179. *Mechanism of Substitution at a Saturated Carbon Atom. Part XIV. Unimolecular Substitutions of* tert.*-Butyl Chloride with Water, and with Anions, as Substituting Agents in Formic Acid Solution.*

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In a previous paper (J., 1937, 1187) we recorded that the rate of reaction of *tert.*-butyl chloride with water in formic acid as solvent was of the first order and independent of the water concentration; we concluded that the reaction was unimolecular. The main products were *tert.*-butyl alcohol and (under some conditions) *iso*butylene. Our conclusion was challenged by Taylor (*ibid.*, p. 1852) on the ground that he had isolated *tert.*-butyl formate " from Kahlbaum's formic acid and *tert.*-butyl chloride at room temperature." He implied that this ester was in our experiments the main product, which we had overlooked through faulty experimental technique.

We have re-examined our technique and found that it is correct: we show that *tert.*-butyl formate cannot be isolated in quantity simply from Kahlbaum's formic acid and *tert.*-butyl chloride at room temperature. In fact, Taylor did not do it in this way, but added an enormous excess of the soluble salt, calcium formate, which we show to be the responsible reagent. Likewise, by adding calcium chloroacetate, we obtain *tert.*-butyl chloroacetate. We show, however, that these salts form their characteristic products without an increase of the total reaction rate, so that even these substitutions are unimolecular, the anions intervening only after the rate-controlling ionisation of the alkyl halide. In the absence of added salts, *tert.*-butyl formate, of which 19% should be present according to Taylor, is actually not formed in more than traces, that can adequately be accounted for by the demonstrated direct esterification of *tert.*-butyl alcohol with formic acid.

Taylor's own explanation of the invariance of rate with water concentration assumes that water and formic acid have equal reactivity in bimolecular attack on *tert.*-butyl chloride. We show on both general and specific grounds that the reactivity of the latter is negligible in comparison with that of the former (cf. the following paper). Thus we confirm our previous conclusions in every detail.

TAYLOR having disagreed with our previous conclusions (J., 1937, 1187) concerning the aqueous hydrolysis of *tert.*-butyl chloride in formic acid as solvent (paper 4; references, this vol., p. 900), we shall here summarise the evidence adduced by both parties, and also submit new evidence.

(i) *Our Previous Evidence and Interpretation.*

Our previous experimental findings were as follows: (*a*) Kinetic study showed that the rate of development of chloride ions from *tert.*-butyl chloride in " anhydrous " formic acid and in formic acid containing various proportions up to 10% of added water is practically constant. (*b*) The main organic product in aqueous media is *tert.*-butyl alcohol, although a second reaction, significant in the most nearly anhydrous solvents, leads to *iso*butylene; furthermore, a doubtful trace (too small for certain identification) of *tert.*-butyl formate is produced. (*c*) The reactions are reversible, and, in contrast to the forward reactions, the rates of the reverse reactions are reduced by added water.

By way of discussion it was stated: " We interpret these results as follows. The rate-determining process in all the media examined is the same, *viz.*, the ionisation of *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 *sequalæ* affects the rate of formation of chloride ions, which is determined solely by the rate of electrolytic dissociation of the alkyl halide." Concerning the retrograde reactions our interpretation was as follows: " 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 the retrograde reactions are strongly affected " (*i.e.*, reduced) " by water solvation of the hydrogen chloride."

(ii) *Taylor's Evidence and Interpretation.*

In considering Taylor's evidence it is necessary to distinguish between what he states to be " fact " in discussion and his experimental record. His opening statement runs thus: "The interpretation offered by Bateman and Hughes . . . is shown to be inadequate, since they did not take into account the formation of *tert.*-butyl formate. An alternative explanation of their kinetic results is based on this fact, *viz.*, that *tert.*-butyl chloride reacts with formic acid to give *tert.*-butyl formate." It is clearly implied here that the chloride and formic acid interact to give *tert.*-butyl formate *under the conditions of our kinetic experiments*: the statement would be meaningless otherwise. It is implied, furthermore, that the *tert.*-butyl formate is produced under these conditions, not merely in traces as we had suggested, or in the way we did take into account as the previous paragraph shows, but as the principal reaction product, which, as Taylor later suggests, we ought to have isolated in quantity instead of *tert.*-butyl alcohol. Taylor claims that he has isolated *tert.*-butyl formate " from Kahlbaum's formic acid and *tert.*-butyl chloride at room temperature."

