250. *Mechanism of Substitution at a Saturated Carbon Atom. Part IX. The Rôle of the Solvent in the First-order Hydrolysis of Alkyl Halides.*

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The hydrolysis of an alkyl halide in an aqueous medium will follow the equation for a reaction of the first order if *either* the reaction is " unimolecular," being determined as to rate by an ionisation :

$$\left\{\begin{aligned} R{\cdot}Hal &\xrightarrow[\text{(slow)}]{} R^+ + Hal^- \\ R^+ + OH^- &\xrightarrow[\text{(fast)}]{} ROH \end{aligned}\right.$$

or it is " bimolecular," being a pseudo-first order reaction involving a solvent molecule as a direct reagent :

$$H_2O + R{\cdot}Hal \longrightarrow H^+ + OH{\cdot}R + Hal^-$$

(The terms " unimolecular " and " bimolecular " refer, as is customary, to the type of mechanism involved, independently of the reaction order.) Indirect methods of distinguishing between the two cases have been based on the kinetic effects of added alkali, of variations in the solvent and of added neutral salts, as well as on the stereochemical effect of the substitution. In this paper a direct kinetic method is elaborated and applied in the case of *tert.*-butyl chloride. It is shown that the rate of reaction of this halide with water in formic acid solution is of the first order, and independent of the (small) concentration of water. The reaction is, therefore, unimolecular, as has already been assumed on other grounds.

IT was shown in Part V (Hughes, J., 1935, 255) that the rate of hydrolysis of *tert.*-butyl chloride in aqueous alcohol or aqueous acetone is independent of the concentration of hydroxide ions : the reaction is of the first order, and its rate constant is the same in acid and in

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(*Note added in proof.*) The distinction between order and mechanism does not appear to be fully understood by Taylor, who, in a paper which has just appeared, misrepresents our view of the first-order reactions of methyl, ethyl, *iso*propyl and *tert.*-butyl bromides with aqueous ethyl alcohol. The reactions of the methyl and ethyl halides are bimolecular, and their rates decrease in the order of naming as they should ; just as the rates of the essentially unimolecular reactions of *iso*propyl and *tert.*-butyl bromides increase in this order as *they* should. Further discussion of these examples is deferred, but additional examples of bimolecular first-order reactions, with evidence of mechanism, are given in an accompanying paper (this vol., p. 1208).

alkaline solution provided the solvent remains unchanged. The rate increases with the ionising power of the medium : it is greater in more aqueous solvents, and greater in aqueous alcohol than in aqueous acetone. The constitutional and environmental factors which govern the operation of this type of substitution have been discussed (Hughes and Ingold, J., 1935, 244). We now bring fresh evidence to bear on the question of the function of the aqueous solvent.

The general problem to which this paper is a contribution may be expressed in the following form. The discovery that a hydrolysis is kinetically of the first order always opens up the possibility that the process in operation is that which we symbolise as S_N1. This mechanism assumes that the rate-controlling process is the ionisation of the alkyl halide, and that ionisation is succeeded by the rapid reaction of the cation with the solvent molecules :

$$\left.\begin{array}{r} R - X \xrightarrow[\text{slow}]{} R^+ + X^- \\ R^+ + H_2O \xrightarrow[\text{fast}]{} R\cdot OH + H^+ \end{array}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad S_N1$$

The order of reaction alone, however, does not distinguish between this mechanism and a single-stage bimolecular substitution involving water as a direct reagent, when, as in the experiments to which reference has been made, the quantity of water in the solvent is so large that its concentration is substantially constant.

$$H_2O + R\cdot X \longrightarrow R\cdot OH + HX \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad S_N2$$

Under the conditions specified, first-order kinetics would still prevail in any one experiment, and any proportionately considerable change in the water contents of the solutions used in different experiments would amount to an alteration of solvent properties.

