalyzed and mechanistically analogous to the numerous reactions of the Michael type. The nucleophilic reagent adds to the β-carbon to give an intermediate carbanion which is of sufficiently low energy relative to unstabilized carbanions to permit rapid reaction. In these examples where the addition is so surprisingly rapid, the lowering of the energy of the intermediate must be large in comparison to that obtaining in the more common Michael additions. It must be inserted that the existence of the intermediate is only inferred and it would be more nearly correct to consider the rate-determining transition state which, with or without a following intermediate, would be approximately represented by a structure similar to that written for the intermediate in the sense of having a high electron density on the α-carbon atom requiring stabilization for realization of the reaction.



$$B^-: + \underset{\text{I}}{CH_2{=}CH-\overset{+}{S}(CH_3)_2} \longrightarrow B-CH_2-\overset{-}{C}H-\overset{+}{S}(CH_3)_2 \xrightarrow{H_2O} \overset{-}{O}H + BCH_2CH_2\overset{+}{S}(CH_3)_2$$

From the facility of the elimination of hydrogen bromide observed in the preparation of vinyldimethylsulfonium bromide (I) and the rapid addition of bases to the vinyl group in I, it is concluded that the grouping $-\overset{-}{C}-\overset{+}{S}-$ is at a considerably lower energy (is formed more rapidly; contains a more stabilized carbanion) than a simple carbanion.

The nature of this stabilization is a matter of theoretical importance demanding further consideration. The pertinent comparison involves the ammonium analogs II, the vinyloxonium salts III being unobtainable. Vinyltrimethylammonium (II, neurine) bromide is easily made by the method of Renshaw and Ware.[14] At room temperature in the presence of hydroxide for 10^4 minutes, II does not react with ethanol, water, 2-phenoxyethanol nor 2-mercaptoethanol and is recovered in recrystallized state in 92, 94, 89 and 84% of the theoretical amount, respectively. In no instance could any other product be detected. At 78° for 1500 minutes, 2-mercaptoethanol and alkali yielded some trimethylamine but the only ammonium salt isolated was starting material in 62% of theory. Similarly, less than 2% of sodium thiosulfate reacted in three days. There is, therefore, *no evidence for any addition of bases to vinyltrimethylammonium ion.* However, a minimum difference in rate between I and II can be calculated roughly using, for example, the reaction with water and the assumption of constant hydroxide ion concentration. Taking the recovery of 94% II to imply 6% addition (for which there is no evidence), the rate constant for II is *ca.* 1×10^{-7} sec.$^{-1}$ compared to *ca.* 1×10^{-2} sec.$^{-1}$ for I. There is, therefore, a minimal difference of 10^5 although the actual figure is certainly larger.

The stabilization of a carbanion by an adjacent positively charged nitrogen atom can be assumed to result from the electrostatic interaction of opposite charges uncomplicated by any appreciable resonance. The octet rule excluding resonance is based on the fact that the next available orbital, the 3s, is of much higher energy than the 2s and 2p. It is clear from our experiments that electrostatic interaction is of insufficient magnitude to permit the fragment $-\overset{+}{N}-\overset{-}{C}-$ to be formed at an appreciable rate from neurine by addition of the nucleophilic reagents in significant equilibrium with hydroxide ion.

In sharp contrast, the experiments with the sulfonium salts require that one ascribe to this group an activating effect comparable to that usually associated, for example, with the carbonyl or cyano groups. The theoretical factors which can be invoked are several. The coulombic energy of attraction, which is inversely proportional to the distance, would be about 25% less in the sulfonium carbanion than in the ammonium carbanion, assuming normal covalent distances of 1.82 and 1.47 Å., respectively. The larger polarizability of sulfur would be expected to increase the stabilization of the sulfonium carbanion. Although it is not possible to estimate the magnitude of this effect precisely, it seems doubtful that it would more than compensate the loss resulting from the increased bond length. Resonance stabilization, of no importance in the ammonium case, can theoretically be of much greater importance in the sulfonium cases. The 3d-orbital of sulfur, involvement of which is required, is only slightly higher in energy than the 3p and therefore offers a reasonable means of stabilizing the fragment $-\overset{+}{S}-\overset{-}{C}-$. We consider the facts of this work (to be interpretable) as strongly consistent with the theory that d-orbital resonance involving 10 electrons about sulfur is of energetic significance in determining the chemistry of sulfur (and other elements below the first row of eight).

Resonance structures of this type, according to current theory,[15] involve overlap of a 2p-orbital of carbon and a 3d-orbital of sulfur superimposed on a normal sigma bond consisting of a $3s{\cdot}3p^3$ sulfur hybrid orbital overlapping a $2s2p^2$ hybrid orbital of carbon. Such resonance structures are to be distinguished from the more conventional sulfur–carbon double bond which involves overlap of a 3p sulfur orbital with a 2p carbon orbital.

Experimental[16]

Methyl Vinyl Sulfide (IV).—2-Hydroxyethyl methyl sulfide, prepared by the methylation of mercaptoethanol[17,18] was characterized as **2-*p*-nitrobenzoyloxyethyl methyl sulfide**, m.p. 68° after recrystallization from methanol.

Anal. Calcd. for $C_{10}H_{11}NO_4S$: C, 49.8; H, 4.6. Found: C, 49.7; H, 4.6.