This apparently simple " fact " appears, however, in the later part of Taylor's paper to be actually the result of an uncertain argument based on a not strictly relevant experiment. It is first stated (also as fact) that there is a balanced process $\mathrm{Bu}^{\gamma}\mathrm{Cl} + \mathrm{H{\cdot}CO_2H} \rightleftharpoons \mathrm{H{\cdot}CO_2Bu}^{\gamma} + \mathrm{HCl}$ which normally proceeds to the extent of 19% towards the right. (All this is assumption, the figure 19% being based, apparently, on Taylor's own interpretation of one of our kinetic observations.) Next it appears that, for the purpose of isolating *tert.*-butyl formate, this " equilibrium " was " pushed over to the right by having present an excess of powdered calcium formate " (in order to remove hydrogen chloride). Only by comparing the experimental particulars with the solubility of calcium formate (which Taylor does not give) can it be discovered that the actual reagent by which, according to his description, he produced *tert.*-butyl formate from *tert.*-butyl chloride was, not formic acid, but a 0·3N-solution of calcium formate in formic acid containing a large excess (66 g. in 200 c.c.) of suspended calcium formate. The evidence that, even under these conditions, Taylor isolated the pure ester is not free from ambiguity, since he records as its molecular weight, obtained by quantitative saponification, " *M*, 113·7 (Calc.: 114)." This excellent agreement is difficult to understand, as the molecular formula of *tert.*-butyl formate is, not $C_6H_{10}O_2$ (*M*, 114), but $C_5H_{10}O_2$ (*M*, 102). The isolation of *tert.*-butyl formate is considered in section (iii) (a) and the mode of action of calcium formate in section (iii) (b).

Taylor's explanation of the fact that in our experiments (in which, of course, no calcium formate was employed) *tert.*-butyl alcohol rather than *tert.*-butyl formate was isolated, is that the ester is very rapidly hydrolysed: " It is mainly to this ease of hydrolysis that Bateman and Hughes's failure to isolate the ester must be attributed, for in order to extract the end-products they added water to the reaction mixture before adding the organic solvent, ether or carbon tetrachloride " (Taylor added the organic solvent before the water). We shall show later that *tert.*-butyl formate can easily be isolated when present (and, according to Taylor's reasoning, 19% is present, without calcium formate), whatever the order of the addition.

Taylor's alternative explanation of our finding that the rate of hydrolysis of *tert.*-butyl chloride is independent of water concentration is that a main bimolecular reaction (I) is " probably " partly replaced when water is present by a bimolecular reaction (II) of approximately equal rate, the total rate being therefore independent of the water concentration :

$$\mathrm{Bu^{\gamma}Cl + H{\cdot}CO_2H \longrightarrow H{\cdot}CO_2Bu^{\gamma} + HCl} \quad . \; . \; . \; . \; . \quad \mathrm{(I)}$$

$$\mathrm{Bu^{\gamma}Cl + H_2O \longrightarrow Bu^{\gamma}OH + HCl} \quad . \; . \; . \; . \; . \quad \mathrm{(II)}$$

His argument is that the comparable reactivities of water and formic acid in these bimolecular substitutions are indicated by the rough equality between our constant rate in aqueous formic acid and the rate of reaction of *tert.*-butyl chloride with 50% aqueous ethyl alcohol (Hughes, J., 1935, 255). We do not understand this reasoning; in particular we fail to see the special relevance of the comparison with 50% aqueous alcohol, or even with aqueous alcohol at all. We shall see in section (iii) (c) and in the following paper whether or not formic acid and water are equally active in nucleophilic bimolecular substitutions.

