180. *Mechanism of Substitution at a Saturated Carbon Atom. Part XV. Unimolecular and Bimolecular Substitutions of* n-*Butyl Bromide with Water, and with Anions, as Substituting Agents in Formic Acid Solution.*

By Leslie C. Bateman and Edward D. Hughes.

This investigation on *n*-butyl bromide was carried out as a control on our study of *tert.*-butyl chloride (preceding paper). It had already been concluded (p. 925) that, whilst in ionising media the solvolytic reactions of tertiary halides are essentially unimolecular, those of primary halides are at least partly (predominantly in some solvents) bimolecular. We have now found that, in contrast to the invariance, with changing water concentration, of the rate of reaction of *tert.*-butyl chloride in formic acid containing water, the rate for *n*-butyl bromide increases linearly with the water concentration. Clearly there is a difference of mechanism, the former reaction being unimolecular, and the latter largely bimolecular. There is, in the case of *n*-butyl bromide, probably some accompanying unimolecular reaction also, but this is extremely slow in comparison with the corresponding reaction of *tert.*-butyl chloride (factor $\sim 10^6$, equivalent to a factor of $\sim 10^8$ for identical halogen atoms).

Similarly, added formate ions, which intervened in the reaction of *tert.*-butyl chloride to produce *tert.*-butyl formate without increasing the total rate, intervene in the reaction of *n*-butyl bromide with a strong acceleration of the rate. Evidently the intervention,

which in the former case was unimolecular, the formate ion attacking the carbonium ion only after the rate-determining ionisation, is in the latter case largely bimolecular, the attack being on the alkyl halide molecule, and making, therefore, an additive contribution to the total rate of its destruction.

These results and others, obtained in a case in which a bimolecular mechanism is agreed to be at work, show the incorrectness of Taylor's suggestion that water and formic acid are about equally reactive in bimolecular substitution, and of his claim that calcium formate is not a direct reagent for the production of formic esters.

OUR investigation (J., 1937, 1187; preceding paper) on the hydrolysis, and other substitutions, of *tert.*-butyl chloride in formic acid seemed to us to create a demand for a parallel investigation of a *n*-alkyl halide. The project was in any case a natural extension of our exposure of Taylor's treatment of the problem of the reactions of the tertiary halide, since nothing could show up more effectively than a control research of the kind indicated the strength or weakness of any treatment.

Tertiary and primary halides are each typical of a class, in that, in general, the unimolecular mechanism predominates in the solvolytic reactions of the former and the bimolecular in those of the latter. Thus in an accompanying paper (this vol., p. 925) it is concluded that the reaction of *tert.*-butyl bromide with aqueous alcohol is exclusively unimolecular, whereas that of ethyl bromide is largely, but perhaps not wholly, bimolecular. A similar distinction of mechanism might be expected to apply to the reaction in formic acid, and in this case added water should produce acceleration in the hydrolysis of the primary halide, although it does not disturb the reaction rate of the tertiary halide. On the other hand, Taylor's explanation of the latter phenomenon as due to the closely similar reactivities of water and formic acid, in analogous bimolecular substitutions, would be shown by such an observation to fail in its direct application to a case in which a bimolecular mechanism is agreed to be at work.

Furthermore, Taylor's argument that water and formic acid had similar reactivities in their bimolecular substitution because the rates of hydrolysis of *tert.*-butyl chloride in formic acid and 50% aqueous alcohol were of the same order of magnitude could be tested by application to the admittedly bimolecular substitutions of the primary halide. Contrary to Taylor we envisaged a difference of mechanism with the result that, as there happens to be rough equality of rates for the one halide in the two solvents, there should not be for the other halide, because the solvent influence on the two mechanisms is different.

We chose for study *n*-butyl bromide rather than a methyl or ethyl halide because we anticipated slow reactions necessitating a fairly high temperature. Furthermore, the products were more conveniently isolated than they would have been with a lower halide.