(a) **Sodium Ethoxide and 2-Bromoethyl Methyl Sulfide (V).**—V, prepared according to Akabori, *et al.*,[19] was added (28.0 g.) to ethanolic sodium ethoxide (from 6.0 g. of sodium and 80 cc. of absolute ethanol). After being refluxed for 0.5 hr., the mixture was diluted with 150 cc. of water to precipitate an organic layer which was separated, washed with water, dried with calcium chloride and distilled. The first fraction, b.p. 69°, was methyl vinyl sulfide[20] (25–30%).

Anal. Calcd. for C_3H_6S: C, 48.6; H, 8.2; S, 43.2. Found: C, 48.6; H, 8.0; S, 43.0.

The second fraction was 2-ethoxyethyl methyl sulfide; b.p. 54–56° at 23 mm., $d^{26}{}_4$ 0.924, $n^{25}D$ 1.4473.

Anal. Calcd. for $C_5H_{12}OS$: C, 50.0; H, 10.1. Found: C, 49.7; H, 10.0.

2-Ethoxyethyl methyl sulfide was prepared from 2-chloroethyl ether[21] (b.p. 107–108°; 10.8 g.) and sodium methyl mercaptide (7.0 g.) in ethanol by refluxing for 3 hr. The organic product was precipitated by adding twice the volume of water, washing with water, drying and distilling to give 2-ethoxyethyl methyl sulfide; 8.5 g. (70%), b.p. 59–60° at 27 mm., $d^{26}{}_4$ 0.923, $n^{26}D$ 1.4479.

Anal. Calcd. for $C_5H_{12}OS$: C, 50.0; H, 10.1; S, 26.7; *MR*D, 34.93. Found: C, 49.8; H, 10.2; S, 26.4; *MR*D, 34.86.

(b) **From 2-Methylmercaptoethyltrimethylammonium Bromide (XVIII).**—The precipitate obtained after several days at 4° from an ethereal solution of 15 g. of trimethylamine and 36 g. of V was filtered and recrystallized from ethanol to give XVIII; m.p. 199–201° with dec.; 35.2 g. (69% yield).

Anal. Calcd. for $C_6H_{16}BrNS$: C, 33.6; H, 7.5; N, 6.5. Found: C, 33.9; H, 7.7; N, 6.3.

A solution of 214 g. of XVIII in a minimum amount of water was added dropwise to 500 cc. of boiling 40% aqueous potassium hydroxide, the product being removed continuously by distillation. The dried organic layer was fractionally distilled to give 30 g. (40%) of IV.

(c) **Potassium *t*-Butoxide and 2-Chloroethyl Methyl Sulfide.**—2-Chloroethyl methyl sulfide (66 g.) was added slowly to a boiling solution of potassium *t*-butoxide (from 26 g. of potassium) in 400 cc. of *t*-butyl alcohol. The product, which codistilled from the reaction, was washed several times with water, dried over sodium sulfate, distilled (b.p. 55–75°) and fractionally redistilled to give 14.5 g., b.p. 65°.

Anal. Calcd. for C_3H_6S containing 23% *t*-butyl alcohol: C, 52.3; H, 9.4; S, 33.3. Found: C, 52.4; H, 8.9; S, 33.1.

The composition of the azeotrope, determined infrared spectroscopically in chloroform solution (25%) by reference to a synthetically prepared mixture, was 22 ± 1.5% of *t*-butyl alcohol and 78% of IV.

(d) **Potassium Hydroxide and V.**—IV distilled when V (78 g.) was added slowly to solid potassium hydroxide at 90°. Dried and redistilled, there was obtained 19 g. (51%) of IV, b.p. 69°.

Methyl Vinyl Sulfide and Methyl Iodide.—After one week at 4°, 3 g. of IV and 5.6 g. of methyl iodide in 5 cc. of acetonitrile had turned black and sirupy and was washed with methanol and chloroform, leaving 500 mg. of trimethylsulfonium iodide, m.p. 185–186° after recrystallization from methanol.

Anal. Calcd. for C_3H_9IS: C, 17.7; H, 4.5. Found: C, 18.1; H, 4.8.

The mercuriiodide, m.p. 161–163° from acetone (reported[22] m.p. 163–164°), and the perbromide, m.p. 94° from alcohol (reported[23] m.p. 94–95°), were prepared.

When the reaction was repeated for 24 hr. and picrylsulfonic acid was added, a small amount of picrylsulfonate, m.p. 183° from alcohol, was obtained.

2-Bromoethyldimethylsulfonium (VI) Bromide.—In a steel bomb 155 g. of 2-bromoethylmethyl sulfide (V) in 300 cc. of acetonitrile was cooled to −5° and treated with 100 g. of liquid methyl bromide. After being shaken for 4 days at room temperature in the closed bomb, the reaction mixture was dissolved in methanol. Addition of ether precipitated material which was crystallized from hot methanol to give a total of 145 g. (58%) of VI, m.p. 146–147° with dec.

Anal. Calcd. for $C_4H_{10}Br_2S$: C, 19.2; H, 4.0; Br, 63.9; S, 12.8. Found: C, 19.5; H, 4.0; Br, 63.6; S, 12.9.

In a similar way, using methyl iodide at 4° for 5 days, V was converted to 2-bromoethyldimethylsulfonium (VI) iodide, m.p. 102° with dec. after crystallization from methanol.

Anal. Calcd. for $C_4H_{10}BrIS$: C, 16.2; H, 3.4. Found: C, 15.9; H, 3.2.

Furthermore, the reaction of methyl iodide and 2-chloroethyl methyl sulfide at 4° for a week afforded **2-chloroethyldimethylsulfonium iodide**, m.p. 82° with dec. after crystallization from methanol.

