181. *Mechanism of Substitution at a Saturated Carbon Atom. Part XVI. Hydrolysis of Methyl, Ethyl,* iso*Propyl and* tert.*-Butyl Bromides in Acidic Solutions under Conditions believed to be conducive to Uniformity of Mechanism.*

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In this paper we present data for the rates of hydrolysis of the halides, named in the title, in wet formic acid, *i.e.*, under conditions especially favourable for the unimolecular mechanism (cf. preceding paper). The order of the alkyl groups is found to be that which we have predicted for the unimolecular reactions, *viz.*, S_N1 :—Me$<$Et$<$Pr$^\beta$$<Bu^\gamma$. By studying the effect of added water on the rate, we show that the bimolecular mechanism, even in this solvent, is important at the left-hand end of the series, though not sufficiently so to produce an actual rate minimum, such as is observed in less ionising media such as wet acetone.

THIS paper is closely related to the three papers immediately preceding, the first of which dealt with the variation of rate with structure in the series indicated in the title.

The theoretical connexion depends on the mechanism of hydrolysis, as determined by the sequences S_N2 :—Me$>$Et$>$Pr$^\beta$$>Bu^\gamma$ and S_N1 :—Me$<$Et$<$Pr$^\beta$$<Bu^\gamma$. In alkaline solution, in which a powerful base such as hydroxide ion may make the dominating contribution to hydrolysis, it was possible kinetically to establish mechanism S_N2 in the first three examples: and, consistently, the rate sequence was found to be S_N2 :—Me$>$Et$>$Pr$^\alpha$. In acid solution, a rate minimum was observed at the second member of the series. Here, first-order kinetics is consistent with either mechanism, but we were able to give a number of reasons for the belief that the mechanism changes in the series; that a second-order mechanism obtains with the first two members, and a first-order with the last two; and that there is probably a certain overlapping of mechanisms in the middle two members of the series. This evidence restored consistency to the observed rate variations: we had S_N2 :—Me$>$Et and S_N1 :—Pr$^\beta$$<Bu^\gamma$.

The present work arose from a desire to improve upon the previous very partial demonstration, represented by S_N1 :—Pr$^\beta$$<Bu^\gamma$, that in unimolecular hydrolysis the rate variation really is governed by the full sequence S_N1 :—Me$<$Et$<$Pr$^\beta$$<Bu^\gamma$. The theoretical conditions for securing the requisite uniformity of mechanism throughout the series are the use of a sufficiently low concentration of a sufficiently weak nucleophilic reagent, in a solvent of sufficiently high ionising power for alkyl halides. The preceding two papers suggest that wet formic acid might largely fulfil these conditions, the most significant indication being our conclusion that, in formic acid containing only small proportions of water, the hydrolysis of the primary halide, *n*-butyl bromide, is mainly unimolecular. We therefore decided to employ wet formic acid.

We record below the first-order rate constants (k_1 in hr.$^{-1}$) of hydrolysis of the four halides, at 100·2°, in " Kahlbaum " formic acid (which contains about 0·5% of water), and in formic acid with 10% of added water. The reaction of *tert.*-butyl bromide is much too fast to measure and the figures in parenthesis are orders of magnitude estimated from the measured rate for the chloride at a lower temperature (Bateman and Hughes, J., 1937, 1187) with reasonable allowances for the change in the temperature and the halogen atom:

	" Kahlbaum " formic acid.				10% Water in formic acid.			
	MeBr.	EtBr.	Pr$^\beta$Br.	Bu$^\gamma$Br.	MeBr.	EtBr.	Pr$^\beta$Br.	Bu$^\gamma$Br.
10^2k_1	0·847	1·45	37·9	(*ca.* 10^8)	2·76	3·15	61·9	(*ca.* 10^8)

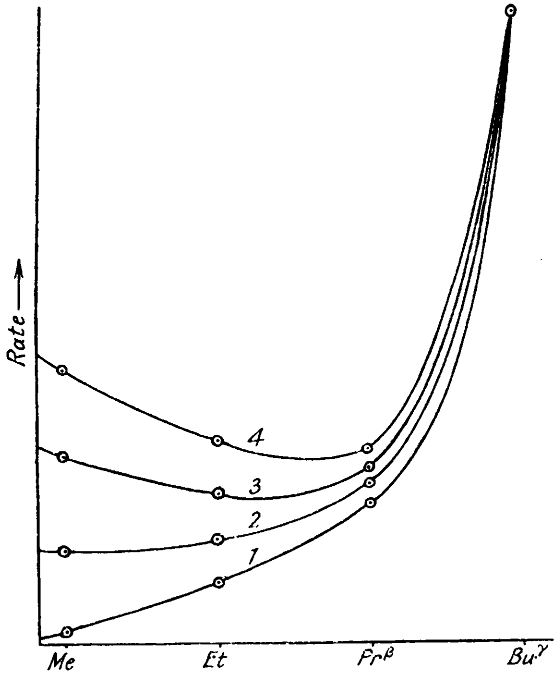
The rate constants for the *iso*propyl and *tert.*-butyl halides are composite inasmuch as small but appreciable proportions of the reactions measured are due to olefin elimination. It is probable, however, that the elimination process is also substantially unimolecular (cf., for example, Hughes, Ingold, and Scott, J., 1937, 1271), the rate-controlling stage in both substitution and elimination being the ionisation of the alkyl halide, which is what the first-order rate constant measures in so far as the reactions are indeed unimolecular. In any case the proportion of olefin is too small to affect the main conclusions. In the case of the primary halides some formate is also produced in the reaction (cf. experimental section), but, as shown in the preceding papers, no special significance attaches to this, since the alcohols react with formic acid under the conditions of the experiments.

