148. *The Alkaline Fission of Some 2-Substituted Dimethylethylsulphonium Iodides.*

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The action of alkali on five compounds of the general structure $R{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{S}Me_2\}I^-$ (R = Ph·CO·O, PhO, MeS, Ph·CO·NH, and Ph·CH_2·NH) has been investigated. The behaviour of the last three compounds is normal but the first two are remarkably sensitive to alkali and undergo " double elimination ", thus :

$$R{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{S}Me_2\}I^- \longrightarrow RH + CH{:}CH + SMe_2 + HI$$

The theoretical basis of this novel reaction is discussed and its possible utility in synthetic and degradative work is pointed out.

The work now described was stimulated by various observations (Northrop; du Vigneaud; Ball; private communications, 1942—1943) that the products of the action of " mustard gas " on proteins were more easily split by alkali than would be expected if they had the simple structure (I). It seemed to us that this alkali-lability might be due to the formation of sulphonium salts of the general type (II), and we accordingly carried out a number of experiments on model compounds of types (III) and (IV), corresponding to (I) and (II), respectively, in which R was Ph·CO·O, PhO, MeS, Ph·CO·NH, and Ph·CH_2·NH to simulate combination with carboxyl, phenolic hydroxyl, thiol, amide, and amino-groups in the protein molecule. The results of these

Protein—$CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}CH_2Cl$ (I.)

Protein—$CH_2{\cdot}CH_2{\cdot}\overset{+}{S}(CH_2{\cdot}CH_2Cl)_2\ \underset{\sim}{Cl^-}$ (II.)

$R{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_3$ (III.)

$R{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{S}(CH_3)_2\ \underset{\sim}{I^-}$ (IV.)

experiments seem of sufficient general interest to warrant publication, irrespective of whether they do or do not throw any light on the mode of action of " mustard gas."

Dimethyl-2-benzoyloxyethylsulphonium iodide (VI) was prepared as follows :

$$HO{\cdot}CH_2{\cdot}CH_2{\cdot}SMe \xrightarrow{Ph{\cdot}COCl} Ph{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}SMe\ (V.) \xrightarrow{MeI} Ph{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{S}Me_2\}I^-\ (VI.)$$

It is remarkably easily decomposed in alkaline solution, liberating two equivalents of acid (one of benzoic acid, one of hydriodic). Under identical conditions (M/100-solution in 60% alcohol at 25° and pH 11) the sulphonium salt (VI) liberates 1 equiv. of acid in 4 mins. whereas the parent *methyl 2-benzoyloxyethyl sulphide* (V) shows no trace of hydrolysis in 9 hours. In aqueous solution the liberation of acid follows first-order kinetics; the following data relate to the liberation of the first equivalent of acid :

Rate of hydrolysis of (VI) *in aqueous solution at* 25°.

Initial concn. of (VI), M	0·01	0·02	0·02
pH (maintained constant)	10	10	11
k (min.$^{-1}$)	0·0089	0·0078	0·079
Time for 50% change (mins.)	77·6	88·6	8·8

Even at pH 7·4 and 37° slight hydrolysis occurs, 0·02 equiv. of acid being liberated under these conditions in 6 hours. Qualitative experiments, in which the sulphonium salt (VI) was boiled with 10% sodium hydroxide solution, resulted in the isolation or detection as reaction products of acetylene (detected qualitatively only), dimethyl sulphide (60% yield), and benzoic acid (100% yield), together with a little methyl iodide. Clearly the main reaction is the following unusual decomposition :

$$Ph\cdot CO\cdot O\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- + 2NaOH \longrightarrow Ph\cdot CO_2Na + CH{:}CH + SMe_2 + NaI + 2H_2O$$

accompanied to a small extent by simple dissociation of the sulphonium iodide into the sulphide (V) and methyl iodide.

