CCCCIX.—*The Influence of the Sulphur Atom on the Reactivity of Adjacent Atoms or Groups. Part V. Comparative Reactivities of a Series of Nine Homologous ω-Hydroxy-sulphides.*

By G. MACDONALD BENNETT and A. NEVILLE MOSSES.

THE quantitative comparison of the reactivities of the chlorine atoms in β- and γ-chloro-sulphides with respect to hydrolysis or to the reaction with iodides, which was described in Part II of this series (J., 1927, 1676), could not be extended to the δ- and ε-chloro-sulphides owing to the fact that internal self-addition takes precedence of other reactions with these substances (Part III, J., 1929, 2567).

A preliminary comparison of the behaviour of γ-, δ-, and ε-hydroxy-sulphides having shown that a hydroxyl group in the δ-position relative to a sulphur atom reacts with hydrobromic acid much faster than one in the γ- or the ε-position (Part IV, J., 1930, 2364), it seemed desirable to make a quantitative comparison of the reactivities of these substances and at the same time to include as long a series of homologues as possible so that the significance of the data for the earlier members of the group might be clearly demonstrated. The possibility that the high reactivity found for the δ-hydroxyl group would recur at some point further along the growing carbon chain also required investigation. The simple aliphatic alcohol cetyl alcohol was, moreover, included in the series for purposes of comparison.

Systematic investigations of the reactivities of alcohols have been made in more than one way during the past fifty years. The classical work of Menschutkin (*Annalen*, 1879, **195**, 334; **197**, 193) relates to the velocities of reaction of alcohols with acetic acid; and a series of papers by Norris and collaborators (*J. Amer. Chem. Soc.*, 1925, **47**, 837; 1927, **49**, 1166, 2640; 1928, **50**, 1000) has dealt with the action of acyl and of diarylmethyl chlorides on alcohols. These reactions are of a different polar type from that between an alcohol and hydrobromic acid with which we are concerned. The latter reaction has received attention recently from Levene and Rothen (*J. Biol. Chem.*, 1929, **81**, 359), who did not, however, obtain constant velocity coefficients. During the progress of the present investigation, a preliminary account of work on this subject has been published by Norris (*Rec. trav. chim.*, 1929, **48**, 885).

According to the method described below, with phenol as solvent, we have found it possible, by use of the equation for a reversible bimolecular reaction, to obtain satisfactory velocity coefficients and consequently a valid comparison of the reactivities of these substances.

General Equation for a Reversible Reaction of the Second Order.—If the concentrations of reactants in the system $A + B \rightleftharpoons C + D$ are initially a, b, c, and d, and after time t are $(a - x)$, $(b - x)$, $(c + x)$, and $(d + x)$ respectively; and if the value of x at equilibrium is n, then

$$dx/dt = k_1(a - x)(b - x) - k_2(c + x)(d + x) \quad . \quad . \quad (1)$$

where k_1 and k_2 are the coefficients of the reaction to the right and the left respectively. Then at equilibrium

$$k_1/k_2 = K = (c + n)(d + n)/(a - n)(b - n)$$

whence

$$n = \frac{K(a+b) + (c+d) - \sqrt{[K(a+b)+c+d]^2 - 4(abK - cd)(K-1)}}{2(K-1)}$$

Substituting for k_2 in equation (1), we have

$$\begin{aligned} dx/dt &= k_1[(a - x)(b - x)K - (c + x)(d + x)]/K \\ &= k_1[Kab - cd - \{K(a + b) + c + d\}x + x^2(K - 1)]/K \\ &= k_1(x - n)(x - \overline{n + E})\,(K - 1)/K \end{aligned}$$

where $E = \dfrac{\sqrt{[K(a + b) + c + d]^2 - 4(abK - cd)(K - 1)}}{K - 1}$

Finally, by integration and simplification, we obtain

$$k_1 = \frac{2{\cdot}3K}{(K - 1)(t_2 - t_1)E} \log_{10} \frac{(x_2 - \overline{n + E})(x_1 - n)}{(x_2 - n)(x_1 - \overline{n + E})}$$

This equation is applied below.