(iii) *New Evidence and Conclusions.*

(a) *The Formation and Significance of* tert.*-Butyl Formate.*—We have repeated and extended our previous experiments, and also Taylor's on the isolation of this ester. We find that his criticism of our extraction method is unwarranted. Provided the elementary precaution is taken of doing the extraction quickly with cooled solutions, it matters not in what order the solvents are added. Even if these precautions are omitted—if the addition of water is carried out at room temperature, and the subsequent extraction with ether is performed at leisure—there is no difficulty in isolating the ester when present, though the yield may be slightly impaired. From solutions equivalent to those obtained at the end of our formerly published kinetic runs, and by employing both methods of isolation, we again found traces, too small for certain identification, of liquid which probably contained *tert.*-butyl formate. From solutions to which much calcium formate had been added as in Taylor's description, we isolated (by both methods), approximately in his yield, *tert.*-butyl formate (of the correct composition and molecular weight). Taylor's phraseology implies that he had established the truth of his explanation of why *tert.*-butyl formate did not appear in quantity in our isolation experiments, but it now appears that his statement was an incorrect guess, and that he had really carried out no direct tests at all.

In case the same significance should be claimed for the probable trace of ester as Taylor applied to the 25% produced in the presence of calcium formate, *viz.*, that it can arise only by direct action of *tert.*-butyl chloride on formic acid, we have now verified the anticipated interaction of *tert.*-butyl alcohol with formic acid, which Taylor disregarded. It follows from our previous considerations that, starting either with *tert.*-butyl chloride, or with equivalent quantities of *tert.*-butyl alcohol and hydrogen chloride, the main substances present (in an analytical sense) in the moist formic acid solvent after a length of time sufficient for the completion of a corresponding kinetic run are those of the equilibrium

$$\mathrm{Bu^{\gamma}Cl + H_2O \rightleftharpoons Bu^{\gamma}OH + HCl}$$

In these new experiments we started with the alcohol, but left out the hydrogen chloride, and after an appropriate length of time isolated about 22% of *tert.*-butyl formate. This shows that the probable trace obtained in the presence of hydrogen chloride, or alternatively when the starting point is *tert.*-butyl chloride, could have been formed by the esterification of *tert.*-butyl alcohol: it is not necessary to assume that it is formed directly from *tert.* butyl chloride and formic acid. Of course, esterification being reversible, the same argument applies the other way round: all we can say on the basis of isolation experiments is that the main product into which *tert.*-butyl chloride is converted (directly or indirectly) is *tert.*-butyl alcohol. In relation to the question of what is the substituting agent (water or formic acid), and to that of the mechanism of its interaction with *tert.*-butyl chloride, isolation experiments alone are, therefore, indecisive; evidence of a different type is considered in the sequel and in the following paper.

(b) *The Mode of Action of Calcium Formate and the Action of Calcium Chloroacetate.*—Although the removal of hydrogen chloride from the balanced action formulated above must promote the production of *tert.*-butyl alcohol, and, therefore, in accordance with the experiments just described, its esterification to *tert.*-butyl formate, there is no doubt that the mode of action of calcium formate in Taylor's experiment is both more profound and more direct than that of a mere absorbent of hydrogen chloride. In order to show this we have investigated the behaviour of calcium chloroacetate with *tert.*-butyl chloride in formic acid. This salt was chosen, first, because its solubility in formic acid is comparable with that of calcium formate; and, secondly, because chloroacetic acid is so much stronger than formic acid that we may expect the chloroacetate ion to remain essentially stable in formic acid solution. We find that much of the ester which in Taylor's experiment was *tert.*-butyl formate appears in this parallel experiment as *tert.*-butyl chloroacetate. We have also shown that the latter does not arise from *tert.*-butyl alcohol, formic acid and calcium chloroacetate. This seems to us definite evidence of interaction between the added salt and *tert.*-butyl chloride, because the only way of explaining the formation of *tert.*-butyl chloroacetate on Taylor's scheme of bimolecular interaction between *tert.*-butyl chloride and an undissociated acid would involve the improbable double assumption that the anion of the stronger acid becomes replaced by that of the weaker, and that the undissociated form of the stronger acid is a more powerful reagent in bimolecular nucleophilic substitution than that of the weaker acid. A part of the total ester isolated in the presence of calcium chloroacetate consists of *tert.*-butyl formate, and the most natural explanation is that it is formed through the expected increase of direct esterification of *tert.*-butyl alcohol; for we have already noted that when hydrogen chloride, and any substance that could yield it, are completely removed, then the main reaction undergone by *tert.*-butyl alcohol is esterification with the formic acid.