Dimethyl-2-phenoxyethylsulphonium iodide (VIII) was prepared as follows :

$$Cl\cdot CH_2\cdot CH_2\cdot SMe \xrightarrow{PhONa} \underset{(VII.)}{PhO\cdot CH_2\cdot CH_2\cdot SMe} \xrightarrow{MeI} \underset{(VIII.)}{PhO\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^-}$$

Once again the sulphonium salt (VIII) is much more alkali-labile than the corresponding sulphide, *methyl 2-phenoxyethyl sulphide* (VII), the latter being quite unaffected by 5 minutes' boiling with 40% sodium hydroxide solution whereas the former is measurably and rapidly hydrolysed at 100°, even at pH 7·4. It will be seen from the details given on p. 770 that the rate of hydrolysis of (VIII) is markedly influenced by pH. The alkaline fission of (VIII) is rather less rapid than that of (VI), an M/100-solution of (VIII) being only 5% hydrolysed in 180 mins. at pH 10 and 25°, conditions under which (VI) is 25% hydrolysed in 78 mins. Nevertheless, the alkali-lability of (VIII) is quite remarkable, decomposition of M/100-solutions being complete within one minute at pH values of 10 or higher. Isolation experiments, in which (VIII) was boiled with 10% sodium hydroxide solution, showed that the main decomposition was into phenol (isolated in 85% yield), dimethyl sulphide (39% yield), and acetylene (detected qualitatively only), thus :

$$PhO\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- + 2NaOH \longrightarrow PhONa + CH{:}CH + SMe_2 + NaI + 2H_2O$$

There was also about 10% of simple dissociation into methyl iodide and the sulphide (VII).

Dimethyl-2-methylthioethylsulphonium iodide (IX) was much less sensitive to alkali; no free thiol groups could be detected by iodometric titration when this compound was kept in M/100-solution at 25° and pH 10, 11, or 12 for periods up to 5½ hours. With boiling 10% sodium hydroxide traces of thiol compounds could be detected by the nitroprusside reaction in the early stages, but the principal reaction appeared to be fission to dimethyl and methyl vinyl sulphides, thus :

$$\underset{(IX.)}{SMe\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^-} + NaOH \longrightarrow SMe\cdot CH{:}CH_2 + SMe_2 + NaI + H_2O$$

No acetylene could be detected in the reaction products; there was a little dissociation into methyl iodide and 1 : 2-bismethylthioethane.

Dimethyl-2-benzamidoethylsulphonium iodide (X), on being boiled with 10% sodium hydroxide gave, as the only isolated products, dimethyl sulphide (65% yield), 2-phenyl-4 : 5-dihydro-oxazole (XII) (43% yield), and benzoic acid (11% yield); monoethanolamine, although almost certainly present, could not be isolated; acetylene could not be detected. Since control experiments showed that (XII) is partly hydrolysed under our reaction conditions, it seems reasonable to represent the action of alkali on (X) as a simple elimination reaction followed by cyclisation

of the intermediate *N*-vinylbenzamide (XI) to the oxazoline (XII), which is then partly hydrolysed :

$$\underset{\text{(X.)}}{Ph\cdot CO\cdot NH\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^-} \longrightarrow Me_2S + \underset{\text{(XI.)}}{[Ph\cdot CO\cdot NH\cdot CH{:}CH_2]}$$

$$Ph\cdot CO_2H + NH_2\cdot CH_2\cdot CH_2\cdot OH \longleftarrow \underset{\text{(XII.)}}{PhC(=N)O\cdot CH_2\cdot CH_2}$$

Dimethyl-2-benzylaminoethylsulphonium iodide (XIII) was very stable to alkali, no free amino-groups being liberated in M/100-solution at pH 12 even at 100°. With boiling 10% sodium hydroxide the decomposition was complex, the isolated reaction products being methyl vinyl sulphide, benzyldimethylamine, *methyl 2-benzylaminoethyl sulphide* (XIV) and *benzyldimethyl-(2-methylthioethyl)ammonium iodide* (XV); no acetylene was formed. Since the ammonium salt (XV), which may be prepared by the action of methyl iodide on the base (XIV) in alkaline solution, is partly split into methyl vinyl sulphide and benzyldimethylamine under our reaction conditions, the following is the probable course of the alkaline fission of (XIII) :

(i) $\underset{\text{(XIII.)}}{CH_2Ph\cdot NH\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^-} \longrightarrow \underset{\text{(XIV.)}}{CH_2Ph\cdot NH\cdot CH_2\cdot CH_2\cdot SMe} + MeI$

(ii) $(XIV) + 2MeI + NaOH \longrightarrow \underset{\text{(XV.)}}{CH_2Ph\cdot \overset{+}{N}Me_2\cdot CH_2\cdot CH_2\cdot SMe\}I^-} + NaI + H_2O$

(iii) $(XV) + NaOH \longrightarrow CH_2Ph\cdot NMe_2 + CH_2{:}CH\cdot SMe + NaI + H_2O$

Clearly, the main initial reaction here is dissociation, followed by a number of secondary reactions.