Anal. Calcd. for $C_4H_{10}ClIS$: C, 19.0; H, 4.0; S, 12.7. Found: C, 18.8; H, 4.0; S, 13.0.

Reactions of 2-Bromoethyldimethylsulfonium (VI) Halide. (a) With Ethanolic Potassium Hydroxide.—A solution of 1.0 g. of the VI iodide was added to 5 cc. of *ca.* 0.6 *N* ethanolic sodium hydroxide. After 10 min., the solution was filtered and diluted with ether precipitating **2-ethoxyethyldimethylsulfonium (VIII) iodide**, m.p. 62° after recrystallization from ethanol–ether, in 90% of the theoretical yield.

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[15] G. E. Kimball, *J. Chem. Phys.*, **8**, 188 (1940); W. E. Moffitt, *Proc. Roy. Soc. (London)*, **A200**, 409 (1950); H. P. Koch and W. E. Moffitt, *Trans. Faraday Soc.*, **47**, 7 (1951); D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel and L. E. Sutton, *J. Chem. Soc.*, 332 (1954).

[16] Melting points are corrected.

[17] E. Booth, V. C. E. Burnop and W. E. Jones, *J. Chem. Soc.*, 666 (1944).

[18] W. Windus and P. R. Shildneck, "Organic Syntheses," A. H. Blatt, Ed., Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 345.

[19] S. Akabori, T. Kaneko and S. Motizuki, *J. Chem. Soc. Japan*, **59**, 1135 (1938).

[20] R. Brown and R. C. G. Moggridge, *J. Chem. Soc.*, 816 (1946).

[21] This was made in 49% yield by the method used by L. W. Jones and D. H. Powers, THIS JOURNAL, **46**, 2518 (1924), to prepare 2-chloroethyl methyl ether.

[22] S. Smiles, *J. Chem. Soc.*, **77**, 160 (1900).

[23] L. Dobbin and O. Masson, *J. prakt. Chem.*, [2] **31**, 36 (1885).

Anal. Calcd. for $C_6H_{15}IOS$: C, 27.5; H, 5.8; I, 48.4; S, 12.2. Found: C, 27.5; H, 5.4; I, 48.8; S, 12.3.

VIII picrylsulfonate was recrystallized from 95% ethanol, m.p. 156° with dec.

(b) **With Aqueous Sodium Hydroxide.**—The addition of 17.74 cc. of 0.2065 *N* sodium hydroxide to a solution of 1.019 g. of the VI bromide in 350 cc. of water was followed by the removal and titration of 10-cc. aliquots. After about 4 min. 99% of the hydroxide had been consumed and 98% of the non-ionic bromide had been liberated. Calculation gave a rough second-order rate constant of 100 l. mole^{-1} sec.$^{-1}$. A picrylsulfonate, m.p. 183° turning black, was obtained.

(c) **With Sodium Acetate.**—A solution of 2.498 g. of VI in 240 cc. of water was mixed with a solution of 1.172 g. of sodium acetate trihydrate in 50 cc. of water. Aliquots were titrated with standard silver nitrate solution over a period of 4 days from which the second order constant was determined: $k = 0.00487 \pm 0.00005$ l. mole^{-1} min.$^{-1}$.

(d) **With Silver Oxide.**—A stirred mixture of 2.3 g. of silver oxide and 5 g. of VI in 100 cc. of water was filtered from silver bromide after 5 min. The slightly basic (*p*H 7.5–8.0) solution was evaporated to dryness under reduced pressure at room temperature leaving a residue, crystallization of which from water–ethanol afforded 2.5 g. of **oxyethylene-bis-(dimethylsulfonium) (IX) bromide**; m.p. 183° with dec.

Anal. Calcd. for $C_8H_{20}Br_2OS_2$: C, 27.0; H, 5.7; Br, 44.9; S, 18.0. Found: C, 27.1; H, 5.9; Br, 44.5; S, 17.5.

IX picrylsulfonate, m.p. 197–198° with dec., was crystallized from water.

Anal. Calcd. for $C_{20}H_{24}N_6O_{19}S_4$: C, 30.8; H, 3.1; N, 10.8; S, 16.4. Found: C, 30.7; H, 3.2; N, 10.7; S, 16.0.

The freezing point depression of 0.428 g. of IX in 19.90 g. of water was 0.268°, corresponding to a cryoscopic mol. wt. of 150.3.

Dimethylvinylsulfonium (I) Bromide.—A solution of 25.0 g. of VI in 500 cc. of water was stirred with 11.5 g. of powdered, freshly prepared silver oxide for 10 min. The filtered solution was then acidified with acetic acid to *p*H 4 and evaporated to dryness at room temperature or below. The residual oil crystallized on being at 4° and was recrystallized from ethanol–ether to give **dimethylvinylsulfonium (I) bromide**: 10 g.; 59% of theory; m.p. 109–110° with dec. I bromide decomposed at room temperature in a few days.

Anal. Calcd. for C_4H_9BrS: C, 28.4; H, 5.4; Br, 47.3; S, 19.0. Found: C, 28.2; H, 5.6; Br, 47.0; S, 18.7.

The freezing point depression of 0.219 g. of I bromide in 19.93 g. of water was 0.207°, corresponding to a molecular weight of 98.7.

Dimethylvinylsulfonium (I) picrylsulfonate was crystallized from ethanol; m.p. 183° with dec. and blackening.

Anal. Calcd. for $C_{10}H_{11}N_3O_9S_2$: C, 31.5; H, 2.9; N, 11.0; S, 16.8. Found: C, 31.6; H, 2.5; N, 11.1; S, 17.1.