The most noteworthy feature of both sets of figures is that the order of the alkyl groups is that which we have predicted for the unimolecular reaction dependent on ionisation (S_N1). It will be observed also that the rate ratios are less divergent from unity in the more aqueous solvent, because the factors by which the 10% of added water increases the rate diminish in the order Me, Et, Pr , Bu :

MeBr.	EtBr.	$Pr^{\beta}Br$.	$Bu^{\gamma}Br$.
3·26	2·17	1·63	(1·0)

The figure in parenthesis is based on the investigation of *tert.*-butyl chloride (Bateman and Hughes, *loc. cit.*).

FIG. 1.



In the case of methyl bromide we made a more detailed study of the variation of the rate with water concentration. The results indicate a linear variation, and suggest the incursion of a bimolecular mechanism of substitution (cf. preceding paper):

Added H_2O (%)	0·0	1·0	2·0	5·0	10·0
10^2k (hours^{-1})	0·847	1·01	1·26	1·67	2·76

In these experiments the initial concentration of methyl bromide was about 0·18M and the quantities of water noted were added to " Kahlbaum " formic acid which already contained about 0·5% of water.

Reviewing the results as a whole, we suppose that even in " Kahlbaum " formic acid the differences of rate between the halides that would characterise a purely unimolecular reaction are modified by bimolecular contributions. These should be most marked in the methyl end of the alkyl series, and will increase with the water content of the medium. It is clear that a more serious incursion of the bimolecular mechanism than appears to arise in any of the experiments here reported would introduce a minimum into the rate series.

This is what happens in less ionising and more strongly nucleophilic solvents such as aqueous alcohol or aqueous acetone. The situation may be schematically pictured with the aid of curves connecting points representing rates plotted on an arbitrary scale (Fig. 1). Curve (1) represents a pure unimolecular mechanism and expresses the sequence S_N1 :—Me<Et<Pr^{β}<Bu^{γ}. Curves (2), (3), and (4) represent a progressively increasing incursion of the bimolecular mechanism. The graded divergence of any of these curves from curve (1) expresses the sequence S_N2 :—Me>Et>Pr^{β}>Bu^{γ}. Only after mechanism S_N2 is well established does a minimum enter, which may shift from the second to the third member as this mechanism gains in importance.

EXPERIMENTAL.

Materials.—The bromides used were carefully purified commercial samples. The formic acid media were made up as previously described (Bateman and Hughes, J., 1937, 1187).

Kinetic Measurements.—A weighed quantity of the halide was dissolved in the medium, and the solution made up to a definite volume, usually at 0°. Portions of 5 c.c. were then enclosed in small sealed tubes and the progress of the reaction (at 100·2° ± 0·1°) was followed as before (cf. this vol., p. 943). It was observed in the experiments with methyl bromide that the reaction rate varied appreciably with the volume of the "free" space above the liquid (Table I). All the comparative experiments were therefore carried out in small bulbs which were specially blown from narrow glass tubing. It was arranged that the portion of reaction mixture introduced filled the bulb and part of the narrow tube, which could then be sealed leaving a minimum of "free" space. Failure to observe this precaution may lead to serious errors in rate measurements with volatile compounds at high temperatures, particularly if the reactants are but sparingly soluble in the medium.

TABLE I.

Illustrating Dependence of Rate on Volume of Reaction Tubes. Initial [CH_3Br] ~0·18N. Constants, k, in hours^{-1}.

Medium.	Total vol. of tube (c.c.).	10^2k.
10% Water in formic acid	6·5	2·76
,, ,, ,,	10	2·45
,, ,, ,,	21	2·12
"Kahlbaum" formic acid	6·5	0·847
,, ,, ,,	21	0·792

As with *n*-butyl bromide (this vol., p. 940) we were able to measure initial rates quite accurately. The results of a few typical experiments are recorded in detail in Table II. All the constants are of the first order, and are calculated from the formula $k = (1/t)\log_e a/(a - x)$. The initial [Halide] was *ca.* 0·18N throughout, and the total volume of the reaction tubes (except in the experiments recorded in Table I) was *ca.* 6·5 c.c.