Focusing attention on the initial changes, we may summarise our results by saying that the alkaline fission of the five β-substituted-ethyldimethylsulphonium iodides studied takes place by way of one or more of the following three reactions :

$$R\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- \begin{cases} \longrightarrow RH + CH{:}CH + SMe_2 + HI & (\text{" Double elimination "}) \\ \longrightarrow R\cdot CH{:}CH_2 + SMe_2 + HI & (\text{" Single elimination "}) \\ \longrightarrow R\cdot CH_2\cdot CH_2\cdot SMe + MeI & (\text{" Dissociation "}) \end{cases}$$

" Double elimination " predominates when R = Ph·CO·O or PhO, " single elimination " when R = MeS or Ph·CO·NH, and dissociation when R = Ph·CH_2·NH. The last two reactions are well known and it is unnecessary to discuss them further; so far as we know, however, the " double elimination " reaction is new and so warrants some discussion.

Before discussion of the reaction its potentialities as a new method for the protection of carboxyl and phenolic hydroxyl groups in sensitive compounds may be pointed out; for instance, such a compound could be converted into the 2-methylthioethyl ester or ether, the derivative subjected to other desired reactions, and the protecting group eventually removed by conversion into the methiodide followed by very mild alkaline treatment.

A thorough kinetic study of the double elimination reaction was not possible, so our discussion of the mechanism of the reaction is necessarily speculative. Our experimental data do not in themselves show whether the liberation of dimethyl sulphide precedes, follows, or is simultaneous with that of benzoic acid (or phenol). Let us consider the possible steps in a two-stage mechanism; it is at once clear that both stages must be eliminations since, were either of them a hydrolysis, the two-carbon reaction product would necessarily be, not acetylene, but acetaldehyde (vinyl alcohol), *e.g.* :

$$RO\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- \xrightarrow{\text{elimination}} HI + SMe_2 + RO\cdot CH{:}CH_2 \xrightarrow{\text{hydrolysis}} ROH + HO\cdot CH{:}CH_2$$

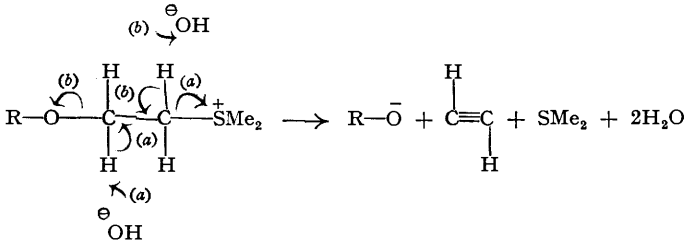
There remain, therefore, only two possible two-stage routes, *viz.* :

(A) $RO\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- \longrightarrow HI + SMe_2 + \underset{\text{(XVI.)}}{RO\cdot CH{:}CH_2} \longrightarrow ROH + CH{:}CH$

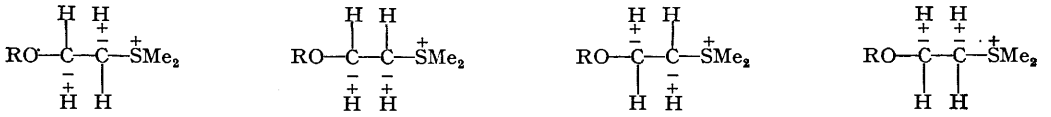
(B) $RO\cdot CH_2\cdot CH_2\cdot \overset{+}{S}Me_2\}I^- \longrightarrow ROH + \underset{\text{(XVII.)}}{CH_2{:}CH\cdot \overset{+}{S}Me_2\}I^-} \longrightarrow CH{:}CH + HI + SMe_2$