Hydrolysis of β- and γ-Chloro-sulphides.—A comparison of the speeds of hydrolysis of β- and γ-chloro-sulphides was made with aqueous-alcoholic solutions in Part II of this series (J., 1927, 1676). In such a reaction, alcoholysis might conceivably occur as a subsidiary reaction (compare Kirner, *J. Amer. Chem. Soc.*, 1928, **50**, 2446), although the isolation of the pure hydroxy-compound formed from *p*-nitrophenyl β-chloroethyl sulphide seemed to negative the idea. We therefore take this opportunity to record an examination of the hydrolysis of a β- and a γ-chloro-sulphide in 50% aqueous acetone. The former substance was hydrolysed according to the unimolecular law and many times faster than the latter, thus confirming the earlier result.

EXPERIMENTAL.

The hydroxy- and chloro-sulphides used in this work were prepared as described elsewhere (this vol., p. 1697).

Experiments on the Hydrolysis of β- and γ-Chloro-sulphides.—The hydrolysis of phenyl β-chloroethyl sulphide proceeds in 50% aqueous acetone at about two-thirds of the rate in aqueous alcohol. The liberated hydrochloric acid was shown by a separate test to be unaffected by the acetone under the conditions of the experiment.

The chloro-sulphide (1/4000 mol.), dissolved in carefully purified acetone (5 c.c. with 5 c.c. of water), was sealed in a glass tube and heated in a constant-temperature bath controlled to $\pm$ 0·1°. The free acid or chlorion was determined in successive tubes removed at intervals.

With phenyl β-chloroethyl sulphide at 60·0° successive values of the velocity coefficient $k \times 10^4$ were 98, 96, 92; mean 96; and at 80·0° 418, 405, 370, 415; mean 402. The temperature coefficient per 10° is therefore 2·05.

With β-chloroethyl *n*-butyl sulphide the hydrolysis at 80° was instantaneous.

On the other hand, the reaction was so slow with phenyl and *n*-propyl γ-chloropropyl sulphides as to make accurate comparative measurement impossible. These substances were practically unaffected after being heated in 50% aqueous acetone at 80° for several weeks. They were, however, hydrolysed to the extent of about 60% when the solutions were heated at 150° for 7 hours.

Measurements of Reactivities of Hydroxy-sulphides with Hydrobromic Acid.—The hydroxy-compound (1/800 mol.), dissolved in phenol (2·0 c.c.) containing hydrogen bromide (1/400 mol.) and water (1/80 mol.), was sealed into glass tubes and heated in a bath kept to constant temperature within $\pm$0·1°. Tubes removed at definite times were rapidly cooled, opened, and their contents titrated with

0·1N-sodium hydroxide, bromophenol-blue being used as indicator. The concentration of bromion was then determined by means of standard silver and thiocyanate solutions. The velocity coefficients below are derived from the acidimetric observations : the significance of the observed bromion concentrations will be referred to later. For the calculation of accurate molar concentrations, the volume (V) of the reaction mixtures at various temperatures was determined with the aid of a small calibrated dilatometer. The data for one sulphide are given in detail :

Phenyl β-hydroxyethyl sulphide at 30°. $V = 2·19$ *c.c.*

t, hrs.	N/10-NaOH, c.c.	k_1.	t, hrs.	N/10-NaOH, c.c.	k_1.
0	25·4	—	1·67	20·95	0·306
0·33	24·2	0·294	2·00	20·75	0·276
0·67	23·1	0·310	2·33	20·15	0·288
1·00	22·2	0·317	∞	(17·0)	Mean 0·299

Phenyl β-hydroxyethyl sulphide at 40°. $V = 2·21$ *c.c.*

0	24·4	—	0·83	19·5	1·03
0·17	22·7	1·07	1·00	18·9	1·15
0·33	21·3	1·16	1·17	18·75	1·05
0·50	20·6	1·06	1·33	18·5	1·10
0·67	19·9	1·07	∞	(17·8)	Mean 1·09

Table I summarises the results for all the substances studied.

TABLE I.

