

CCXIV.—*The Influence of the Sulphur Atom on the Reactivity of Adjacent Atoms or Groups. Part II. Comparative Reactivities of Chlorine in some β - and γ -Chloro-sulphides.*

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IN Part I of this series (this vol., p. 477), a qualitative comparison was made of the reactivities of the chlorine atoms in the β -, γ -, and δ -positions relative to a sulphur atom. In the present communication, we describe quantitative measurements of the reactivities of the chlorine atoms in some β - and γ -chloro-sulphides, namely, in the *o*-, *m*-, and *p*-nitrophenyl β -chloroethyl sulphides, *p*-nitrobenzyl β -chloroethyl sulphide, and *p*-nitrophenyl γ -chloropropyl sulphide, described in the preceding paper, together with the unsubstituted phenyl β -chloroethyl- and γ -chloropropyl-sulphides.

Comparative measurements were first made of the extent of their interaction with aqueous alcoholic sodium hydroxide solution during a short interval of time at 55°. With respect to this test, the substances arrange themselves in order of diminishing reactivity as follows: *o*- and *p*-nitrophenyl β -chloroethyl sulphide > *m*-isomeride \gg phenyl β -chloroethyl sulphide > phenyl γ -chloropropyl sulphide and its *p*-nitro-derivative.

The nitrobenzyl sulphide suffered some profound decomposition in presence of alkali, doubtless owing to the activation of the methylene group situated between the sulphur atom and the nucleus. No attempt was made to calculate a velocity coefficient for this reaction, since from analogy with the behaviour of other chloro-sulphides (compare Bales and Nickelson, J., 1922, **121**, 2137) it is probable that two reactions are involved, namely, a true hydrolysis

to the corresponding hydroxy-compound and the formation of an unsaturated sulphide by removal of one molecular proportion of hydrogen chloride. The result does, however, show that, in agreement with the conclusions previously reached concerning β - and γ -chloro-sulphides (Bennett and Hock, J., 1925, 127, 2671; this vol., p. 477), the γ -chloropropyl sulphide is in each case less reactive than the closely related β -chloroethyl compound.

In order to obtain a more accurate comparison of the reactivities of these substances we examined their hydrolysis by 50% aqueous alcohol at 75°, a reaction similar to that used by Olivier for a similar purpose (*Rec. trav. chim.*, 1922, 41, 646) and likely to be free from the defect of subsidiary reactions. We have therefore made a comparison of the initial velocities of hydrolysis; the results are in column 4 of Table I.

The reaction of the chloro-sulphides with piperidine was also examined with a view to quantitative measurement, but it was discarded when the product of the reaction was found to be a mixture. Finally, we also examined the reaction of these substances with potassium iodide, since this had been found to be quantitative and free from subsidiary reactions in the preparation of the β -iodo-sulphides (see preceding paper). Similar reactions have, moreover, been studied by Conant and his colleagues (Conant, Kirner, and Hussey, *J. Amer. Chem. Soc.*, 1925, 47, 488) and found suitable for accurate measurement. The velocities of reaction of these chloro-sulphides have been measured in acetone solution at 55°. The method of determining ionic iodine described by these authors was found to be unsuitable and a modified procedure was worked out. The reaction was in all cases bimolecular and the coefficients are given in Table I.

TABLE I.

| Substance. | Reaction with potassium iodide at 55°. | | Hydrolysis at 75°. |
|---|--|------------------|--------------------|
| | <i>k</i> . | Relative values. | Relative values. |
| Ph·S·C ₂ H ₄ Cl | 0·091 | 1·00 | 1·00 |
| <i>o</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 0·180 | 1·98 | 0·023 |
| <i>m</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 0·189 | 2·09 | 0·083 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 0·257 | 2·62 | 0·052 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·CH ₂ ·S·C ₂ H ₄ Cl | 0·215 | 2·36 | — |
| Ph·S·C ₃ H ₆ Cl | 0·330 | 3·52 | 0·0031 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₃ H ₆ Cl | 0·836 | 9·19 | 0·0010 |

Interpretation of the Results.