Measurements have been made at 100° in " Kahlbaum " formic acid, which contains about 0·5% of water, and in aqueous mixtures containing up to 10% of added water. As will be seen from the right-hand side of Fig. 1, the rates increase sharply and approximately linearly with the water concentration, in marked contrast with the behaviour of the tertiary halide, which is illustrated for comparison on the left. It is our provisional opinion * that the residual rate for the primary halide at low water concentration is due largely to a unimolecular reaction which is (as it should be) exceedingly slow in comparison with the corresponding reaction of the tertiary compound, *viz.*, about 200 times slower at a temperature 85° higher, the factor of difference at equal temperatures being probably of the order of 10^6. Our comparison is, of course, between *n*-butyl bromide and *tert.*-butyl chloride, but bromides are more reactive than chlorides, and hence the difference of rate between, for example, the primary and the tertiary chloride would be even larger. Concerning the linear increase of rate, Taylor will no doubt agree with us that it represents a

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* An alternative explanation would be that the residual rate is due to a bimolecular reaction with formic acid in one of its various modifications. A study of the effect produced by extraneous formate ions, however, eliminates the ionised form of the acid (in its equilibrium concentration) from serious consideration, and the work of Dawson (cf. preceding paper) makes it improbable that the undissociated form has any appreciable influence in bimolecular substitution. Valuable confirmation of the interpretation adopted is provided by the work described in the following paper.

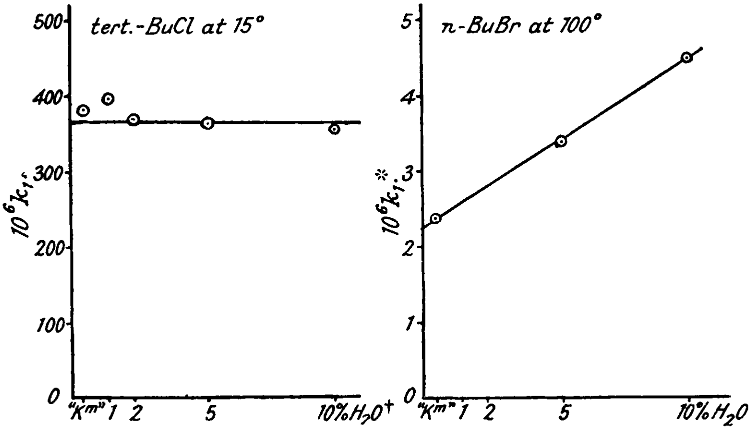
bimolecular reaction; nevertheless, there is no question of equal activity between water and formic acid as reagents.

A study of the reaction products in " Kahlbaum " formic acid showed the presence of *n*-butyl alcohol, *n*-butyl formate and olefin, although the amount of olefin formed was negligible, in agreement with previous observations relating to the hydrolysis of primary halides (cf. this vol., p. 899). No special significance can be attached to the production of the formate, for we have isolated it from *n*-butyl alcohol and formic acid under the conditions obtaining in the hydrolysis experiments (cf. preceding paper). The production of olefin is trivial also when the solvent is " Kahlbaum " formic acid with 10% of added water.

We can obtain a further check on these conclusions. If water participates in a bimolecular reaction with *n*-butyl bromide, formate ions must do so too, because formate ions are more strongly nucleophilic than water molecules. In the case of *tert.*-butyl chloride we found that calcium formate in homogeneous solution had a negligible effect on the rate. If the mechanism for *n*-butyl bromide is different and, in particular, if any considerable part of the reaction is bimolecular, then we should observe a marked increase of rate due to the greater nucleophilic activity of formate ion than of water. Using calcium formate, we found a strong effect of this kind: a 0·1N-concentration of the salt increased the rate as much as an extra 1·7M-concentration of water would have done. The amount of olefin formed under these conditions remained insignificant.

FIG. 1.