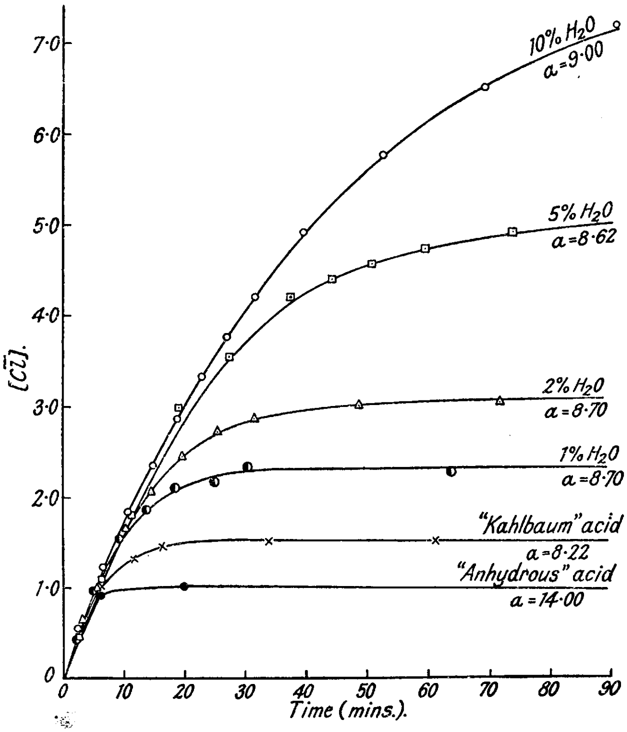
Several methods of distinguishing between the two mechanisms have already been suggested. It was pointed out (Hughes and Ingold, *loc. cit.*) in relation to the example of *tert.*-butyl chloride that, when in hydrolysis the water molecule functions as a primary reagent, it does so either as an acid or as a base or as both, and that, accordingly, either the stronger acid H_3O^+ or the stronger base $\overline{OH}$ or both act very much more powerfully. This did not happen in the case of *tert.*-butyl chloride and mechanism S_N1 was, therefore, indicated unequivocally. The result of applying this criterion will always be definite and certainly correct when there is no difference of rate as between acid, neutral, and alkaline solutions. The criterion becomes progressively less valuable and certain as the rate of the reaction in the presence of added hydroxide ions increases above that of the acid hydrolysis.

Other criteria, however, have been proposed. We have shown theoretically that in the hydrolysis of alkyl halides by mechanism S_N1 the rate of reaction should increase with the ionising power of the medium, whereas in the hydrolysis by mechanism S_N2 the rate should decrease. This criterion has been applied by Nixon and Branch (*J. Amer. Chem. Soc.*, 1936, **58**, 492) to their experiments on the alcoholysis of triarylemthyl chlorides, and we agree with their statement of the matter. As, however, they refer to a paper from this laboratory dealing with the hydrolysis of 'onium salts, we take this opportunity to make it clear that the particular type of solvent effect which characterises the hydrolysis and alcoholysis of alkyl halides by mechanisms S_N1 and S_N2 does not apply to nucleophilic substitutions generally, or even to all types of hydrolysis. For instance, the hydrolysis of an 'onium cation by mechanism S_N1 would be retarded by an increase in the ionising power of the medium. It is necessary in each individual case to apply the solvent theory of Hughes and Ingold in order to discover the relation of solvent effect to mechanism.

A third criterion can be based on the direction of the neutral-salt effect on reaction velocity. A fourth, based on the steric orientation of substitution, is available when there is asymmetry at the seat of substitution. These matters are, however, dealt with in accompanying papers (this vol., pp. 1196, 1201, 1208, 1252) and require no discussion here.

In this paper we attempt to work out, in the example of *tert.*-butyl chloride, a direct kinetic method of distinguishing between mechanisms S_N1 and S_N2. The method is to use as solvent a substance which has an ionising power towards alkyl halides as great as or greater than that of water ; so that small additions of water do not bring about any profound change in the ionising properties of the medium towards these halides. The mass law can then be applied, and the dependence of the reaction rate on water concentration determined. Formic acid (dielectric constant = 57) has proved a suitable solvent, and the only complicating factors encountered, neither of which presented an insuperable obstacle, arose from the reversibility of the hydrolysis and a reversible side reaction leading to olefin formation.

Measurements have been made at 15° in " anhydrous " formic acid, *i.e.*, formic acid containing a very small amount of water, " Kahlbaum " acid which appears to contain about 0·5% of water, and various synthetic solutions of water in formic acid. The reaction was followed by determining the concentrations of chloride ions. In anhydrous formic acid reaction proceeded to the extent of 7% and no further. We proved the presence at this equilibrium of olefin and hydrogen chloride, but cannot exclude the possibility that some part of the observed reaction is due to the presence of traces of water. In Kahlbaum acid the reaction was more extensive, and the progressive addition of water caused a progressive increase in the percentage of reaction at equilibrium. The most significant fact, however, is that the concentration of water had no appreciable effect on the *initial* velocity of formation of chloride ions within the range investigated. This is shown in the figure, in which chloride ion concentration is plotted against time. The initial slopes of all the graphs are the same to within the error of experiment. The subsequent curvature of each graph is due to the reversibility of the reaction. These statements are confirmed by a calculation of the rate constant k_1 of the forward reaction from the integrated equation for the speed of a first-order reaction with second-order reversal $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B + C$. The reactions all obey this equation satisfactorily, and the first-order constants k_1 are practically independent of the concentration of water as is shown in Table I.