The substances are arranged with respect to the hydrolysis in an order which is the opposite of that shown in the reaction with potassium iodide. This contrast must depend on the nature and

mechanism of the two reactions used. It may be explained if the reactions involved are of opposite polar type. A similar contradiction was pointed out by Conant, Kirner, and Hussey (*loc. cit.*), who remark with reference to certain chloro-compounds that the increased reactivity with potassium iodide "appears to be just the reverse of what would be predicted from a consideration of polarity." A consideration of the influence of certain activating groups "would," they point out, "lead to the conclusion that the chlorine atom of Ph·CO·CH₂Cl was more *positive* than the chlorine atom of benzyl chloride: yet it is 500 times more reactive in a reaction in which the chlorine is *eliminated as a negative ion* and is *replaced by a negative ion*. . . . It seems evident that no adequate interpretation of the facts can be stated solely in terms of polarity." This difficulty is in reality the same as that presented by our own opposed sets of reaction velocities. A further clear case of the same kind is shown in Table II, which gives the results of the comparison of benzyl chloride and its nitro-compounds as determined by hydrolysis (Olivier, *loc. cit.*) and by the potassium iodide reaction (Conant and others).

TABLE II.

| Substance. | Relative reactivity with | |
|--|--------------------------|---------------|
| | KI at 50°. | water at 30°. |
| Ph·CH ₂ Cl | 1 | 1 |
| <i>o</i> -NO ₂ ·C ₆ H ₄ ·CH ₂ Cl..... | 0.15 | 0.047 |
| <i>m</i> -NO ₂ ·C ₆ H ₄ ·CH ₂ Cl | 3.96 | 0.057 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·CH ₂ Cl | 6.95 | 0.044 |

All these anomalies disappear if it be admitted that, whilst a negative charge on the chlorine atom accelerates the hydrolysis (compare Oxford and Robinson, J., 1926, 384), it is a positive charge on the chlorine atom that makes it react more rapidly with potassium iodide. This will be the case if, as we suggest, the latter reaction involves two stages, the first of which is the formation of a complex between the organic chloro-compound and the iodide ion. In the second stage, the neutral organic iodo-compound is formed by the ejection of a chlorine ion from the complex. The first stage of the reaction will proceed at a higher velocity the greater the *positive* charge on the chlorine atom, since this will favour combination with the negative iodine ion. On this assumption, our two sets of data become consistent among themselves, and with the electron distribution deduced for β- and γ-chloro-sulphides in Part I of the series. The reaction velocities observed for Ph·S·C₂H₄Cl and Ph·S·C₃H₆Cl lie respectively below and above that found by Conant and his colleagues for Ph(CH₂)₄Cl, namely, 0.211.* This confirms

* This value has been obtained from their figure by use of their interpolation formula and multiplication by 2.302.

the suggestion made in Part I that actually the chlorine atom in the β -position is negatively, and in the γ -position positively, charged as compared with the normal.

Kirner (*J. Amer. Chem. Soc.*, 1926, **48**, 2745) has recently found three ethers to have reactivities in the order $\text{PhO}\cdot\text{C}_2\text{H}_4\text{Cl} < \text{PhO}\cdot\text{C}_3\text{H}_6\text{Cl} > \text{PhO}\cdot\text{C}_4\text{H}_8\text{Cl}$, with respect to the potassium iodide reaction. The influence of an atom of oxygen and one of sulphur in a molecule should be similar, if similarly situated, so that this result is in qualitative agreement with the conclusion arrived at in Part I that chlorine varies in reactivity (to hydrolysis) with position relative to sulphur in the order: $\beta > \gamma < \delta$.

The introduction of a nitro-group into the nucleus of any of these compounds—chloro-sulphides or benzyl chlorides—gives a positive charge to the chlorine atom and so alters the velocities of the two reactions discussed in the directions observed. No large difference of effect was found with orientation of the nitro-group in the *o*-, *m*-, and *p*-positions in the sulphides, which is consistent with the conclusion of Oxford and Robinson (*loc. cit.*) that “the alternating effect of a nitro-group cannot be discerned beyond the limits of the conjugated system of which it forms a part.” In the case of the reaction with aqueous alcoholic sodium hydroxide, the introduction of the nitro-group actually increases the reactivity in the β -chloro-sulphides. Since in the true hydrolysis the converse effect is observed, the increase must be due to the subsidiary reaction involving the elimination of hydrogen chloride.

EXPERIMENTAL.

Preparation of β -Hydroxyethyl and γ -Hydroxypropyl Phenyl Sulphides.—These compounds were obtained by the condensation of sodium thiophenoxide and the respective chlorohydrins: The thiophenol (15 g.), a solution of sodium hydroxide (6 g. in 100 c.c. of water), and ethylene chlorohydrin (12 c.c., or 15 c.c. of trimethylene chlorohydrin in the case of the propyl compound) were mixed and heated to about 60°. When the solution had become neutral to litmus, 20 c.c. of *N*-sodium hydroxide and 4 c.c. of the chlorohydrin were added and the mixture was heated for a further 15 minutes. The precipitated oil was removed in ether.