Direct interaction between a formate or chloroacetate ion and *tert.*-butyl chloride could be unimolecular, bimolecular, or, under Taylor's conditions, which involve the presence of a very large excess of suspended salt, heterogeneous. In the last two cases the addition of the salt should produce an increase in the reaction rate. We have studied the kinetics of the reactions taking place in the presence of an excess of suspended salt, and find that there is no increase of rate, but in both cases a small decrease. We have also examined the effect of a 0·1N-concentration of calcium formate (homogeneous) and find a rate constant in good agreement with our previous result in the absence of added salt. The decrease in rate is therefore associated with the presence of undissolved salt, and may be due to the temporary removal of part of the *tert.*-butyl chloride by adsorption on the saline surface. We conclude that the reaction with formate or chloroacetate ions, as with water molecules, is unimolecular, the salts intervening after the reaction-stage which fixes the rate:

$$\begin{array}{rcll} \mathrm{Bu^{\gamma}Cl} & \longrightarrow & \mathrm{Bu^{\gamma+} + Cl^{-}} & \text{(slow)} \\ \mathrm{Bu^{\gamma+} + H_2O} & \longrightarrow & \mathrm{Bu^{\gamma}OH + H^{+}} & \multirow{2}{*}{$\left.\vphantom{\begin{array}{c}a\\a\end{array}}\right\}\text{(fast)}^{*}$} \\ \mathrm{Bu^{\gamma+} + R{\cdot}CO_2^{-}} & \longrightarrow & \mathrm{R{\cdot}CO_2Bu^{\gamma}} & \end{array}$$

If this is so, the conclusion that the solvolytic process is also unimolecular is almost inescapable, because water must be a much weaker reagent in bimolecular nucleophilic substitution than the formate ion, and formic acid enormously weaker still (next sub-section). The argument is just the same as that which has been based on the failure of sodium hydroxide to increase the hydrolysis rate in aqueous solvents.

(c) *Activity of Formic Acid and Water in Bimolecular Substitution.*—As has been indicated on numerous occasions, the activity of undissociated carboxylic acids in

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[*] Calculation shows (cf. this vol., p. 979) that, under the conditions of our experiments in homogeneous solution, the "ionic strength effect" of calcium formate is probably within the limits of precision of the measurements.

the bimolecular substitution reactions of alkyl halides must be small in comparison with that of water. Independently of general chemical theory, the point has been clearly established in the work of the late Professor Dawson. For example, Brooke and Dawson (J., 1936, 497) wrote down the ten possible reactions that might (without the guidance of theory) be supposed to contribute to the displacement of bromine in the aqueous hydrolysis of bromoacetic acid (either as acid or anion); and they showed experimentally that, of these ten, six had finite rates, including the reactions in which the water molecule was the substituting agent, and four had zero rates. These four were just those in which the assumed reagents were undissociated carboxylic acids. This, and indeed much more widespread, evidence of specificity in reagents is neglected by Taylor when he assumes that molecular formic acid and water have nearly equal activity in what he regards as similar bimolecular substitutions. In the following paper this assumption is subjected to a further experimental test.

(d) *Conclusions.*—Having regard to the additional evidence described in section (iii) of this paper, we have no desire to change anything in our previous conclusions, which are quoted in full in section (i) (p. 935).

EXPERIMENTAL.

(1) *Reaction of* tert.-*Butyl Chloride with Wet Formic Acid and Calcium Formate.*—(A) *Products.* (*a*) From a repetition of Taylor's experiment (*loc. cit.*) we obtained a 25% yield of *tert.*-butyl formate of the correct composition and molecular weight [Found: C, 59·4; H, 9·9; *M* (by quantitative saponification), 103·1. Calc. for $C_5H_{10}O_2$: C, 58·8; H, 9·8%; *M*, 102].