Dimethylvinylsulfonium (I) picrate was crystallized from ethanol; m.p. 154–155° with dec.

Anal. Calcd. for $C_{10}H_{11}N_3O_7S$: C, 37.9; H, 3.5; N, 13.3; S, 10.1. Found: C, 37.9; H, 3.5; N, 13.0; S, 10.1.

Reactions of Dimethylvinylsulfonium (I) Bromide with Nucleophilic Reagents. (a) **Ethanol.**—Five minutes after the addition of a drop of 5% aqueous sodium hydroxide to 2 g. of I bromide, in 10 cc. of ethanol, ether was added precipitating 2.4 g. of oil which was converted to **2-ethoxyethyldimethylsulfonium (VIII) picrylsulfonate**, m.p. 156° with dec.

Anal. Calcd. for $C_{12}H_{17}N_3O_{10}S_2$: C, 33.7; H, 4.0; N, 9.8; S, 15.0. Found: C, 33.5; H, 3.8; N, 10.1; S, 15.2.

(b) **Water.**—After five minutes, a solution of 1 g. of I bromide in 20 cc. of water containing a few drops of 5% sodium hydroxide was evaporated under reduced pressure at room temperature, leaving 0.98 g. (94%) of oxyethylene-bis-(dimethylsulfonium) (IX) bromide; m.p. 183° with dec. after crystallization from water–ethanol.

Anal. Calcd. for $C_8H_{20}Br_2OS_2$: C, 27.0; H, 5.7; Br, 44.9; S, 18.0; C–CH_3, 0.0. Found: C, 27.1; H, 5.5; Br, 45.0; S, 17.6; C–CH_3, 0.0.

The picrylsulfonate of IX was crystallized from water: m.p. 196–198° with dec.

Anal. Calcd. for $C_{20}H_{24}N_6O_{19}S_4$: C, 30.8; H, 3.1; N, 10.8; S, 16.4. Found: C, 31.1; H, 3.1; N, 10.7; S, 16.4.

(c) **Concentrated Potassium Hydroxide.**—A solution of 0.1 mole of potassium hydroxide in 25 cc. of water reacted with 5 g. (0.03 mole) of I bromide for 15 min. at room temperature, was then made acid with 48% hydrobromic acid, and concentrated *in vacuo* until precipitation occurred. Water was added till clear, followed by a large amount of absolute ethanol to give a precipitate of IX which was recrystallized from water–ethanol; m.p. 183° with dec.; picrylsulfonate, m.p. 197° with dec. The aqueous ethanol filtrate afforded 2-hydroxyethyldimethylsulfonium (X) picrylsulfonate, m.p. 154° with dec.

(d) **2-Phenoxyethanol.**—To 2.0 g. of I covered with 15 cc. of 2-phenoxyethanol, a drop of 5% aqueous sodium hydroxide was added. After 15 min., the addition of ether precipitated an oil which was washed twice with ether and crystallized from acetonitrile–ether to give 2.1 g. (72%) of **2-(2-phenoxyethoxy)-ethyldimethylsulfonium (XI) bromide**, m.p. 67–69° in a sealed tube.

Anal. Calcd. for $C_{12}H_{19}BrO_2S$: C, 46.9; H, 6.2; Br, 26.0; S, 10.4; C–CH_3, 0.0. Found: C, 47.0; H, 6.0; Br, 25.9; S, 10.2; C–CH_3, 0.0.

XI picrylsulfonate, m.p. 174°, was crystallized from water.

Anal. Calcd. for $C_{18}H_{21}N_3O_{11}S_2$: C, 41.6; H, 4.1; N, 8.1; S, 12.3. Found: C, 41.4; H, 4.1; N, 8.2; S, 12.0.

XI picrate, m.p. 144°, was crystallized from absolute ethanol.

Anal. Calcd. for $C_{18}H_{21}N_3O_9S$: C, 47.5; H, 4.7; N, 9.2; S, 7.0. Found: C, 47.4; H, 4.5; N, 9.0; S, 6.8.

(e) **Methyl Acetoacetate.**—On adding a drop of 5% aqueous sodium hydroxide to 2.0 g. of I bromide covered with 12 cc. of methyl acetoacetate, heat was evolved at once. After 5 min., the addition of 35 cc. of ether precipitated material which was crystallized from acetonitrile–ether as well as from alcohol–ether to yield 2.3 g. (68% of theory) of **3-acetyl-3-carbomethoxypropyldimethylsulfonium (XIII) bromide**, too hygroscopic for m.p. determination.

Anal. Calcd. for $C_9H_{17}BrO_3S$: C, 37.9; H, 6.0; Br, 28.0; S, 11.2. Found: C, 37.7; H, 6.0; Br, 27.9; S, 10.9.

The picrylsulfonate of XIII, m.p. 142–143°, was crystallized from water.

Anal. Calcd. for $C_{15}H_{19}N_3O_{12}S_2$: C, 36.2; H, 3.9; N, 8.5; S, 12.9. Found: C, 36.4; H, 3.5; N, 8.2; S, 12.4.

(f) **Diethyl Malonate.**—A mixture of 1.0 g. of I bromide, 10 cc. of diethyl malonate and a few drops of 5% aqueous sodium hydroxide was shaken for 15 min. whereupon a semi-solid oil had separated. The very hygroscopic product was crystallized from alcohol–ether and converted to **3,3-dicarboethoxypropyldimethylsulfonium (XII) picrylsulfonate**; 1.4 g.; 48%; m.p. 168–169° with dec., crystallized from water.

