

THE SULFONIUM SALT OF MUSTARD GAS: BIS- $\beta$ -[BIS( $\beta$ -HYDROXYETHYL) SULFONIUM] ETHYLSULFIDE DICHLORIDE (H·2TDG)\*

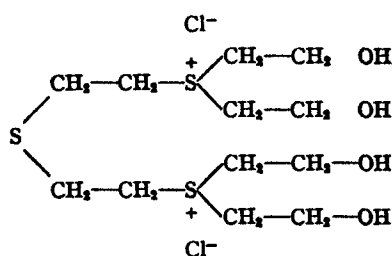
By ROGER M. HERRIOTT

(From the Laboratories of The Rockefeller Institute for Medical Research, Princeton, New Jersey)

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The results of some solubility determinations of H (1) indicated that in dilute aqueous solutions, H participates in the formation of compounds resembling the sulfonium salts described by Davies and Oxford (2). These authors prepared the H·2TDG sulfonium salt bis- $\beta$ -[bis ( $\beta$ -hydroxyethyl) sulfonium] ethylsulfide dichloride from a non-aqueous mixture of mustard (bis ( $\beta$ -chloroethyl)

Formula I



sulfide) (H) and thiodiglycol (TDG). They stated that this compound is a true salt, both chlorine atoms being ionized, and that aqueous solutions of it are relatively stable at room temperature but decompose rapidly at 100°C., liberating 2 equivalents of HCl.

The experiments reported here show that in dilute aqueous solutions of TDG and H, the sulfonium salt H·2TDG is formed in appreciable amounts (see Fig. 1 and Table I). Similar observations were made by others (4, 6). During the hydrolysis of dilute aqueous solutions of H, a compound is formed which hydrolyzes faster than H·2TDG but not as fast as H and which is probably H·1TDG. The latter was not isolated.

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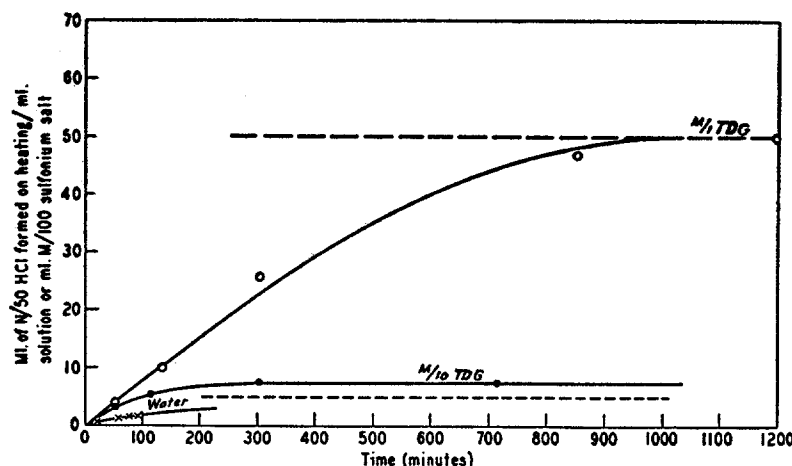
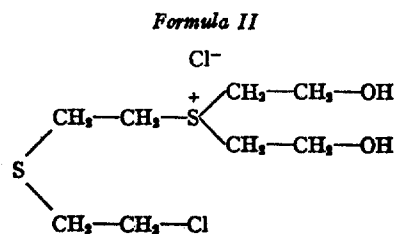


FIG. 1. Formation of  $H \cdot 2TDG$  sulfonium salt by stirring  $H$  in  $M/10$  and  $M/1$   $TDG$  solutions. The broken lines are the limiting values expected from a stoichiometric reaction in which one mol of  $H$  reacts with two mols of  $TDG$ .

*I. Formation of the Sulfonium Salt  $H \cdot 2TDG$  in Dilute Aqueous Solutions of  $TDG$  and  $H$*

Fig. 1 represents the formation of a sulfonium salt when  $H$  is shaken in  $M/10$  and  $M/1$   $TDG$  solutions at room temperature. The two to one stoichiometric relationship between the concentration of  $TDG$  and the equilibrium concentration of the sulfonium salt was indicative of the nature of the compound. The slightly higher than stoichiometric equilibrium value obtained with  $M/10$   $TDG$  (see Fig. 1) may have been due to the formation of  $TDG$  during the reaction as a result of hydrolysis of  $H$  or to the formation of some sulfonium compound  $H \cdot 1TDG$ .