Rate of formation of Cl^- *ions from* tert.*-butyl chloride in formic acid solutions at* 15°: $[Cl^-]$ *expressed in c.c. of* $N/10$-NH_4CNS *per* 5 *c.c. of solution,* "a" = *initial* $[Bu^{\gamma}Cl]$ *in the same units.*

An examination of the products of reaction showed that the formation of olefin is rapidly suppressed by small additions of water. In all solvents, except the anhydrous acid, olefin

TABLE I.

			Units % of water added to Kahlbaum acid.			
Formic acid medium.	Anhydrous.	Kahlbaum.	1.	2.	5.	10.
% Reaction at equilm.	7·1	18·5	25·9	34·9	58·0	84·2
10^4k_1 (sec.$^{-1}$)	—	3·84	3·98	3·70	3·66	3·53

production is a minor reaction, and in the presence of the larger concentrations of water it is completely suppressed. In these circumstances the only isolable product is *tert.*-butyl alcohol.

We interpret these results as follows. The rate-determining process in all the media examined is the same, *viz.*, the ionisation of the *tert.*-butyl chloride. The ionising medium for the halide is primarily the formic acid and not the water, and hence the velocity of ionisation is not appreciably changed by increasing the concentration of water within the experimental limits. The fate of the *tert.*-butyl cation depends, however, on the conditions. It may eliminate a proton with the formation of *iso*butylene. If water is present it will largely or exclusively undergo the more facile reaction with a water molecule to produce *tert.*-butyl alcohol. The formation of *tert.*-butyl formate by reaction with formic acid cannot be excluded. But none of these *sequelæ* affects the rate of production of chloride ions, which is determined solely by the rate of electrolytic dissociation of the alkyl halide.

Although the addition of small proportions of water to formic acid does not affect the rate of ionisation of *tert.*-butyl chloride, it does considerably influence the activity of the hydrogen chloride formed, water being more efficient than formic acid for the solvation of a proton. The solvated form of hydrogen chloride $[H_3O]^+Cl^-$ is comparatively inactive in additions to olefins and reactions with alcohols; and hence the rates of these retrograde reactions are strongly affected by water-solvation of the hydrogen chloride; and the equilibrium becomes shifted, as is shown in the figure.

EXPERIMENTAL.

Materials.—The *tert.*-butyl chloride used had b. p. 50·0°/749 mm. The anhydrous formic acid was prepared from " Kahlbaum " formic acid (m. p. *ca.* 7·5°) by fractional freezing, special care being taken to exclude moisture. The technique employed was similar to that described by Smith (J., 1931, 3257) for the purification of formamide. Four freezings usually gave an acid, m. p. 8·4°, which was not improved by further treatment. This m. p. is in good agreement with most of the values recorded in the literature for the m. p.'s of samples purified either by partial freezing or by fractional distillation from an anhydrous salt at low pressures [cf. Garner, Saxton, and Parker, *Amer. Chem. J.*, 1911, **46**, 236 (8·35°); Ewins, J., 1914, **105**, 350 (8·39°); Turner and Pollard, J., 1914, **105**, 175 (8·4°); Kendall, *J. Amer. Chem. Soc.*, 1914, **36**, 1228 (8·5°); Timmermans and Hennaut-Roland, *J. Chim. physique*, 1930, **27**, 401 (8·4°)]. The anhydrous acid deteriorates on keeping, owing to decomposition into carbon monoxide and water which takes place even at low temperatures (Coolidge, *J. Amer. Chem. Soc.*, 1928, **50**, 2166; 1930, **52**, 1874). For this reason it was used as soon as possible after the last freezing. The aqueous mixtures were prepared from Kahlbaum acid, and were made up by volume. The figures recorded in the tables refer to the number of c.c. of *added* water per 100 c.c. of the mixture. Thus " 10% " water in formic acid refers to the mixture resulting when 10 c.c. of water are made up to 100 c.c. with Kahlbaum acid.