Anal. Calcd. for $C_{17}H_{23}N_3O_{13}S_2$: C, 37.7; H, 4.3; N, 7.8; S, 11.8. Found: C, 37.6; H, 4.2; N, 7.7; S, 11.5.

(g) **Methyl Mercaptan.**—Five minutes after adding 2 g. of I bromide to an aqueous solution of 1.5 g. of sodium methyl mercaptide, 48% hydrobromic acid was added at 0° until the solution was slightly acid. Distillation of the water under reduced pressure left crystalline material which was recrystallized from methanol to yield 2.4 g. (85%) of **2-methylmercaptoethyldimethylsulfonium (XIV) bromide**, m.p. 108–109° with dec.

Anal. Calcd. for $C_5H_{13}BrS_2$: C, 27.7; H, 6.0; Br, 36.8; S, 29.5; C–CH_3, 0.0. Found: C, 27.9; H, 6.2; Br, 36.9; S, 29.3; C–CH_3, 0.0.

XIV picrylsulfonate, crystallized from water, melted with dec. at 216–217°.

Anal. Calcd. for $C_{11}H_{15}N_3O_9S_3$: C, 30.8; H, 3.5; N, 9.8; S, 22.4. Found: C, 30.9; H, 3.5; N, 9.9; S, 22.0.

(h) **2-Mercaptoethanol.**—Upon adding a drop of 5% aqueous sodium hydroxide at 0° to 2.0 g. of I bromide suspended in 25 cc. of 2-mercaptoethanol, the mixture warmed at once. After shaking five minutes, the excess 2-mercaptoethanol was removed by washing several times with ether. The residue, not easily purified by crystallization, was converted to **2-(2-hydroxyethylmercapto)-ethyldimethylsulfonium (XV) picrylsulfonate** in a yield of 4.5 g. (83% of theory), m.p. 195–197° with dec. after crystallization from methanol.

Anal. Calcd. for $C_{12}H_{17}N_3O_{10}S_3$: C, 31.4; H, 3.7; N, 9.2; S, 20.9; C–CH$_3$, 0.0. Found: C, 31.0; H, 3.5; N, 9.0; S, 20.6; C–CH$_3$, 0.0.

The picrate of XV, m.p. 162° with dec., was crystallized from absolute ethanol.

Anal. Calcd. for $C_{12}H_{17}N_3O_8S_2$: C, 36.5; H, 4.3; N, 10.6; S, 16.2. Found: C, 36.2; H, 4.1; N, 10.9; S, 16.0.

(i) **Thiourea.**—After a solution of 2.0 g. of I and 0.9 g. of thiourea in the minimum amount of water had been shaken 15 min., the calculated amount of 48% hydrobromic acid (1.5 cc.) was added, followed by a large amount of absolute ethanol. The precipitated **2-isothiouronium-ethyldimethylsulfonium (XVII) bromide hydrobromide** weighed 1.85 g. (48%) and melted at 146° with dec.

Anal. Calcd. for $C_5H_{14}Br_2N_2S_2$: C, 18.4; H, 4.3; Br, 49.0; N, 8.6; S, 19.7; C–CH$_3$, 0.0. Found: C, 18.4; H, 4.6; Br, 49.3; N, 8.6; S, 20.0; C–CH$_3$, 0.0.

XVII dipicrate, m.p. 191° with dec., was crystallized from water.

Anal. Calcd. for $C_{17}H_{18}N_8O_{14}S_2$: C, 32.8; H, 2.9; N, 18.0; S, 10.3. Found: C, 32.9; H, 3.0; N, 17.9; S, 10.2.

2-Ethoxyethyldimethylsulfonium (VIII) Iodide.—A solution of 3.0 g. of 2-ethoxyethyl methyl sulfide and 3.5 g. of methyl iodide in 5 cc. of acetonitrile deposited, after 4 days at room temperature, a precipitate from which VIII iodide was obtained by crystallization from ethanol–ether: 5.3 g.; 82% of theor. yield; m.p. 60–62° with dec.

Anal. Calcd. for $C_6H_{15}IOS$: C, 27.5; H, 5.8; I, 48.4; S, 12.2. Found: C, 27.5; H, 5.9; I, 48.2; S, 11.9.

VIII picrylsulfonate, m.p. 156–157° with dec., was crystallized from 95% ethanol.

Anal. Calcd. for $C_{12}H_{17}N_3O_{10}S_2$: C, 33.7; H, 4.0; N, 9.8; S, 15.0. Found: C, 34.0; H, 4.1; N, 9.6; S, 14.8.

With methyl bromide an oily bromide giving the same picrylsulfonate was obtained.

Oxyethylene-bis-(dimethylsulfonium) Bromide (IX).—Bis-(2-mercaptoethyl) ether was prepared from bis-(2-chloroethyl) ether by the thiourea method.[24] A stirred solution of 34 g. of bis-(2-mercaptoethyl) ether and 20 g. of sodium hydroxide in 400 cc. of 50% aqueous ethanol was treated with 71 g. of methyl iodide and refluxed for 4 hr. Addition of 600 cc. of water caused the separation of an organic layer which was dried over sodium sulfate and carefully fractionated to give 25 g. (61%) of **bis-(2-methylmercaptoethyl) ether (XIX)**; b.p. 97° at 4 mm., d^{26}_4 1.049, n^{26}_D 1.5059.

Anal. Calcd. for $C_6H_{14}OS_2$: C, 43.3; H, 8.5; S, 38.6; MR_D, 47.5. Found: C, 43.5; H, 8.6; S, 38.3; MR_D, 47.1.