It should be mentioned that whereas the formation of  $H \cdot 2TDG$  almost certainly takes place in solution, the system studied was heterogeneous,  $H$  being only slightly soluble in water (saturated = 1 mg. per ml.). The suspensions were shaken mechanically until all the  $H$  had dissolved and presumably reacted with either the  $TDG$  or water.

TABLE I  
Preparation of the Sulfonium Chloride Salt  $H \cdot 2TDG$  from  $H$  and Dilute TDG

	No.	Vol.	Melting point (corrected)
		mi.	°C.
10 ml. of TDG (carbon-carbide kromfax solvent) was diluted to 100 ml. with water then 5 ml. redistilled $H$ was added and shaken vigorously for 8 hrs. 2 ml. more $H$ was added and shaken 10 hrs. Practically all the $H$ had disappeared. This was then mixed with 1 liter of acetone; shaken and the two layers allowed to separate.			
Upper layer.....	1		
Lower layer.....	2	20	
No. 2 shaken with 80 ml. acetone and centrifuged.			
Upper layer.....	3		
Lower layer.....	4	15	
No. 4 warmed to 55°C. and absolute alcohol added until the solution remained turbid. On cooling two layers separated.			
Upper layer.....	5		
Lower layer.....	6		
A few drops of the upper layer No. 5 were placed on a microscope slide or evaporating dish and soon crystallized. Using these for inoculation of the lower layer, No. 6, set to a solid crystalline paste which was washed with 95 per cent alcohol and dried.....	7		97-100
No. 7 recrystallized from 200 ml. of hot 95 per cent alcohol plus water to dissolve, filtered, and washed with alcohol and dried.....	8		100.5
No. 8 recrystallized from 200 ml. of hot 95 per cent alcohol plus water to dissolve, cooled to 5°C., filtered, and washed.....	9		103
Davies and Oxford product.....			103

*Elementary Analyses of Sulfonium Chloride Salt*

Element	Calculated from formula	Found	Davies and Oxford
	per cent	per cent	per cent
C	35.7	35.7	35.5
H	6.94	7.0	7.0
Total Cl	17.6	17.5	17.5
Chloride ion	17.6	17.5	
S	23.8	23.4	23.5

It may be seen from the results in Fig. 1 that the rate of formation of the sulfonium salt in TDG solutions was greater than in water and the equilibrium quantity was approximately proportional to the TDG concentration. A large proportion of the reaction product was demonstrated to be  $H \cdot 2TDG$  by its isolation and identification, the details of which are described in Table I.

*Formation in Aqueous Solutions of H*

Since TDG is a product of hydrolysis of H, it was of some interest to determine to what extent  $H \cdot 2TDG$  was formed during the hydrolysis of H solutions. The complete course of hydrolysis of an aqueous solution of H is shown in Fig. 2. In the first hour during which the free H disappeared, the liberation of acid was logarithmic ( $K = 0.12$ ) but after this there was an abrupt change in rate followed by a gradual change continuing for many hours. Approximately 93 per cent of the calculated quantity of acid was liberated during the initial drop.

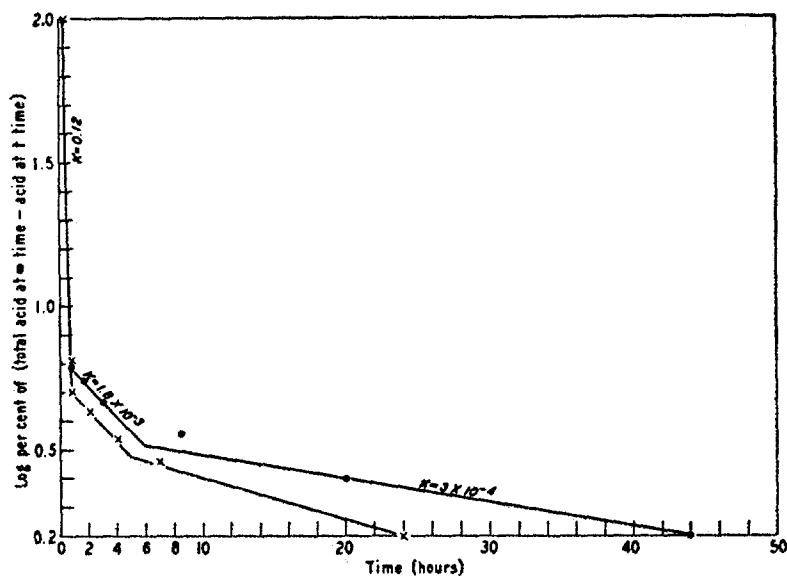


FIG. 2. Hydrolysis of  $3.2 \times 10^{-3}$  M H at  $25^\circ\text{C}$ ., in distilled water.