Neither vinyl benzoate (XVI; R = Ph·CO) nor phenyl vinyl ether (XVI; R = Ph) appears to be specially sensitive to alkali, and so Route (A) may be discarded. The perchlorate of (XVII) was prepared by Hofmann, Höbold, and Quoos (*Annalen*, 1912, **386**, 317) who make no mention of any marked instability to alkali; neurine iodide, the nitrogen analogue of (XVII), is alkali-stable (cf. Renshaw and Ware, *J. Amer. Chem. Soc.*, 1925, **47**, 2993), and the corresponding hydroxide decomposes on distillation into trimethylamine, dimethylvinylamine, and acetaldehyde (Meyer and Hopff, *Ber.*, 1921, **54**, 2278); clearly Route (B) is, by itself, no more acceptable than Route (A).

We are thus led to postulate some kind of single-stage process, such as :



in which the two electronic processes (*a*) and (*b*) (which correspond to Routes A and B respectively) are coupled in some way, perhaps somewhat along the lines suggested by Robinson (*J.*, 1941, 220) for the benzidine change. The same idea may be expressed in different terms (cf. Hughes and Ingold, *ibid.*, p. 608) as a lowering of the activation energy resulting from resonance between the various possible ionic structures of the activated molecule :



In either case the necessary conditions for the occurrence of " double elimination " are, first, the presence on the α-carbon atom of a positively charged atom with a sufficient tendency to lose its positive charge [providing the driving force of electronic process (*a*)] and, secondly, the presence on the β-carbon atom of a sufficiently powerfully electron-attracting group [providing the driving force of electronic process (*b*)]. The first of these requirements probably explains why similar phenomena are not, apparently, exhibited by the nitrogen analogue of (VI), *viz.*, benzoylcholine (cf. Easson and Stedman, *Proc. Roy. Soc.*, 1936, *B*, **121**, 142; cf. acetylcholine, Renshaw and Bacon, *J. Amer. Chem. Soc.*, 1926, **48**, 1726; Kahane and Rousseau, *Bull. Soc. chim.*, 1939, **6**, 647). The second requirement fits in well with our observation that, of the five compounds of type (IV) which we have investigated, only those in which RH is most acidic [*viz.*, (VI) in which RH = Ph·CO_2H and (VIII) in which RH = PhOH] show the " double elimination " reaction.

Experimental.

1. *Dimethyl-2-benzoyloxyethylsulphonium Iodide.*—(a) *Preparation.* Methyl 2-hydroxyethyl sulphide (51 g.) was added slowly, with cooling and shaking, to a mixture of benzoyl chloride (86 g.) and dry pyridine (60 g.). After being heated on the water-bath for 2 hours, the mixture was cooled and treated with water. The precipitated oil was taken up in light petroleum (b. p. 40—60°), dried, and distilled, yielding 54 g. (50%) of *methyl 2-benzoyloxyethyl sulphide* (V) as a colourless oil, b. p. 137—138°/2·5 mm. (Found : C, 61·2; H, 5·9. $C_{10}H_{12}O_2S$ requires C, 61·2; H, 5·1%). This sulphide (14 g.) was kept at room temperature for 20 hours with methyl iodide (12 g.). The resulting crystalline mass was washed with dry ether and twice recrystallised from absolute alcohol, yielding *dimethyl-2-benzoyloxyethylsulphonium iodide* (VI) as colourless plates, m. p. 128—129° (decomp.) (Found : C, 39·0; H, 4·4. $C_{11}H_{15}O_2IS$ requires C, 39·1; H, 4·5%). The *picrate* crystallised from acetone in silky yellow needles, m. p. 151—152° (Found : C, 46·4; H, 3·8. $C_{17}H_{17}O_9N_3S$ requires C, 46·4; H, 3·9%).