Effect of Water Concentration on Rate of Hydrolysis of a Tertiary and a Primary Halide in Formic Acid. (*Note temperature and scale difference.*)



* For *n*-butyl bromide the initial rates are calculated formally as first-order constants for comparison with the first-order constants of *tert.*-butyl chloride. In both diagrams k_1 is in sec.$^{-1}$.

† The aqueous mixtures were made up from " Kahlbaum " formic acid (cf. experimental section).

Finally, in the case of *n*-butyl bromide we do not find even an approximate equality of rates in 50% aqueous ethyl alcohol and in " Kahlbaum " formic acid—the first-order rate constant is forty times larger in the former medium. This is, again, in marked contrast with the behaviour of *tert.*-butyl chloride, for which the constant in the alcohol solvent is nearly four times smaller than that in formic acid. With both halides the hydrolysis in aqueous alcohol is accompanied by alcoholysis and the measured rate includes both, a circumstance which still further invalidates Taylor's choice of the 50% mixture for the purpose of assessing the activity of water in comparison with that of formic acid in bimolecular substitution.

From our point of view, the experiments with *n*-butyl bromide form an exceedingly satisfactory control on the conclusions which we drew in 1937 relating to the reaction of *tert.*-butyl chloride.

EXPERIMENTAL.

(1) *Reaction of* n-*Butyl Bromide with Aqueous Formic Acid.*—(A) *Rate measurements.* Owing to the slow reaction of the primary halide, and to the development of considerable pressure in

the tubes after long heating, we have not yet determined the composition at equilibrium from kinetic data, but we have been able to measure initial rates quite accurately. Measurements were carried out in " Kahlbaum " formic acid and in " 5% " and " 10% " aqueous solutions (cf. Bateman and Hughes, J., 1937, 1187). The method was as follows : A known quantity of *n*-butyl bromide was dissolved in the medium, and the solution made up to 100 c.c. at room temperature. Portions of 5 c.c. were enclosed in sealed tubes, which were then heated for a known time at 100°, cooled in solid carbon dioxide–alcohol, and broken under 75 c.c. of carbon tetrachloride, and the contents estimated by the method previously adopted for the tertiary halide (Bateman and Hughes, *loc. cit.*). The results, together with those of an experiment with added calcium formate (cf. below), are in Table I, where a is the initial concentration of *n*-butyl bromide, x the concentration of hydrogen bromide after t hours (both expressed in equivalent c.c. of 0·0294N-silver nitrate per 5 c.c. sample), and k_1(sec.$^{-1}$) is the formal first-order rate constant, $(1/t)\log_e a/(a - x)$.

TABLE I.

Development of Bromide Ion from n-*Butyl Bromide in Formic Acid at* 100°.

(a = 14·50 throughout.)

" Kahlbaum " formic acid.			" Kahlbaum " + " 5% " H_2O.			" Kahlbaum " + " 10% " H_2O.			" Kahlbaum " formic acid +0·101N-calcium formate.		
t.	x.	10^6k_1.	t.	x.	10^6k_1.	t.	x.	10^6k_1.	t.	x.	10^6k_1.
3·75	0·43	2·25	2·0	0·33	3·22	5·0	1·26	5·05	2·75	0·43	3·08
6·0	0·72	2·35	4·0	0·68	3·33	9·7	1·99	4·22	5·0	0·73	2·86
9·3	1·03	2·20	6·6	1·06	3·66	15·0	2·97	4·26	7·0	1·11	3·16
13·5	1·65	2·49	9·5	1·55	3·31	20·0	4·01	4·50	9·0	1·28	2·86
17·5	2·06	2·44	14·5	2·36	3·41	27·0	5·16	4·53		Mean	2·99
20·0	2·31	2·41	19·5	3·12	3·44	32·75	5·90	4·44			
23·25	2·67	2·43	23·5	3·58	3·36	44·0	7·35	4·47			
	Mean	2·37		Mean	3·39	63·3	9·24	4·44			
							Mean	4·49			