Hydroxy-compound, Ph·S·[CH$_2$]$_n$·OH : value of n.	Temp.	K.	Limits of k_1.	k_1.	$\log_{10} k_1$.
2	30°	21·1	0·288—0·317	0·299	
	40	14·8	1·03 —1·16	1·09	
	80		(extrapolated)	192	2·28
3	80	47·1	0·061—0·075	0·066	$\bar{2}$·82
	90	42·8	0·215—0·260	0·237	
4	30	14·8	0·255—0·291	0·276	
	40	21·1	0·694—0·817	0·775	
	80		(extrapolated)	47·6	1·68
5	80	52·4	0·498—0·554	0·520	$\bar{1}$·72
6	80	52·4	0·179—0·262	0·209	$\bar{1}$·32
7	80	52·4	0·171—0·260	0·224	$\bar{1}$·35
8	80	52·4	0·191—0·253	0·218	$\bar{1}$·34
9	80	72·2	0·155—0·201	0·182	$\bar{1}$·26
10	80	14·8	0·126—0·196	0·160	$\bar{1}$·20
	90	14·8	0·600—0·688	0·635	
Cetyl alcohol	80	16·8	0·147—0·181	0·165	$\bar{1}$·22

Titration showed that with each hydroxy-sulphide the fall of bromion concentration during the reaction was not as rapid as that of hydrion. With the δ- and the ε-hydroxy-sulphide, the bromion concentration remained constant throughout, as was to be expected from the earlier experiments, the rapid internal formation of a sulphonium salt liberating the whole of the halogen in the ionic form. All the bromo-sulphides must tend to undergo self-addition

to some extent (compare Bell, Bennett, and Hock, J., 1927, 1803), but whereas this type of reaction is intramolecular and complete with the δ- and ε-members, it is no doubt mainly intermolecular and partial in the other cases. Although this behaviour may affect the position of final equilibrium in the reaction of hydroxy-sulphide with hydrobromic acid, it should not affect the validity of the values of k_1 derived from the acidimetric observations. This complication does, on the other hand, make it out of the question to obtain true values of the velocity of the reverse reaction k_2 from these experiments, and it is also not surprising that the equilibrium value n found to give steady values of k_1 was only approximately the same as that found with mixtures heated for long periods.

The heats of activation q (in cals.) for the forward reaction in four cases, calculated from the variation of $\log_e k_1$ with temperature, are : phenyl β-hydroxyethyl sulphide, 24,400; phenyl γ-hydroxypropyl sulphide, 32,400; phenyl δ-hydroxybutyl sulphide, 19,500; phenyl κ-hydroxydecyl sulphide, 35,000.

Influence of an Added Sulphide on the Reaction.—Two experiments were carried out to test the influence of ethyl sulphide on the reactivity of cetyl alcohol. (1) For a reaction mixture similar to that used in the determination above, but with 5 in place of 10 mols. of water present, k_1 at 80° was 0·86. (2) This experiment was repeated with identical concentrations except that the phenol used as solvent was replaced by a mixture of phenol and ethyl sulphide (50% by volume) : k_1 at 80° was then 2·17.

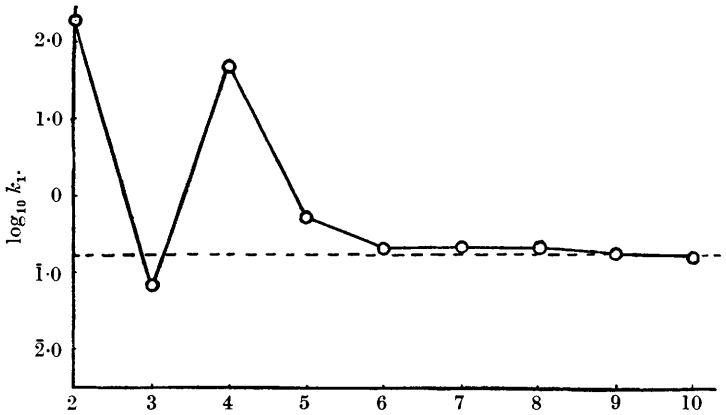
Discussion of Results.—The variation of the reactivity of the hydroxyl group towards hydrobromic acid in this series of hydroxy-sulphides is shown in Fig. 1, in which $\log_{10} k_1$ has been plotted against the number of carbon atoms in the chain separating the hydroxyl group from the sulphur atom.