(b) *Isolation of alkali fission products.* The sulphonium iodide (VI) (11·6 g.) was slowly distilled with 10% sodium hydroxide solution (33 c.c.) for 2 hours. The volatile oil which collected (1·3 g.) was identified as dimethyl sulphide (62% yield) by its b. p. (37—38°) and by conversion into the mercurichloride, m. p. and mixed m. p. 149—151°; the presence of a little methyl iodide was shown by the deposition of a small amount of trimethylsulphonium iodide, decomp. 215°, when the volatile oil was kept for a few days. Exhaustive ether extraction of the aqueous residue in the reaction flask failed to yield any methyl 2-hydroxyethyl sulphide; acidification of the aqueous residue yielded benzoic acid (4·2 g.; 100%), m. p. and mixed m. p. 121—122°. In a separate experiment, the presence of acetylene

in the gaseous products of the decomposition was demonstrated by the formation of a red precipitate of copper acetylide with cuprous chloride–hydroxylamine.

(c) *Quantitative experiments.* The rate of production of acid in dilute aqueous solution at 25° at pH 10 (phenolphthalein) and pH 11 (alizarin-yellow) was determined by continuous titration with baryta, using the apparatus of Powell and Trendall (*Chem. and Ind.*, 1943, **62**, 368). The velocity constants given on p. 767 were obtained by the usual logarithmic plotting method, the experimental points (20—40 for each experiment) falling satisfactorily on straight lines over the major portion of the experiment. The rate of hydrolysis at pH 7·4 and 37° was determined manometrically in a Warburg apparatus using bicarbonate buffer.

For comparative purposes, since the sulphide (V) is very sparingly soluble in water, its rate of fission was compared with that of the sulphonium iodide (VI) by continuous titration at 25° in 60% alcohol, alizarin-yellow being used as indicator, with the results quoted on p. 767.

2. *Dimethyl-2-phenoxyethylsulphonium Iodide.*—(a) *Preparation.* Methyl 2-chloroethyl sulphide (55 g.) was added to a solution of phenol (47 g.) and sodium hydroxide (20 g.) in 95% alcohol (500 c.c.). After 4 hours' refluxing the neutral product was filtered, concentrated under reduced pressure, diluted with water, and extracted with ether. The ethereal extract contained much phenol and was washed with 10% sodium hydroxide solution until the washings no longer gave a positive reaction with Folin's phenol reagent. The extract, washed once more with water, was dried and distilled, giving *methyl 2-phenoxyethyl sulphide* (VII) as a colourless oil, b. p. 120°/7 mm., $n_D^{19°}$ 1·5419 (Found: C, 64·05; H, 6·95. $C_9H_{12}OS$ requires C, 64·3; H, 7·1%). This substance still gave a negative reaction with Folin's phenol reagent after being boiled for 5 mins. with 40% sodium hydroxide solution.

The sulphide (VII) (30 g.) was refluxed on the water-bath for an hour with methyl iodide (51 g.). The almost solid product was triturated with ether and separated; crystallisation from methanol–ether yielded *dimethyl-2-phenoxyethylsulphonium iodide* (VIII) (34 g.; 61%) in beautiful leaflets, m. p. 104° (decomp.) (Found: C, 38·9; H, 5·0. $C_{10}H_{15}OIS$ requires C, 38·7; H, 4·85%).

(b) *Isolation of alkali fission products.* The sulphonium iodide (VIII) (15·5 g.; 0·05 mol.) was distilled with 2N-sodium hydroxide (100 c.c.), distillation being stopped when no more oil came over (15 mins.). The oil was separated, dried, and distilled. The low-boiling fraction (1·2 g.; 39%) was identified as dimethyl sulphide by b. p. (37—42°) and by conversion into the mercurichloride, m. p. and mixed m. p. 148°; the presence of a little methyl iodide was shown by the deposition of a small amount of trimethylsulphonium iodide, decomp. 215°, on keeping. The high-boiling fraction (1·4 g.; 9%), b. p. 108—110°/4 mm., was identified as methyl 2-phenoxyethyl sulphide (VII) by conversion into the methiodide (VIII), m. p. and mixed m. p. 102—103°. The aqueous residue from the alkali fission was acidified and extracted with ether; evaporation yielded phenol (4·0 g.; 85%), identified by conversion into tribromophenol and picric acid. In a separate experiment the presence of acetylene in the gaseous products was established by the formation of a red precipitate of copper acetylide with cuprous chloride–hydroxylamine.