Kinetic Measurements.—The temperature throughout was 15·00° ± 0·02°. In the experiments in Kahlbaum and more aqueous acids an approximately measured volume (*ca.* 2 c.c.) of *tert.*-butyl chloride was dissolved in a suitable volume of the solvent (*ca.* 100 c.c.), both being kept in the thermostat before admixture. At suitable intervals 5 c.c. portions of the reaction mixture were withdrawn and run into 50 c.c. of carbon tetrachloride. The carbon tetrachloride solution was extracted twice with 25 c.c. of water, and to the aqueous extracts were added a few drops of concentrated nitric acid, 10 or 20 c.c. (excess) of a standard solution of silver nitrate, the ferric alum indicator, and about 10 c.c. of ether. The excess of silver ions was determined by titration with standard ammonium thiocyanate solution. The presence of ether eliminates the necessity of removing the silver halide [cf. Treadwell and Hall, " Analytical Chemistry," Vol. 2, p. 604 (1930)]. Blank experiments with standard hydrochloric acid solutions were performed to check the reliability of the method in the presence of formic acid. The total chloride-ion concentration was determined by running 5-c.c. portions of the reaction mixture into 50 c.c. of water, leaving the mixture overnight to complete the hydrolysis, and estimating chloride as above. Experiments in which accurately weighed quantities of *tert.*-butyl chloride were made up to a standard volume showed that this procedure gives a reliable estimate of the initial concentration of the halide. In the experiments in anhydrous formic acid, the *tert.*-butyl chloride was placed in a flask through which dry nitrogen was passed, and the medium was introduced through a glass tube directly from the freezing vessel by applying pressure to the latter. With the exception of this precaution to exclude moisture, the technique was the same as in the other experiments.

Calculations of First-order Constants.—The first-order rate constants are calculated from the integrated rate equation of a reversible reaction of the form $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B + C$. If a is the concentration of *tert.*-butyl chloride initially, and x and x_∞ the concentrations of the products of reaction after t seconds and infinite time respectively, then

$$dx/dt = k_1(a - x) - k_2x^2$$

and at equilibrium

$$k_1(a - x_\infty) - k_2x^2_\infty = 0$$

wherefore

$$k_1 = \frac{x_\infty}{t(2a - x_\infty)} \log_e \left\{\frac{ax_\infty + x(a - x_\infty)}{a(x_\infty - x)}\right\}$$

In Table II, a, x, and x_∞ are expressed as equivalent c.c. of $1{\cdot}004N/10$-ammonium thiocyanate (per 5 c.c. of reaction mixture); t is in secs., and k_1* is in sec.$^{-1}$. In one case only (col. 4, last section of table) the values of the "constants," calculated from the equation for a non-reversible unimolecular reaction, $k_1' = (1/t).\ \log_e \{a/(a - x)\}$, are recorded for comparison.

TABLE II.

t.	x.	10^4k_1.
"*Anhydrous formic acid.*"		
$a = 14{\cdot}00$, $x_\infty = 1{\cdot}00$.		
360	0·90	(2·25)
"10%" *Water in formic acid.*		
$a = 9{\cdot}00$, $x_\infty = 7{\cdot}58$.		
150	0·54	4·11
396	1·20	3·62
648	1·82	3·50
894	2·33	3·38
1134	2·85	3·40
1380	3·30	3·36
1626	3·75	3·39
1902	4·19	3·40
2388	4·90	3·47
3162	5·76	3·54
4176	6·49	3·60

t.	x.	10^4k_1.
"1%" *Water in formic acid.*		
$a = 8{\cdot}70$, $x_\infty = 2{\cdot}25$.		
156	0·51	3·91
312	0·95	3·90
558	1·53	4·12
822	1·85	3·98
"2%" *Water in formic acid.*		
$a = 8{\cdot}70$, $x_\infty = 3{\cdot}04$.		
198	0·63	3·83
336	0·99	3·69
624	1·65	3·68
882	2·06	3·60
1188	2·44	3·64
1518	2·71	3·74

t.	x.	10^4k_1.	$10^4k_1'$.
"*Kahlbaum*" *formic acid.*			
$a = 8{\cdot}22$, $x_\infty = 1{\cdot}52$.			
156	0·45	3·70	—
378	1·01	4·11	—
702	1·32	3·72	—
"5%" *Water in formic acid.*			
$a = 8{\cdot}62$, $x_\infty = 5{\cdot}00$.			
162	0·46	3·39	3·38
378	1·08	3·57	3·54
690	1·80	3·48	3·39
1158	2·97	3·97	3·65
1650	3·53	3·67	3·19
2256	4·19	3·84	2·95
2658	4·38	3·69	2·67
3054	4·55	3·66	2·46
3576	4·71	3·63	2·20