An attempt to distil phenyl β -hydroxyethyl sulphide under diminished pressure gave an unsaturated compound, probably due to the splitting out of water from the side chain giving rise to phenyl vinyl sulphide. The preparation of the chloroethyl sulphide was therefore carried out with the crude hydroxy-compound by means of the Darzens reaction (preceding paper, p. 1671). The products were removed by ether extraction.

Phenyl β -chloroethyl sulphide is a colourless liquid with a rather pungent smell and a very slight vesicant action; b. p. $117^{\circ}/12$ mm. (Found: Cl, 20.4. Calc.: Cl, 20.55%). Phenyl γ -chloropropyl sulphide is a colourless liquid and is not appreciably vesicant; b. p. $137^{\circ}/13$ mm. (Found: Cl, 18.8. $C_9H_{11}ClS$ requires Cl, 19.0%).

Reaction of the Chloro-sulphides with Piperidine.—This reaction was investigated with a view to employ it as a means of determining the relative reactivities of the chloro-compounds.

o-Nitrophenyl β -chloroethyl sulphide (1 g.) was boiled under reflux for 8 hours with piperidine (1.2 g.) and alcohol (10 c.c.). The mixture was then made slightly alkaline and distilled in steam to remove the alcohol and excess of piperidine. The remaining oil was dissolved in ether, and the solution dried. On passing dry hydrogen chloride into the ethereal solution, a precipitate was formed (0.7 g.), m. p. 231° . This compound was soluble in water and the addition of sodium hydroxide caused the precipitation of an oil, which solidified to give pale yellow crystals, m. p. 45° , of *o*-nitrophenyl β -piperidinoethyl sulphide (Found: N, 10.7. $C_{13}H_{18}O_2N_2S$ requires N, 10.5%). The compound precipitated from the ethereal solution was therefore the hydrochloride of this base.

Evaporation of the remaining ethereal solution gave a dark oil which did not crystallise. It gave a negative result with a test for chlorine, but its reaction with potassium permanganate as compared with that of the original chloro-sulphide indicated the presence of an unsaturated group. It was therefore probably *o*-nitrophenyl vinyl sulphide.

Further experiments with only one equivalent of piperidine did not give improved yields of the hydrochloride.

p-Nitrophenyl β -chloroethyl sulphide, when subjected to the same reaction, also gave similar products, namely, a base and an unsaturated compound. The hydrochloride had m. p. 217° and the free base, *p*-nitrophenyl β -piperidinoethyl sulphide, melted at 52° .

Reaction of the Chloro-sulphides with Alcoholic Sodium Hydroxide.—A comparison of the reactivities of the chloro-sulphides with alcoholic sodium hydroxide was made in the following way: The chloro-sulphide (0.001 mol.) was weighed into a test-tube, 5 c.c. of absolute alcohol were pipetted on to it, and the mixture was gently warmed to bring the organic matter into solution. *N*/5-Sodium hydroxide (5 c.c.) was added, and the tube was stoppered and immediately immersed in a thermostat. After a definite period of time, the contents of the tube were washed out and titrated with standard hydrochloric acid.

The following table summarises the results :

| Compound. | Temp. | Time (hrs.). | Titration of reaction mixture (c.c. of 0.1N-HCl). | Amount of NaOH (expressed as c.c. of acid). |
|--|-------|--------------|---|---|
| <i>o</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 55° | 0.5 | 1.87 | 8.13 |
| <i>m</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 55 | 0.5 | 2.87 | 7.13 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 55 | 0.5 | 1.75 | 8.25 |
| Ph·S·C ₂ H ₄ Cl | 55 | 2.0 | 7.16 | 2.84 |
| Ph·S·C ₃ H ₆ Cl | 55 | 2.0 | 9.24 | 0.76 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₃ H ₆ Cl | 55 | 2.0 | 9.22 | 0.78 |

Some experiments were also conducted at 42° :

| | | | | |
|--|-----|-----|------|------|
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 42° | 0.5 | 4.00 | 6.00 |
| Ph·S·C ₂ H ₄ Cl | „ | „ | 9.55 | 0.45 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₃ H ₆ Cl | „ | „ | 9.80 | 0.20 |
| Ph·S·C ₃ H ₆ Cl | „ | „ | 9.75 | 0.25 |

When *p*-nitrobenzyl β-chloroethyl sulphide was subjected to this reaction, some other reaction than replacement of chlorine by hydroxyl took place, for a brown compound was produced along with a peculiar odour which was always present when an attempt to condense the sodium salt of *p*-nitrobenzyl mercaptan with ethylene chlorohydrin did not give the desired thioether. The hydroxy-compound is also decomposed by sodium hydroxide in a manner similar to that of the chloro-compound.