(c) *Quantitative experiments.* M/100-Solutions of the sulphonium iodide (VIII) in appropriate buffers (M/10-borate for pH 8, 9, 10, and 11; M/15-phosphate for pH 7·4) were kept at specified temperatures for various times. To 1 c.c. of the resulting solutions 5 drops of Folin's phenol reagent were added, followed by 1 c.c. of 10% sodium hydroxide. After 5 mins.' keeping the mixture was centrifuged and the supernatant liquid matched visually, after suitable dilution, with standards prepared from M/1000-phenol. The results, expressed as % fission, were as follows:

pH.	Temp.: 25°.	37°.	100°.
7·4	—	2% in 48 hrs.	10% in 1 min.
8·0	—	2% in 16 hrs.	10% in 1 min.
9·0	—	10% in 16 hrs.	20% in 1 min.
10·0	5% in 3½ hrs.	15% in 16 hrs.	100% in 1 min.
11·0	10% in 1 hr.	33% in 16 hrs.	100% in 1 min.
12·0	100% in 20 mins.	—	100% in 1 min.

3. *Dimethyl-2-methylthioethylsulphonium Iodide* (IX).—(a) *Preparation.* 1 : 2-Bismethylthioethane (10 g.) was refluxed on the water-bath for 2½ hrs. with methyl iodide (12 g.) and alcohol (5 c.c.). After cooling, the yellow crystalline product was washed with acetone and recrystallised from alcohol, from which the *iodide* (IX) (14·2 g.; 64%) separated in prisms, m. p. 94—95° (Found: C, 22·9; H, 4·8; I, 48·4. $C_5H_{13}IS_2$ requires C, 22·7; H, 4·9; I, 48·1%).

(b) *Isolation of alkali fission products.* The sulphonium iodide (IX) (22 g.) was slowly distilled with 10% sodium hydroxide solution (134 c.c.) for 2½ hours, the distillate being collected in two portions. The first portion contained 8·1 g. of a light oil which was separated, dried, and heated on the water-bath for 30 mins. with thiophenol (2·5 g.); fractionation of the product yielded dimethyl sulphide, b. p. 37—38° (mercurichloride, m. p. and mixed m. p. 151—152°), which contained a little methyl iodide since it deposited trimethylsulphonium iodide, decomp. 212°, on keeping, and phenyl 2-methylthioethyl sulphide, b. p. 117°/2 mm. (mercurichloride, m. p. and mixed m. p. 81—82°), derived from methyl vinyl sulphide present in the fission product. The oil in the second portion of the fission distillate was identified as 1 : 2-bismethylthioethane by conversion into the mercurichloride, m. p. and mixed m. p. 106—107°.

In a separate experiment no acetylene could be detected in the gaseous products of the fission; a positive nitroprusside reaction was given by the reaction mixture after 2—3 mins.' boiling but disappeared later.

(c) *Quantitative experiments.* Iodometric titration of M/100-solutions of the sulphonium iodide (IX) in M/10-borate buffers, pH 10, 11, and 12, kept at 25° for periods up to 5½ hrs., revealed no appreciable thiol formation.

4. *Dimethyl-2-benzamidoethylsulphonium Iodide.*—(a) *Preparation.* Methyl 2-aminoethyl sulphide was best prepared by the following application of the method of Brighton and Reid (*J. Amer. Chem. Soc.*,

1943, **65**, 458): An alcoholic solution of sodium thiomethoxide (from 9·3 g. of sodium, 63 g. of methyl*iso*thiourea sulphate, and 150 c.c. of absolute alcohol) was added to an alcoholic solution of 2-bromoethylamine (from 82·5 g. of the hydrobromide, 9·3 g. of sodium, and 150 c.c. of absolute alcohol), and the mixture heated under reflux for 4 hrs.; sodium bromide was filtered off from the cooled solution, and the alcohol distilled off after addition of concentrated hydrochloric acid (31 c.c.). The residue was treated with 50% potassium hydroxide solution, and the liberated base extracted with ether, dried, and distilled, b. p. 148—150° (25·5 g., 50%).