The abrupt change in logarithmic plot (Fig. 2) at this point was taken as indicating the presence of another acid-liberating product. It is noteworthy that even at its slowest, the rate of acid formation was many times faster than the rate of acid formation in dilute solutions of crystalline  $H \cdot 2TDG$  at  $25^\circ\text{C}$ . for which  $K =$  about  $3 \times 10^{-5}$  (see Table II). A difference was also noted in the hydrolysis rates at  $100^\circ\text{C}$ . The unstable material formed during the hydrolysis of H in aqueous solutions at  $25^\circ\text{C}$ . decomposed at  $100^\circ\text{C}$ . liberating acid within a minute whereas  $H \cdot 2TDG$  required 20 to 30 minutes (see Table II).

Rydon (3), Stein, Moore, and Bergmann (4), and Powell and Rydon (5) have noted that the sulfonium salt  $H \cdot 1TDG$  hydrolyzes considerably faster than  $H \cdot 2TDG$  and that it hydrolyzes in two steps. The formation of acid in solutions of pure mustard (Fig. 2) after the first hour is strikingly similar to the results of Stein *et al.* (4) for the formation of acid in solutions of pure  $H \cdot 1TDG$ .

In both instances the slope of the logarithmic plot changes when about half the acid is liberated and the slopes of the curves for the two materials agree within a factor of 1.5.

The material formed in water solutions of H has not been studied further except to show that it is precipitated from dilute solution by the reagent  $\text{KHgI}_3$  (6) as readily as is  $\text{H}\cdot 2\text{TDG}$ . An estimation of the concentration from the hydrolysis curves in Fig. 2 indicates that between 5 and 8 per cent of the active H in an aqueous solution goes into the formation of this salt. This was qualitatively confirmed by comparing the quantity of precipitate formed by addition of  $\text{KHgI}_3$  with that formed with various concentrations of purified  $\text{H}\cdot 2\text{TDG}$ . No purified  $\text{H}\cdot 1\text{TDG}$  was available for comparison.

TABLE II  
*Hydrolysis of M/100 H·2TDG at different temperatures*

Temperature	$K$ (monomolecular)*	$\frac{Q_0}{Q_1}$ or $\left(\frac{K_{12}}{K_{11}}\right)^{10/(t_2 - t_1)}$
°C.		
20	$1.45 \times 10^{-4}$	4.0
25.5	$3.1 \times 10^{-4}$	4.0
37	$1.5 \times 10^{-4}$	3.6
75	$2.0 \times 10^{-4}$	2.4
100	$1.8 \times 10^{-4}$	

\* In calculating these hydrolysis constants, the time was measured in minutes.

It may be tentatively concluded from the rates of hydrolysis that the unknown fraction in water is  $\text{H}\cdot 1\text{TDG}$  rather than  $\text{H}\cdot 2\text{TDG}$ . Other things being equal this would be expected from a simple kinetic theory, when the concentration of H is high in proportion to the TDG.

### II. Method of Preparation of $\text{H}\cdot 2\text{TDG}$

The results in an earlier section are strong evidence that  $\text{H}\cdot 2\text{TDG}$  is formed when H reacts with aqueous solutions of TDG. More conclusive evidence was obtained by its isolation as described in Table I from an aqueous solution of TDG after shaking with H overnight. The table is self-explanatory and needs no comment except to state that it is unfortunate that the products were not weighed, thus no quantitative figure of the yield could be included. However, it is estimated that the yield of once crystallized product was reasonably good.

### III. Hydrolysis of $m/100$ H·2TDG at Different Temperatures

The rate of hydrolysis of  $m/100$  crystalline H·2TDG has been determined at different temperatures and the results are shown in Table II. A temperature coefficient,  $Q_{10}$ , *i.e.* the ratio of the velocity constants at temperatures differing by  $10^{\circ}\text{C}$ , for this reaction was 3-4. This is slightly higher than many chemical reactions but is close to that obtained by Hopkins (7) for the hydrolysis of H in aqueous solutions.