It follows that with respect to the reaction with sodium hydroxide in alcoholic solution, these compounds may be arranged as follows in descending order of reactivity: *p*-NO₂·C₆H₄·S·C₂H₄Cl > *o*-NO₂·C₆H₄·S·C₂H₄Cl > *m*-NO₂·C₆H₄·S·C₂H₄Cl > Ph·S·C₂H₄Cl > Ph·S·C₃H₆Cl and *p*-NO₂·C₆H₄·S·C₃H₆Cl. The method used is not sufficiently accurate to enable a statement to be made as to which of the last two compounds is the more reactive.

Hydrolysis of the Chloro-sulphides.—The chloro-sulphide (0.001 g.-mol.) was dissolved in alcohol (25 c.c.), and the solution placed in a thermostat at 75° for several minutes. Water (25 c.c.) which had been immersed in the thermostat was then added, the time noted, and the reaction flask stoppered. After a definite time interval, the contents of the flask were cooled, diluted with water, and titrated with standard sodium hydroxide solution.

From this titration value, the proportion of hydrolysis (*x*) was calculated, and values for the relative reactivities were obtained from the expression

$$\text{Relative reactivity} = t_1 \log \{1/(1 - x_2)\} / t_2 \log \{1/(1 - x_1)\},$$

*t*₁ and *x*₁ being the values found for Ph·S·C₂H₄Cl.

The following table summarises the results :—

| Substance. | α . | Time (mins.). | Rel. reactivity. |
|---|------------|---------------|------------------|
| Ph·S·C ₂ H ₄ Cl..... | 0·748 | 15 | 1·0 |
| <i>o</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl..... | 0·243 | 130 | 0·023 |
| <i>m</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl..... | 0·628 | 130 | 0·083 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl..... | 0·460 | 130 | 0·052 |
| Ph·S·C ₃ H ₆ Cl..... | 0·081 | 300 | 0·003 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₃ H ₆ Cl..... | 0·027 | 300 | 0·0010 |

This order of relative reactivities was confirmed in two further sets of experiments.

p-Nitrobenzyl β -chloroethyl sulphide is omitted from the above list, since the product of its hydrolysis was undoubtedly a mixture. After the hydrolysis of *p*-nitrophenyl β -chloroethyl sulphide, the corresponding hydroxy-compound crystallised from the reaction mixture. *p*-Nitrobenzyl β -chloroethyl sulphide, however, yielded an oily product which did not crystallise even on inoculation with a crystal of the pure hydroxy-compound. An unsaturated impurity was found to be present.

Reaction of the Chloro-sulphides with Potassium Iodide.—This reaction was applied under conditions similar to those used by Conant and others (*loc. cit.*), namely, the initial concentrations of the organic chloro-compound and the potassium iodide were in the ratio 5 : 1, the iodide concentration being approximately 0·04*N*. Absolute acetone, purified as described by Conant and Kirner (*J. Amer. Chem. Soc.*, 1924, **46**, 233), was used as solvent.

Andrews's method for estimation of iodide in presence of chloride (*J. Amer. Chem. Soc.*, 1903, **25**, 756), as used by Conant and others, was found to be unsatisfactory in the present investigation, owing to reaction between the iodic acid and the organic sulphide in the chloroform used for indicator. Even after removal of the organic compound, the end-point with chloroform as indicator was not well defined, and starch could not be used owing to the great acidity of the solution.

A convenient method in which starch can be used as indicator was found in that described by Lang (*Z. anorg. Chem.*, 1922, **122**, 332), depending on the addition of an oxidising agent (*e.g.*, potassium iodate) to an acid solution of an iodide in presence of hydrogen cyanide. The iodine is converted quantitatively into iodine cyanide, which does not colour starch. As the acidity of the solution is approximately normal (when hydrochloric acid is used), starch can be used as indicator. Acetone in the titration flask causes a temporary fading of the blue starch-iodide colour when near the end-point, *e.g.*, a further drop of iodate solution regenerates the blue colour, which then fades again on standing : this occurs until the true end-point is reached, after which addition of iodate no longer causes an evanescent blue colour. Thus, although the

acetone does not affect the value for the end-point, its presence makes the determination difficult. The acetone was therefore removed by passing a current of steam through the solution before titrating it.