Methyl 2-aminoethyl sulphide (30 g.) was added, in small portions, with cooling and shaking, to a mixture of benzoyl chloride (50 g.) and pyridine (100 c.c.). After being heated on the water-bath for an hour, the product was cooled and diluted with water; crystallisation of the precipitated solid from benzene–light petroleum (b. p. 60—80°) yielded methyl 2-benzamidoethyl sulphide (28 g.; 47%) in pearly plates, m. p. 60—61° (Schneider, *Annalen*, 1912, **386**, 338, gives m. p. 57°) (Found: C, 61·1; H, 6·8; N, 7·8. Calc. for $C_{10}H_{13}ONS$: C, 61·5; H, 6·7; N, 7·2%). This sulphide (16 g.) was kept for 24 hrs. at room temperature with methyl iodide (22 g.) in absolute alcohol (15 c.c.); crystallisation of the precipitate from alcohol yielded *dimethyl-2-benzamidoethylsulphonium iodide* (X) (21·7 g.; 80%) in plates, m. p. 121—122° (Found: C, 39·4; H, 4·7; N, 4·6. $C_{11}H_{16}ONIS$ requires C, 39·2; H, 4·75; N, 4·2%).

(b) *Isolation of alkali fission products.* The sulphonium iodide (X) (16 g.) was slowly distilled (2 hrs.) with 10% sodium hydroxide solution (76 c.c.). A light oil distilled over first, followed by a heavy oil which only distilled over with difficulty. The reaction mixture was finally refluxed for a further hour.

The light oil was identified as dimethyl sulphide (65% yield) by conversion into the mercurichloride, m. p. and mixed m. p. 150—151°. The heavy oil remaining in the flask was extracted with ether, dried, and distilled; the distillate, b. p. 80—81°/1 mm., was identified as 2-phenyl-4 : 5-dihydro-oxazole (XII) (3 g.; 43%) (Found: C, 73·6; H, 6·5; N, 9·3. Calc. for C_9H_9ON: C, 73·5; H, 6·1; N, 9·5%) by conversion into the hydrochloride, plates, m. p. 81° (lit. m. p. 81°), from light petroleum (b. p. 40—60°), and the picrate, yellow needles from benzene, m. p. and mixed m. p. 177—178°, which, on boiling with water, yielded 2-benzoyloxyethylamine picrate, orange plates from water, m. p. and mixed m. p. 195°. The aqueous residue in the reaction flask was acidified, yielding 0·6 g. (11%) of benzoic acid, m. p. and mixed m. p. 119—120°. No acetylene could be detected as a reaction product.

In a control experiment, the compound (XII) (Wenker, *J. Amer. Chem. Soc.*, 1935, **57**, 1079) was boiled with 10% sodium hydroxide solution for 3 hrs.; 65% of the oxazoline was recovered unchanged and a 20% yield of benzoic acid was isolated. In a second control experiment, methyl 2-benzamidoethyl sulphide was refluxed for 1·25 hrs. with 10% sodium hydroxide solution; 86% was recovered unchanged, some 2·5% being hydrolysed to benzoic acid and methyl 2-aminoethyl sulphide (picrate, m. p. and mixed m. p. 119—120°).

5. *Dimethyl-2-benzylaminoethylsulphonium Iodide.*—(a) *Preparation.* Following Dawson (*J. Amer. Chem. Soc.*, 1933, **55**, 2070), methyl 2-chloroethyl sulphide (22·1 g.) and benzylamine (21·4 g.) were refluxed on the water-bath for 23 hrs. with absolute alcohol (100 c.c.) and anhydrous sodium carbonate (21·2 g.). The cooled product was filtered and evaporated to small bulk under reduced pressure; the residue was treated with 30% potassium hydroxide solution, extracted with ether, and dried over potassium hydroxide. Two distillations yielded 8 g. (25%) of *methyl 2-benzylaminoethyl sulphide* (XIV), b. p. 139—140°/5·5 mm. (Found: C, 66·8; H, 8·2; N, 7·4. $C_{10}H_{15}NS$ requires C, 66·2; H, 8·3; N, 7·7%), which was characterised as its *hydrochloride*, plates, m. p. 238—240°, from alcohol (Found: C, 54·8; H, 7·7. $C_{10}H_{16}NSCl$ requires C, 55·2; H, 7·4%), and its *picrate*, fine needles from aqueous alcohol, m. p. 116—117° (Found: C, 46·7; H, 4·2. $C_{16}H_{18}O_7N_4S$ requires C, 46·8; H, 4·4%). This sulphide (XIV) (11·1 g.), in absolute alcohol (20 c.c.), was kept for some days with methyl iodide (8·7 g.); the crystalline precipitate obtained on adding ether was recrystallised from alcohol–ether, yielding *dimethyl-2-benzylaminoethylsulphonium iodide* (XIII) (5·5 g.; 30%) as shining plates, m. p. 132—133° (Found: C, 40·7; H, 5·8; N, 3·9. $C_{11}H_{18}NIS$ requires C, 40·9; H, 5·6; N, 4·3%).