Reaction Products.—Previous experience (cf. this vol., pp. 935, 940) had shown that a study of the proportions of alcohol and alkyl formate in the final products gives no reliable information about the mechanism of hydrolysis in aqueous formic acid. Consequently we did not undertake an extended investigation of this subject, but, employing the technique previously described (this vol., p. 943), we were able to show that the yield of *iso*propyl formate in the reaction of *iso*propyl bromide in "Kahlbaum" formic acid is very small, the secondary halide resembling *tert.*-butyl chloride in this respect. The situation with regard to a typical primary halide (*n*-butyl bromide) is described elsewhere (*loc. cit.*). We also carried out olefin estimations with *iso*propyl bromide in "Kahlbaum" formic acid, and in "10%" aqueous formic acid, employing the technique previously described (this vol., p. 943). The results indicated 6% elimination in the former medium, and 7% in the latter. In "10%" aqueous formic acid the propylene dibromide was isolated as follows: *iso*propyl bromide (43 g.) and the medium (400 c.c.) were refluxed for 19 hours, and the olefin was absorbed in a solution of bromine in methylene chloride. The methylene chloride solution was washed with water, with dilute aqueous thiosulphate, and again with water, dried, and distilled. The solvent was removed below 45°, and the residue (4·4 g.) was fractionated under reduced pressure: (1) 0·8 g., b. p. below 59°/47 mm.; (2) 3·0 g., b. p. 59°/47 mm. (Found: C, 18·3; H, 3·0; Br, 78·7. Calc. for $C_3H_6Br_2$: C, 17·8; H, 3·0; Br, 79·2%). As in the case of *n*-butyl bromide (*loc. cit.*), olefin elimination in ethyl bromide is negligible under the experimental conditions here employed.

TABLE II.

Illustrating Determination of First-order Rate Constants. a (initial [RBr]) and x ([HBr]) expressed as equivalent c.c. of 0·0249N–$AgNO_3$ per 5 c.c. of solution. t is in hours and k in hours^{-1}.

1. Hydrolysis of MeBr in " Kahlbaum " formic acid (a = 37·55).

t	1·0	2·0	3·4	4·2	5·0
x	0·32	0·65	1·00	1·30	1·52
10^2k	0·875	0·875	0·793	0·839	0·829

2. Hydrolysis of MeBr in " 5% " aqueous formic acid (a = 40·88).

t	0·5*	1·0	1·5	2·0*	2·5	3·5*	4·1
x	0·36	0·70	0·96	1·36	1·60	2·28	2·58
10^2k	1·79	1·75	1·60	1·70	1·60	1·64	1·60

* These tubes contained *ca.* 0·5 g. of crushed glass.

3. Hydrolysis of MeBr in " 10% " aqueous formic acid (a = 37·97).

t	1·2	2·35	3·5	5·0	6·7	8·5
x	1·25	2·35	3·41	4·88	6·71	7·81
10^2k	2·78	2·72	2·68	2·75	2·90	2·71

4. Hydrolysis of EtBr in " Kahlbaum " formic acid (a = 34·47).

t	1·0	2·0	2·5	3·0	3·5	4·0
x	0·45	0·97	1·33	1·45	1·72	1·98
10^2k	1·31	1·41	1·58	1·44	1·47	1·49

5. Hydrolysis of EtBr in " 10% " aqueous formic acid (a = 43·42).

t	1·0	2·0	3·0	4·0	5·75	8·5
x	1·30	2·66	3·88	5·29	7·46	10·69
10^2k	3·04	3·17	3·12	3·25	3·28	3·06

6. Hydrolysis of $Pr^{\beta}Br$ in " Kahlbaum " formic acid (a = 36·58).

t	0·10	0·20	0·30	0·40	0·57	0·85
x	1·39	2·65	3·98	5·18	6·70	10·17
$10k$	3·89	3·77	3·85	3·83	3·55	3·83

7. Hydrolysis of $Pr^{\beta}Br$ in " 10% " aqueous formic acid (a = 39·14).

t	0·10	0·20	0·30	0·40	0·60	0·90
x	2·33	4·56	6·58	8·70	12·10	16·77
$10k$	6·15	6·19	6·13	6·28	6·16	6·22

Reaction of Methyl Bromide in 50% *Aqueous Ethyl Alcohol at* 100·2°.—The method employed was similar to that described for the corresponding reaction of *n*-butyl bromide (*loc. cit.*) except that the sealed tubes employed were specially designed (cf. p. 947). In Table III, a is the initial concentration of methyl bromide, x the concentration of hydrogen bromide (both expressed in equivalent c.c. of 0·0422N-sodium hydroxide per 5 c.c. of solution), t the time in mins., and k the first-order rate constant in min.$^{-1}$. This constant is nearly two hundred times larger than the corresponding first-order rate constant in " Kahlbaum " formic acid (cf. preceding paper).

TABLE III.

a = 19·73.

t	5	10	15	20	30	40	60
x	2·54	4·60	6·33	8·31	10·74	13·45	16·34
10^2k	2·82	2·66	2·58	2·73	2·62	2·86	2·94

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