(B) *Reaction products.* (a) n-*Butyl alcohol and* n-*butyl formate.* *n*-Butyl bromide (48 g.) and " Kahlbaum " formic acid (400 c.c.) were refluxed for 28 days and cooled in ice, ether (200 c.c.) and then water (800 c.c.) added, and the mixture shaken. The aqueous layer was extracted with ether (*ca.* 30 c.c.), and the combined ethereal extracts were washed (4—5 times) with water (300 c.c.) until the washings were substantially free from formic acid. Distillation of the dried ethereal portion gave a fraction, b. p. 103—106°, which when redistilled gave 5·3 g. (15%) of pure *n*-butyl formate, b. p. 104·5—105·5°/750 mm. (Found : C, 58·2; H, 9·7. Calc. : C, 58·8; H, 9·8%). The aqueous portion was neutralised with sodium carbonate, saturated with sodium chloride, and extracted thrice with ether (total, *ca.* 250 c.c.). Distillation of the dried extract gave *ca.* 1·5 g., b. p. 114°, of slightly impure *n*-butyl alcohol (Found : C, 63·1; H, 13·6. Calc. : C, 64·9; H, 13·5%). This was treated with *p*-nitrobenzoyl chloride and the *p*-nitrobenzoate was crystallised from light petroleum (m. p. and mixed m. p. 35·5°) (Found : C, 59·7; H, 5·9. Calc. : C, 59·2; H, 5·8%).

The isolation of these products is, of course, far from complete. We did not attempt to develop a quantitative separation, because no special significance can be attached to the results on account of the esterification of *n*-butyl alcohol [cf. section (3)]. The amount of *n*-butyl formate formed under the strict conditions of our kinetic experiments is probably considerably less than that which is formed in the isolation experiments, because the latter were conducted in open vessels and were accompanied by the partial loss of hydrogen bromide, a circumstance which increases the final yield of ester (cf. preceding paper). It is noteworthy that the quantity of formate is increased by the presence of calcium formate [section (2) (B)] and that an even better yield is easily obtainable from *n*-butyl alcohol and formic acid in the complete absence of hydrogen bromide [section (3)].

(b) *Olefin.* We employed an aspiration method similar in its essential features to that previously described (this vol., p. 901). The reaction mixture was kept at 100° in a flask connected to a long vertical condenser, and the volatile products were swept in a slow current of air through a trap at 0° and two bubbling tubes containing a standard solution of bromine in methylene chloride. The second tube was kept at −78°, and a trap containing aqueous potassium iodide was placed at the end of the gas train. After about 50 hours' heating, the experiment was discontinued, the absorption tubes were allowed to attain room temperature, and the remaining bromine was finally estimated by the usual method. Since the hydrolysis was generally incomplete under these conditions, it was also necessary to estimate the amount of unchanged halide. The combined contents of the flask and the first trap (free from olefin) were, therefore, extracted with ether, and, after washing and distillation of the ether, the *n*-butyl bromide was completely hydrolysed with hot aqueous alcoholic potassium hydroxide and estimated by Volhard titrations. The results were in substantial agreement with estimations based on kinetic data obtained as described in section (1) (A). Estimations were carried out in " Kahlbaum " formic acid, in 10% water in formic acid, and in " Kahlbaum " formic acid containing calcium formate; the amount of unsaturated material thus indicated was always less than 2% of the total decomposition.

(2) *Reaction of* n-*Butyl Bromide with Wet Formic Acid and Calcium Formate.*—(A) *Rate measurements.* Powdered calcium formate and *n*-butyl bromide were made up to 100 c.c. with " Kahlbaum " formic acid ([calcium formate] = 0·101N), and the reaction followed as described above [section (1) (A)]. The results are in Table I.

(B) *Reaction products. n*-Butyl bromide (48 g.), anhydrous calcium formate (70 g.), and " Kahlbaum " formic acid (400 c.c.) were refluxed for 28 days. Fractionation of an ethereal extract, obtained as previously described [section (1) (B)], gave 7·8 g. (22%) of *n*-butyl formate (Found : C, 59·0; H, 9·9%). The aqueous portion was not examined. Olefin estimations were carried out with the results indicated in section (1) (B).