(b) *Alkaline fission.* (i) Isolation of reaction products. The sulphonium iodide (XIII) (8 g.) was slowly distilled for 2 hrs. with 10% sodium hydroxide, 25 c.c. of water being added during this period. The distillate, collected in two portions, contained 2 g. of an oil lighter than water and 0·8 g. of an oil heavier than water; the residue in the distilling flask contained an oil and deposited a crystalline solid on cooling.

The light oil in the distillate was separated, dried, and distilled, yielding three fractions. Fraction (1), 0·2 g., b. p. 25—60°, was too small for further separation but was probably a mixture of dimethyl and methyl vinyl sulphides; fraction (2), 0·65 g., b. p. 60—155°, was basic and was identified as benzyldimethylamine by conversion into the picrate, yellow needles from water, m. p. and mixed m. p. 94—95°. Fraction (3), 0·4 g., b. p. >155°, was identified as methyl 2-benzylaminoethyl sulphide (XIV) by conversion into the picrate, m. p. 114—115°, mixed m. p. 116—117°. The heavy oil in the distillate and that remaining in the reaction flask were collected by ether extraction and identified as methyl 2-benzylaminoethylsulphide (XIV) by conversion into the picrate, m. p. and mixed m. p. 115—116°, and hydrochloride, m. p. and mixed m. p. 235—237°. The crystalline solid remaining in the reaction flask was not extracted by ether; it was filtered off and recrystallised from alcohol, forming long needles, m. p. 149—150°, identified as benzyldimethyl-(2-methylthioethyl)ammonium iodide (XV) by mixed m. p., 150—151°, with a synthetic specimen (below). Acetylene could not be detected as a reaction product.

In a control experiment the sulphide (XIV) was recovered unchanged (96% yield) after refluxing for 2½ hrs. with 10% sodium hydroxide solution.

(ii) Quantitative experiments. No liberation of free primary amino-groups could be detected, a volumetric Van Slyke apparatus being used, in 2 hrs. when the sulphonium iodide (XIII) was kept in M/100-solution in water at 25°, in borate buffer pH 12 at 25° and 100°, or in 10% sodium hydroxide at 25°.

(iii) Synthesis of reaction products. Methyl 2-benzylaminoethyl sulphide (XIV) (3 g.) was treated, with shaking, with methyl iodide (5 g.) and 10% sodium hydroxide solution (10 c.c.). On cooling *benzyldimethyl-(2-methylthioethyl)ammonium iodide* (XV) crystallised out, and recrystallised from alcohol

in long silky needles, m. p. 150—151° (Found : C, 42·6; H, 5·9; I, 36·9. $C_{12}H_{20}NIS$ requires C, 42·7; H, 5·9; I, 37·7%). This iodide (XV) (13·8 g.) was distilled for 3 hrs. with 10% sodium hydroxide solution (56 c.c.); on cooling, 3·3 g.(24%) of unchanged iodide crystallised out in the distillation flask. The volatile product (5·7 g.) was separated, dried, and distilled, yielding two fractions. Fraction (1), b. p. 65—70°, was identified as methyl vinyl sulphide by heating on the water-bath with thiophenol, whereupon it yielded phenyl 2-methylthioethyl sulphide, characterised as its *mercurichloride*, m. p. and mixed m. p. 81—82° (Found : C, 24·0; H, 3·0. $C_9H_{12}Cl_2S_2Hg$ requires C, 23·7; H, 2·6%). Fraction (2), b. p. 165—172°, was identified as benzyldimethylamine by conversion into the picrate, m. p. and mixed m. p. 94—95°.

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