Sealed in an ampoule at −10°, 3.5 g. of XIX and 2 g. of methyl bromide in absolute ethanol were at room temperature for 3 days. The resulting precipitate of IX was recrystallized from water–ethanol, m.p. 182° with dec.

Anal. Calcd. for $C_8H_{20}Br_2OS_2$: C, 27.0; H, 5.7; Br, 44.9; S, 18.0. Found: C, 26.7; H, 5.6; Br, 44.5; S, 17.8.

The picrylsulfonate of IX, m.p. 197° with dec., was recrystallized from water.

Anal. Calcd. for $C_{20}H_{24}N_6O_{19}S_4$: C, 30.8; H, 3.1; N, 10.8; S, 16.4. Found: C, 30.5; H, 3.0; N, 10.5; S, 16.8.

2-Hydroxyethyldimethylsulfonium (X) Salts.—After 5 hr. at room temperature, a solution of 1.8 g. of 2-hydroxyethyl methyl sulfide and 2.8 g. of methyl iodide gave a precipitate which was recrystallized from methanol–water to yield 4.1 g. (89%) of the X iodide; m.p. 61–62° with dec. (reported m.p. 60–62°[25]).

Anal. Calcd. for $C_4H_{11}IOS$: C, 20.5; H, 4.7; I, 54.2; S, 13.7. Found: C, 20.5; H, 4.5; I, 54.0; S, 13.3.

X picrylsulfonate, m.p. 153–154° with dec., was crystallized from 95% ethanol.

Anal. Calcd. for $C_{10}H_{13}N_3O_{10}S_2$: C, 30.1; H, 3.3; N, 10.5; S, 16.1. Found: C, 29.9; H, 3.3; N, 10.4; S, 16.1.

A mixture of 14 g. of X iodide and 0.04 g. of sodium hydroxide in 10 cc. of water reacted for 24 hr. and was then extracted with three 25-cc. portions of ether, no organic material remaining after evaporation of the ether. Evaporation of the aqueous solution to dryness *in vacuo* left a residue which was crystallized from methanol–ether to give 12.9 g. (92%) of recovered X iodide; m.p. 60–61.5° with dec.; X picrylsulfonate, m.p. 153–154° with dec.

2-(2-Phenoxyethoxy)-ethyldimethylsulfonium (XI) Salts.—The reaction mixture obtained by adding 47 g. of 2-bromoethyl methyl sulfide (V) to a hot solution prepared from 130 g. of 2-phenoxyethanol and 7 g. of sodium, was heated on the steam-bath for 2 hr. The organic product, separated by adding 200 cc. of water, was dried and fractionally distilled to give 44 g. (58%) of **2-(2-phenoxyethoxy)-ethyl methyl sulfide (XX)**; b.p. 115–116° at 0.5 mm., d^{26}_4 1.079, n^{26}_D 1.5331.

Anal. Calcd. for $C_{11}H_{16}O_2S$: C, 62.2; H, 7.6; S, 15.1; MR_D, 61.1. Found: C, 62.6; H, 7.7; S, 15.1; MR_D, 61.1.

A solution of 4 g. of XX and 2 g. of methyl bromide in 2 cc. of acetonitrile was sealed in an ampoule, allowed to react for 4 days at room temperature and diluted with ether. Recrystallization of the resulting precipitate from alcohol–ether afforded 3.5 g. (60%) of **2-(2-phenoxyethoxy)-ethyldimethylsulfonium (XI) bromide**; m.p. 69–70° with dec.; very hygroscopic.

Anal. Calcd. for $C_{12}H_{19}BrO_2S$: C, 46.9; H, 6.2; Br, 26.0; S, 10.4. Found: C, 46.8; H, 6.1; Br, 25.8; S, 10.1.

XI picrylsulfonate, m.p. 174°, was recrystallized from water.

Anal. Calcd. for $C_{18}H_{21}N_3O_{11}S_2$: C, 41.6; H, 4.1; N, 8.1; S, 12.3. Found: C, 41.5; H, 4.1; N, 8.2; S, 12.1.

3-Acetyl-3-carbomethoxypropyldimethylsulfonium (XIII) Salts.—A solution of sodio methyl acetoacetate, made from 35 g. of methyl acetoacetate and 7 g. of sodium in 120 cc. of absolute ethanol, to which 47 g. of 2-bromoethyl methyl sulfide (V) had been added slowly, was refluxed for 1 hr. The organic layer, separated by adding 350 cc. of water, was dried over sodium sulfate and fractionally distilled, giving 31.0 g. of methyl (2-methylmercaptoethyl)-acetoacetate (XXI); b.p. 116–117° at 3 mm., d^{26}_4 1.073, n^{26}_D 1.4709.

Anal. Calcd. for $C_8H_{14}O_3S$: C, 50.5; H, 7.4; S, 16.9; MR_D, 48.8. Found: C, 50.8; H, 7.7; S, 16.5; MR_D, 49.6.

A mixture of 1.0 g. of methyl bromide and 1.9 g. of XXI in acetonitrile was sealed in an ampoule and let be at room temperature for 4 days. Dilution with ether afforded a precipitate which was crystallized from acetonitrile–ether to yield 1.7 g. (58%) of **XIII bromide**, too hygroscopic for m.p. determination.

Anal. Calcd. for $C_9H_{17}BrO_3S$; C, 37.9; H, 6.0; Br, 28.0; S, 11.2. Found: C, 37.7; H, 6.1; Br, 27.7; S, 11.0.