Fig. 3 is a plot of the logarithm of the velocity constant against the reciprocal of the absolute temperature. The straight line obtained shows that the

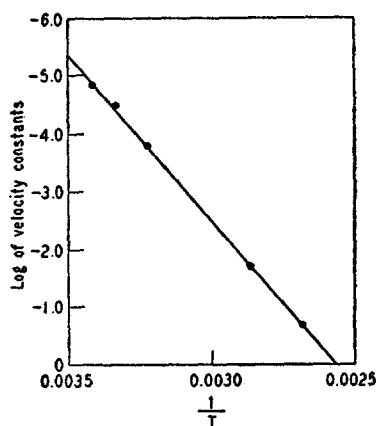


FIG. 3. The effect of temperature on the hydrolysis of  $m/100$  H·2TDG as indicated by Arrhenius equation  $\ln k = -\frac{A}{RT} + C$ .

Arrhenius equation,  $\ln k = -\frac{A}{RT} + C$ , relating the reaction rate  $k$  to the temperature is applicable to this reaction. The slope of this curve gives a value of the activation energy  $A$  equal to 26,000 calories.

#### SUMMARY

1. The sulfonium salt H·2TDG is formed when H is mixed with even dilute solutions of TDG. Crystalline H·2TDG was isolated from such a reaction mixture. A simple method of preparation of this salt is outlined.

2. A material which differs from H·2TDG in that it hydrolyzes faster, is formed when H hydrolyzes in water. This material is probably H·1TDG but it was not isolated. Approximately 5 to 8 per cent of the original H is converted to this sulfonium salt.

3. The hydrolysis constant of  $M/100$   $H \cdot 2TDG$  has been determined at  $20^\circ$ ,  $25.5^\circ$ ,  $37^\circ$ ,  $75^\circ$ , and  $100^\circ C.$ , a temperature coefficient,  $Q_{10}$ , of 3-4 was obtained. The effect of temperature is in agreement with that predicted by the Arrhenius equation. An activation energy of 26,000 calories was calculated.

#### EXPERIMENTAL DETAILS

##### *Titrimetric Method of Determining Sulfonium Compounds*

A method of determining the sulfonium compounds  $H \cdot 1TDG$  and  $H \cdot 2TDG$  was developed, based on their low rate of hydrolysis relative to  $H$ . The method is applicable to mixtures of  $H$  and the sulfonium compounds. It consists of diluting an aliquot to reduce the concentration of any inhibiting substances such as chloride ion; allowing the free  $H$  to hydrolyze during a 30 minute period at  $25^\circ C.$  followed by a titration of the free acid; and finally heating this same aliquot in a water bath until there is no further liberation of acid. At  $100^\circ C.$  the period of heating was 20 to 30 minutes. A titration of this second liberation of acid served as a measure of the sulfonium compound. Some additional and independent information is required to decide whether the compound is  $H \cdot 1TDG$  or  $H \cdot 2TDG$ .

##### *Experimental Procedure used in Fig. 1*

1.0 ml. of c.p. mustard was added to 15 ml. of  $M/10$  and  $M/1$   $TDG$  solutions in glass-stoppered bottles and shaken mechanically at  $25^\circ C.$  Aliquots were removed, diluted 5 to 50 times to lower the chloride concentration, and the solution allowed to stand 30 minutes to allow the free  $H$  to hydrolyze. The free acid thus liberated was neutralized and then the sample heated until no more acid was liberated. The second titration was plotted in Fig. 2 against the time when the sample was taken from the reaction mixture.

##### *Experimental Procedure Used in Fig. 2*

To 500 ml. of distilled water at  $25^\circ C.$  was added 0.2 ml. of c.p.  $H$  (m.p. 14.2 to 14.5) and the flask shaken hard for a minute. The  $H$  dissolved completely. The entire contents was then titrated at intervals with  $NaOH$  using methyl red as an indicator. The concentration of  $NaOH$  was  $N/1$  during the first 30 minutes and  $N/50$  thereafter. The logarithm of the unliberated acid is plotted in Fig. 2 against the time of titrating. The total acid liberated agreed closely with the value expected from the concentration of  $H$  used. In calculating the hydrolysis constants  $K$  shown in Fig. 2 the time was measured in minutes, not hours as used in the abscissa of this figure.

##### *Experimental Procedure Used in Table II*

202 mg. ( $5 \times 10^{-4}$  mols) of twice crystallized  $H \cdot 2 \cdot TDG$  was dissolved in 50 ml. of distilled water at various temperatures and the liberation of acid determined titrimetrically on 5 ml. aliquots. The temperatures were controlled to  $\pm 0.5^\circ$  except at  $75^\circ C.$  which was  $\pm 1^\circ C.$

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