The experimental procedure adopted in these measurements was as follows: 50 C.c. of 0.04*N*-potassium iodide (in the pure acetone) were added to 0.01 g.-mol. of the organic halide contained in a conical flask. The organic compound dissolved rapidly and as soon as it was thoroughly mixed, 5 c.c. of the mixture were pipetted into a separating funnel containing 20 c.c. of water. This precipitated the organic halide and prevented any reaction: in the estimation as subsequently described, this reading gave the blank for calculating the concentration of the potassium iodide in the reaction and also the value for A_0 in the formula (below). 5 C.c. lots of the mixture were pipetted into each of a series of nine tubes (made of stout glass tubing, about 6 in. long and 0.5 in. inside diameter) which were then sealed up in the blow-pipe flame. These tubes were placed in a thermostat at 55.0°.

After about 30 minutes, one of the tubes was removed and opened and the contents were washed into water (10 c.c.). The time was noted and this was counted as the zero time of the readings. The whole was then extracted with chloroform (four portions of 5 c.c.), the chloroform extracts being washed with water (10 c.c.) to recover any potassium iodide solution which may have been removed mechanically in the chloroform. This aqueous washing of the chloroform was finally extracted with 5 c.c. of chloroform. The aqueous solution was then distilled in steam for 3 minutes to remove the chloroform and acetone, a splash-bulb being used to prevent any loss. The mixture, which then had a bulk of about 70 c.c., was cooled and concentrated hydrochloric acid (15 c.c.) and potassium cyanide solution (8 c.c. of *N*/2) were added. It was titrated against 0.003*M*-potassium iodate solution, starch being used as indicator.

At definite time intervals, tubes were removed from the thermostat and worked up as indicated above. The velocity coefficient was calculated from the bimolecular formula

$$k = \frac{2.302}{4b(t_2 - t_1)} \log_{10} \frac{(4A_0 + A_2)A_1}{(4A_0 + A_1)A_2},$$

where A_0 = blank titration value at the commencement of reaction, A_1 = titration value at time t_1 , A_2 = titration value at time t_2 , and b = the concentration of potassium iodide in the reaction (calc. from A_0), time being measured in hours and the concentrations in g.-mol. per litre.

Except in one instance, the greatest percentage variation among the values for k in a series of measurements is less than 10%, which

is satisfactory in view of the necessarily complicated experimental procedure.

o-Nitrophenyl β -Chloroethyl Sulphide.—0.01 G.-mol. mixed with 50 c.c. of 0.04*N*-potassium iodide in pure acetone. Temperature of thermostat 55.0°. The titrations (*A*) are expressed as c.c. of 0.003*M*-potassium iodate.

| $(t_2 - t_1)$ in hrs. | <i>A.</i> | <i>k.</i> | $(t_2 - t_1)$ in hrs. | <i>A.</i> | <i>k.</i> |
|-----------------------|---------------------------------|-----------|-----------------------|-----------|------------|
| — | 32.55 (<i>A</i> ₀) | — | 10 | 22.16 | 0.181 |
| 0 | 31.11 (<i>A</i> ₁) | — | 14 | 19.46 | 0.181 |
| 2 | 28.89 | 0.193 | 18 | 17.39 | 0.176 |
| 4 | 27.04 | 0.184 | 22 | 15.44 | 0.174 |
| 6 | 25.55 | 0.173 | 27 | 13.42 | 0.177 |
| | | | | | Mean 0.180 |

Mean value in an independent experiment, 0.177.

The following table summarises the measurements of the reaction velocities of the remaining compounds studied.

In each case 0.01 g.-mol. of the chloro-sulphide was dissolved in 50 c.c. of 0.04*N*-potassium iodide solution, and the temperature of the reaction was 55.0°.

| Substance. | Limits of <i>k.</i> | <i>k.</i> | <i>k</i> (independent observation). |
|---|---------------------|-----------|-------------------------------------|
| <i>m</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 0.180—0.198 | 0.189 | 0.187 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₂ H ₄ Cl | 0.250—0.267 | 0.257 | 0.252 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·CH ₂ ·S·C ₂ H ₄ Cl ... | 0.206—0.227 | 0.215 | 0.235 |
| <i>p</i> -NO ₂ ·C ₆ H ₄ ·S·C ₃ H ₆ Cl | 0.817—0.886 | 0.836 | 0.820 |
| Ph·S·C ₂ H ₄ Cl | 0.084—0.100 | 0.091 | 0.086 |
| Ph·S·C ₃ H ₆ Cl | 0.321—0.342 | 0.330 | 0.343 |

We wish to thank the Chemical Society for assistance in the purchase of materials, and the Department of Industrial and Scientific Research for a maintenance grant which has enabled one of us (W. A. B.) to take part in the work described in this and the preceding paper.

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[Received, April 8th, 1927.]