If the behaviour of cetyl alcohol be taken as a standard from which to judge the degree of reactivity, the following points are clearly apparent. (*a*) In the β- and the δ-position ($n = 2$ and 4) the hydroxyl group has a very high reactivity; (*b*) in the ε-position ($n = 5$) the reactivity is high but less than that in the δ-position (ratio 1 : 90, as compared with 1 : 76 found for relative velocities of closure of the corresponding chloro-sulphides to cyclic sulphonium salts); (*c*) the reactivity is still appreciably above the standard from the ζ- to the θ-position ($n = 6, 7$, and 8), but at the ι- and κ-positions it is identical with that of cetyl alcohol; (*d*) the variations in the values for $n = 6$, 7, and 8 are probably too small to be of significance, but the reactivity of the γ-hydroxy-sulphide ($n = 3$) is definitely less than the normal.

Of these conclusions, (*a*) and (*d*) confirm the comparisons deduced

from earlier qualitative experiments (Part I, J., 1927, 477). Moreover, the effect (*c*) is consistent with the explanation of the large reactivity of the δ-hydroxy-sulphide as being due to the influence of the sulphur atom on the CH_2·OH group at moments when the ends of the chain approach each other : for it is known that the ease of closure of 7-, 8-, and 9-membered rings, although smaller than for 5- and 6-membered ones, is not negligible (compare Ruzicka and others, *Helv. Chim. Acta*, 1926, **9**, 249, 339), so that some increased reactivity was to be expected in these cases from a similar cause. It is noteworthy that there is no recurrence in any higher member of the series of the specially high reactivity found in the δ-hydroxy-compound.

FIG. 1.



Number of carbon atoms in the growing chain.

Variation of reactivity in the series Ph·S·$[CH_2]_n$·OH (n = 2—10).
(– – – – – *represents the value for cetyl alcohol.*)

The interpretation of the influence of the sulphur atom in these compounds given in Part I (*loc. cit.*) requires little modification to bring it into line with more recent conceptions or nomenclature. If the Flürscheim–Lapworth terms are used (see Lapworth and Manske, J., 1928, 2533; Cocker, Lapworth, and Walton, J., 1930, 440), the sulphur atom appears to cause a high reactivity in the group CH_2·OH or CH_2Cl separated from it by a single carbon atom (as in R·S·CH_2·CH_2·OH) by its "primary interior effect," but the interposition of one more carbon atom prevents the operation of this effect and leaves the slight deactivation resulting from the ordinary electropolar effect of the sulphur atom.

The enhanced reactivity of the δ- and the ε-hydroxy-sulphide resembles that of the β-hydroxy-sulphide attributed to the "primary interior effect." The influence of the sulphur atom on the δ-CH_2·OH

group has been regarded as a " direct effect through space," special experiments in Part IV having confirmed the fact that ring closure does not precede the reaction with halogen acid. The increased reactivity in question is not necessarily inconsistent with the depressed reactivity found in the γ-hydroxy-sulphide : for the field in space near the sulphur atom in a direction remote from the attached groups will be of the opposite sign from that in the direction of the growing chain (compare Part IV, p. 2367). It is also possible that, in the course of the reaction of the δ-hydroxy-sulphide with hydrobromic acid, the sulphur atom not only approaches within atomic distance of the terminal group but actually allows one of its lone pairs of electrons to take part in the process whereby the hydroxyl group becomes separated from the carbon atom to which it was attached. If this be so, the effect here may be regarded as at the moment an " interior " one, although it is clear from the experiment mentioned above that the reaction complex may finally yield either the bromo-sulphide or the cyclic sulphonium salt.

A further application of these conceptions may be made to the influence of a solvent on the velocity of the reaction. It appeared that the effect on a hydroxyl group of the sulphur atom from a relatively distant part of the same molecule might be imitated by that exercised by sulphur atoms in other molecules present as solvent, provided that the concentration of the latter were high enough to cause the probability of approach of a sulphur atom to the reacting $CH_2 \cdot OH$ group to be of a similar order. Other physical influences of the solvent doubtless help to determine the velocity of reaction, but the chemical effect now suggested is probably an important factor in causing the observed increase in the reactivity of cetyl alcohol with hydrobromic acid from 0·86 to 2·17 when half the phenol used as solvent is replaced by ethyl sulphide.

THE UNIVERSITY, SHEFFIELD. [*Received, May* 21*st*, 1931.]