Reversibility of the Hydrolysis.—The reversible nature of the hydrolysis was confirmed when *tert.*-butyl alcohol was allowed to react with hydrogen chloride in aqueous formic acid solution. *tert.*-Butyl alcohol (0·0180 mol.) was made up to 100 c.c. at 15·0° with the medium obtained by mixing 90 c.c. of "Kahlbaum" formic acid and 10 c.c. of approximately 1·8N-hydrochloric acid. At intervals, 5-c.c. portions were withdrawn, and their chloride-ion contents determined by the method described for the kinetic experiments. The initial concentration of chloride ions was obtained as before by running 5 c.c. portions into water. The results are appended :

Time (hrs.)	0	2	19	20
[Cl$^-$], (N)	0·179	0·150	0·154	0·149
% Cl as ions	100	83·8	86·6	83·2

It is to be noted that the conditions employed in this experiment are similar to those obtaining in the hydrolysis experiments in "10%" water in formic acid, and that the position of equilibrium is practically the same in each case (cf. Table I).

Reaction Products.—(a) *Olefin.* Reaction mixtures similar to those employed for the kinetic experiments were made up in a jar provided with an inlet and an outlet tube, the former reaching

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* Some of the constants recorded are probably not very accurate owing to the short range over which measurements are possible before equilibrium is reached.

to the bottom. The latter was connected in series to a trap at 0°, a tube packed with powdered potash, two bubbling tubes containing known quantities of bromine in carbon tetrachloride the second of which was kept at 0°, and a trap containing aqueous potassium iodide. After a period of time sufficient for the attainment of equilibrium, a slow stream of nitrogen was blown through the inlet tube. A blank experiment with the medium substituted for the reaction mixture was conducted in exactly the same way for the same length of time. The olefin was estimated by titrating the remaining bromine with standard thiosulphate after addition of potassium iodide, and applying a small correction for the results of the blank experiment. The yield of olefin depended on the time of bubbling, owing, no doubt, partly to inefficient sweeping from the reaction mixture and partly to the effect on the equilibrium of removing one of the products of reaction. In " anhydrous " formic acid 10—15% of olefin was carried over after about 5 hours' bubbling. The yield decreased with increasing water content of the medium, and with 10% water in formic acid no olefin could be detected by this method. Attempts were made to determine accurately the amount of olefin formed in the reaction in " anhydrous " formic acid by adding a standard solution of bromine in carbon tetrachloride directly to the reaction mixture after equilibrium had been reached, shaking to extract the olefin into the tetrachloride layer, and estimating the halogen left after a standard period of time. In order to avoid the loss of olefin, the bromine–carbon tetrachloride was introduced through a tap-funnel into a partial vacuum created in the reaction vessel by cooling it in solid carbon dioxide–alcohol. The accuracy of the method, however, was vitiated by the fact that bromine reacts with formic acid. By applying a correction for the amount of halogen used up by the medium alone, determined in a separate experiment under similar conditions, it was found that the olefin estimation accounted for only about 50% of the chloride-ion concentration at equilibrium. In spite of the difficulties attending the experiment, we believe that this deficiency is real and is due to hydrolysis by traces of water and/or reaction with formic acid.

(b) tert.-*Butyl alcohol.* In order to obtain a more complete reaction, " 15% " water in formic acid was used as the medium of hydrolysis. *tert.*-Butyl chloride (20 c.c.) and the medium (100 c.c.) were shaken mechanically for 4 hours. The small upper layer was removed and shown to be unchanged *tert.*-butyl chloride (7 c.c.). The remainder was diluted with water (100 c.c.) and extracted with carbon tetrachloride (80 c.c.). The carbon tetrachloride was fractionated but no residue was obtained. The aqueous layer was neutralised with anhydrous sodium carbonate, saturated with sodium chloride, and fractionated over an 8-pear still-head. The fraction, b. p. 78·5°/735 mm. (6·5 c.c.), was repeatedly distilled from barium oxide. It finally had b. p. 82·5°; it solidified on cooling and was identified as *tert.*-butyl alcohol by direct comparison with an authentic specimen. In other similar experiments in various media ranging from Kahlbaum formic acid to " 15% " water in formic acid, the carbon tetrachloride used in the extraction was replaced by ether, and careful fractionation of the ethereal layer gave but a trace of residue which may have been *tert.*-butyl formate.

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