(3) *Reaction of* n-*Butyl Alcohol with Wet Formic Acid.*—*n*-Butyl alcohol (26 g.) and " Kahlbaum " formic acid (400 c.c.) were refluxed for 24 hours. Ether was added, and the solution washed with water, dried, and distilled. A fraction, b. p. 104—106°, was redistilled and gave 18 g. (50%) of pure *n*-butyl formate, b. p. 105·5—106°/760 mm. (Found : C, 59·0; H, 9·9%). The formate was also obtained in 25% yield when the alcohol (9·6 g.) was mixed with formic acid (400 c.c.) and left for only 15 minutes at room temperature.

(4) *Reaction of* n-*Butyl Bromide with* 50% *Aqueous Ethyl Alcohol.*—(A) *Rate measurements.* A known quantity of *n*-butyl bromide was dissolved in the medium, and the solution made up to 100 c.c. at room temperature. Aliquot portions were enclosed in sealed tubes. Each tube was shaken vigorously in the thermostat at 100° for 1 minute, left at this temperature for known times, quenched rapidly, and broken under 100 c.c. of absolute alcohol. The acidity was titrated against standard alkali with lacmoid as indicator. An " initial " estimation was made on a sample which had been shaken in the thermostat for 1 minute and immediately quenched. The results are in Table II, where t is the time in minutes, $a - x$ the concentration of *n*-butyl bromide, expressed in c.c. of 0·0490N-alkali per 5 c.c. of solution, and k_1 the first-order rate constant in sec.$^{-1}$.

TABLE II.

t	0	15	30	50	75	105	145	180	235	295	355
$a - x$	8·59	7·80	7·27	6·43	5·69	4·91	3·82	3·25	2·44	1·67	1·16
$10^5 k_1$	—	10·7	9·28	9·65	9·15	8·89	9·32	9·00	8·97	9·25	9·40

(B) *Isolation of* n-*butyl ethyl ether. n*-Butyl bromide (32 g.) and 50% aqueous ethyl alcohol (500 c.c.) were refluxed in an all-glass apparatus. Frequent and exact neutralisation (phenolphthalein) of the mixture was effected by cautious addition of a concentrated solution of sodium hydroxide in a medium of the same composition. After completion of the reaction, the mixture (vol., 600 c.c.) was diluted with water (400 c.c.) and distilled with an 8-pear column to give the following fractions : (1a) 10·5 c.c., b. p. 72—75°; (1b) 8 c.c., b. p. 75—78·8°; (1c) 20 c.c., b. p. 78·8—80·8°; (1d) 25 c.c., b. p. 80·8—81°. With water (1a), (1b), and (1c) gave an upper layer, which was washed with water, but (1d) gave no separation of layers. The aqueous portions and washings from (1a), (1b), and (1c) were combined, diluted with water, and distilled : (2a) 2 c.c., b. p. 72—78·8°; (2b) 4 c.c., b. p. 78·8—85°; (2c) 10 c.c., b. p. 85—88°. With water (2a) gave an upper layer, which was washed with water, but (2b) and (2c) gave no separation. Fraction (1d), water, and the aqueous portions and washings from (2a), (2b), and (2c) were now combined and distilled : (3a) 2 c.c., b.p. 72—85°. Addition of water and calcium chloride gave an upper layer. The top layers (crude ether) from (1a), (1b), (1c), (2a), and (3a) totalled 10 c.c. This was subjected to the following distillations : (I) From fused barium oxide : yield 9·0 c.c., b. p. 91—96°. (II) From potassium : yield 7·9 c.c., b. p. 91—92° (Found : C, 70·2; H, 13·5. Calc. for $Bu^{a}OEt$: C, 70·6; H, 13·7%).

THE SIR WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C. 1.

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