XIII picrylsulfonate, m.p. 142–143° with dec., was crystallized from water.

Anal. Calcd. for $C_{15}H_{19}N_3O_{12}S_2$: C, 36.2; H, 3.9; N, 8.5; S, 12.9. Found: C, 36.3; H, 4.2; N, 8.4; S, 12.5.

2-Methylmercaptoethyldimethylsulfonium (XIV) Salts.—Prepared from ethylene bromide and sodium mercaptide,[26] 4.0 g. of 1,2-bis-methylmercaptoethane and 1.5 g. of methyl bromide were cooled at −10° and sealed in an ampoule. After 24 hr., the precipitate (3.8 g., 88%) was filtered and recrystallized from methanol to give **XIV bromide**, m.p. 108–109° with dec.

Anal. Calcd. for $C_5H_{13}BrS_2$: C, 27.7; H, 6.0; Br, 36.8; S, 29.5. Found: C, 27.4; H, 6.2; Br, 37.1; S, 29.4.

XIV picrylsulfonate, m.p. 216–217° with dec., was crystallized from water.

Anal. Calcd. for $C_{11}H_{15}N_3O_9S_3$: C, 30.8; H, 3.5; N, 9.8; S, 22.4. Found: C, 31.0; H, 3.6; N, 10.0; S, 22.1.

2-(2-Hydroxyethylmercapto)-ethyldimethylsulfonium (XV) Picrylsulfonate.—A boiling solution of 40 g. of 2-bromoethyl methyl sulfide (V), 10.5 g. of sodium hydroxide, 20 g. of mercaptoethanol and 150 cc. of methanol was re-

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(24) C. M. Hull, L. A. Weinland, S. R. Olsen and W. G. France, *Ind. Eng. Chem.*, **40**, 513 (1948).

(25) J. v. Braun, E. Anton and K. Weissbach, *Ber.*, **63**, 2847 (1930).

(26) G. T. Morgan and W. Ledbury, *J. Chem. Soc.*, **121**, 2882 (1922).

fluxed for one hour. The organic product, separated by adding 300 cc. of water, was dried, together with a chloroform extract of the aqueous layer, over sodium sulfate and distilled *in vacuo* to give 29 g. of **2-hydroxy-2'-methylmercaptodiethyl sulfide (XVI)**; b.p. 122–123° at 4 mm., d^{26}_4 1.135, n^{26}_D 1.5440.

Anal. Calcd. for $C_5H_{12}OS_2$: C, 39.4; H, 8.0; S, 42.1; *MR*D, 42.6. Found: C, 39.2; H, 7.9; S, 41.9; *MR*D, 42.6.

A mixture of 1.5 g. of XVI and 1 g. of methyl bromide, cooled to 0°, was sealed in an ampoule for 2 days at room temperature. The separated oil was washed twice with ether and twice with ethyl acetate, could not be crystallized conveniently and was converted to **XV picrylsulfonate**; m.p. 195–197° with dec. after crystallization from methanol.

Anal. Calcd. for $C_{12}H_{17}N_3O_{10}S_3$: C, 31.4; H, 3.7; N, 9.2; S, 20.9. Found: C, 31.2; H, 3.8; N, 9.3; S, 20.7.

XV picrate was crystallized from absolute ethanol; m.p. 162° with dec.

Anal. Calcd. for $C_{12}H_{17}N_3O_8S_2$: C, 36.5; H, 4.3; N, 10.6; S, 16.2. Found: C, 36.8; H, 4.1; N, 10.7; S, 16.0.

2-Isothiouroniumethyldimethylsulfonium (XVII) Bromide Hydrobromide.—A solution of 15 g. of thiourea in 100 cc. of 95% ethanol containing 31 g. of 2-bromoethyl methyl sulfide (V) was refluxed for 3 hr. The resulting precipitate was recrystallized from ethanol to yield 40 g. (86%) of **S-2-methylmercaptoethylisothiouronium bromide (XXII)**; m.p. 104–105° with dec.

Anal. Calcd. for $C_4H_{11}BrN_2S_2$: C, 20.8; H, 4.8; Br, 34.6; N, 12.1; S, 27.7. Found: C, 20.9; H, 4.7; Br, 34.8; N, 12.4; S, 27.7.

At room temperature for 3 days, a sealed ampoule containing 2 g. of XXII, 5 cc. of methanol and 3 g. of methyl bromide, yielded a precipitate which was crystallized from water–ethanol. There was obtained 4.2 g. (91%) of XVII bromide hydrobromide, m.p. 145–146° with dec.

Anal. Calcd. for $C_5H_{14}Br_2N_2S_2$: C, 18.4; H, 4.3; Br, 49.0; N, 8.6; S, 19.7. Found: C, 18.7; H, 4.2; Br, 48.8; N, 8.8; S, 19.2.

XVII dipicrate, m.p. 191°, was crystallized from water.

Anal. Calcd. for $C_{17}H_{18}N_8O_{14}S_2$: C, 32.8; H, 2.9; N, 18.0; S, 10.3. Found: C, 32.7; H, 3.1; N, 17.9; S, 10.3.

2-Methoxyethyldimethylsulfonium Iodide.—A solution of equivalent amounts of sodium methyl mercaptide and 2-chloroethyl methyl ether was refluxed 6 hr. and diluted with water to yield an organic layer which was separated. This layer and an ether extract of the aqueous phase were dried and distilled, giving 2-methoxyethyl methyl sulfide, b.p. 132° (reported[27] b.p. 131° at 755 mm.). A mixture of 4 g. of this sulfide and 5 g. of methyl iodide reacted 3 days at 4° to produce an oil which was washed with ethyl acetate and crystallized from methanol–ether to give 6.5 g. (72%) of **2-methoxyethyldimethylsulfonium iodide**.

Anal. Calcd. for $C_5H_{13}IOS$: C, 24.2; H, 5.3; I, 51.2; S, 12.9. Found: C, 24.5; H, 5.1; I, 51.0; S, 13.0.

The picrylsulfonate, m.p. 216° with dec., was crystallized from 95% ethanol.

Anal. Calcd. for $C_{11}H_{15}N_3O_{10}S_2$: C, 32.0; H, 3.6; N, 10.2; S, 15.5. Found: C, 31.8; H, 3.6; N, 9.8; S, 15.6.

2-Acetoxyethyldimethylsulfonium Iodide.—2-Acetoxyethyl methyl sulfide, prepared according to Challenger and Simpson,[28] reacted with methyl iodide in acetonitrile, giving an oil which was washed with ethyl acetate thrice and recrystallized from ethanol–ether; m.p. 72–73° with dec.

Anal. Calcd. for $C_6H_{13}IO_2S$: C, 26.1; H, 4.7; I, 46.0; S, 11.6. Found: C, 26.3; H, 5.1; I, 46.1; S, 11.8.

The picrate, m.p. 133°, was recrystallized from ether.

The picrylsulfonate, m.p. 161–162° with dec., was crystallized from 95% ethanol.

Anal. Calcd. for $C_{12}H_{15}N_3O_{11}S_2$: C, 32.7; H, 3.4; N, 9.5; S, 14.5. Found: C, 32.9; H, 3.6; N, 9.8; S, 14.1.

Ethyl S-(2-Methylmercaptoethyl)-xanthate.—A solution of potassium ethyl xanthate (76 g.) and 2-bromoethyl methyl sulfide (V, 73 g.) in 160 cc. of 95% ethanol was refluxed for 3 hr. and diluted with twice the volume of water. The ether extract was dried and distilled to give 45 g. (50%) of ethyl S-(2-methylmercaptoethyl)-xanthate, b.p. 110° at 2 mm., d^{25}_4 1.159.

Anal. Calcd. for $C_6H_{12}OS_3$: C, 36.7; H, 6.2; S, 49.0. Found: C, 36.8; H, 6.2; S, 48.6.

Reaction of Bromocholine Bromide (VII) with Sodium Hydroxide.—A mixture of 60 g. of choline chloride was refluxed 48 hr. with 300 cc. of 48% hydrobromic acid and freed of water and excess acid by distillation *in vacuo*. Recrystallization of the residue from absolute ethanol afforded 59 g. (55%) of bromocholine bromide; m.p. 232–234° with dec.; reported[29] m.p. 230–231°.

This method is less convenient than the preparation from trimethylamine and excess ethylene bromide.[29]

The reaction of 6.556 millimoles of VII in 240 cc. of water with 31.81 cc. of 0.2065 *N* sodium hydroxide was followed by removing aliquots and titrating with standard silver nitrate solution, the second-order rate constant being 0.00362 ± 0.00001 l. mole^{-1} sec.$^{-1}$. After two weeks, the reaction was concentrated *in vacuo* leaving a residue which was converted to the picrate. Choline picrate was isolated in amount of 1.0 g. (59%); m.p. 246°, reported m.p. 246°.[30]

Reaction of Neurine (II) Bromide with Nucleophilic Reagents.—Neurine bromide, prepared from bromocholine bromide by the method of Renshaw and Ware[14] (m.p. 192–193° with dec., reported[14] m.p. 192–193°), was hydrogenated with platinum catalyst in water, 98% of one mole of hydrogen being absorbed. The hygroscopic residue remaining after removal of water *in vacuo* was converted to trimethylethylammonium picrate in 85% of the theoretical yield; m.p. 299–300°, reported m.p. 299–300°.[31]

(a) **Ethanol.**—A solution of 5 g. (0.03 mole) of neurine (II) bromide in 30 cc. of absolute ethanol containing 0.05 g. of sodium hydroxide reacted 7 days at room temperature and was diluted with ether to precipitate recovered neurine bromide; 4.6 g. (92%) after three recrystallizations from ethanol--ether; m.p. 192° with dec.

(b) **Water.**—A similar experiment in water afforded recovery of II in 94% of theoretical, no other product being detectable.

(c) **2-Phenoxyethanol.**—A similar experiment in 2-phenoxyethanol as solvent led again to recovered starting material (89%) only.

(d) **2-Mercaptoethanol.**—The mixture of 60 g. of 2-mercaptoethanol, 10 g. of neurine (II) bromide and 0.05 g. of sodium hydroxide, after 7 days at room temperature, was diluted with three volumes of ether. The precipitated oil was washed twice with ether and crystallized 5 times from ether, giving 8.4 g. of recovered neurine bromide; m.p. 191–192° with dec. Distillation of the ether solution yielded 40.5 g. (81%) of 2-mercaptoethanol.

Repeated at 78° for 24 hr., the same reaction afforded 6.2 g. of recovered II; m.p. 192° with dec. Decomposition was inferred from the odor of trimethylamine.

(e) **Sodium Thiosulfate.**—Neurine bromide (440 mg.) was added to 25 cc. of 0.2019 *M* sodium thiosulfate and brought to 50 cc. in a volumetric flask. Ten-cc. aliquots were removed and titrated. After three days, 98% of the original thiosulfate had remained unreacted.

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