(*b*) The reaction with calcium formate was again repeated, but the isolation technique was changed. The mixture was now diluted with water (600 c.c.) and then extracted with ether (250 c.c. and 25 c.c.). The ethereal extract, after washing, etc., gave a 20% yield of *tert.*-butyl formate (Found: C, 59·4; H, 9·8%). In this illustrative experiment no special precautions were taken, the dilution and extraction processes being carried out at room temperature.

(B) *Rate measurements.* (*a*) For the reaction in the presence of an excess of suspended salt, finely powdered calcium formate (35 g.) and *tert.*-butyl chloride (2 c.c.) were made up to 100 c.c. at 15·00° ± 0·02° with "Kahlbaum" formic acid. At suitable intervals 5 c.c. portions were removed, and the chloride-ion concentration determined as previously described (Bateman and Hughes, *loc. cit.*). The results are in Table I, where a is the initial concentration of the organic halide, x and x_∞ are the concentration of hydrogen chloride after t seconds and after large times respectively (all expressed as equivalent c.c. of 0·100N-silver nitrate per 5 c.c. sample), and k_1 (sec.$^{-1}$) is the first-order rate constant, calculated as before.

TABLE I.

$a = 10·09$, $x_\infty = 9·16$.

t	138	258	456	666	1002	1530	2238	3012	5034
x	0·35	0·75	1·18	1·61	2·35	3·35	4·50	5·50	7·33
10^4k_1	2·53	2·99	2·73	2·61	2·65	2·65	2·67	2·69	2·77

(*b*) The homogeneous reaction ([calcium formate] = 0·101N) was carried out similarly. The results are in Table II, where the previous definitions of quantities apply, except that the concentrations are now expressed as equivalent c.c. of 0·1024N-silver nitrate per 5 c.c. sample.

TABLE II.

$a = 8·30$, $x_\infty = 4·67$.

	156	288	492	750	1032	1620	2400
x	0·51	0·87	1·37	1·92	2·47	3·38	4·09
10^4k_1	4·07	3·87	3·72	3·63	3·65	3·77	3·93

(2) *Reaction of* tert.-*Butyl Chloride with Aqueous Formic Acid.*—We have repeated and extended our previous experiments on the isolation of *tert.*-butyl formate under the conditions of our kinetic measurements. In particular we applied the method of isolation which Taylor employed in his experiment with calcium formate, and obtained, after fractionation of the ether, traces of liquid, b. p. > 52°, which probably contained the ester.

(3) *Reaction of* tert.-*Butyl Alcohol with Wet Formic Acid.*—*tert.*-Butyl alcohol (19 g.) and " Kahlbaum " formic acid (200 c.c.) were left for 1 day at room temperature. Ether was then added and the solution was washed with water, dried, and distilled. A fraction (16 g.), b. p. 78—82°, was redistilled and gave 5·8 g. (22%) of pure *tert.*-butyl formate, b. p. 82°/760 mm. (Found: C, 59·2; H, 10·1%; *M*, 102·4).

(4) *Reaction of* tert.-*Butyl Chloride with Wet Formic Acid and Calcium Chloroacetate.*—(A) *Products.* *tert.*-Butyl chloride (24 g.), anhydrous calcium chloroacetate (124 g.), and " Kahlbaum " formic acid (200 c.c.) were kept at room temperature for 2 days. Fractionation of an ethereal extract, obtained as above [section (3)], gave three crude fractions: (1) b. p. 40—75° (1 g.), (2) b. p. 75—83° (6 g.), (3) b. p. > 83° (4 g.). Redistillation of (2) gave: (2a) b. p. 76—81° (1·5 g.), (2b) b. p. 81—82° (3 g.) (Found: C, 59·2; H, 10·2%), (2c) b. p. > 82° (*ca.* 1 g.). Redistillation of (2c) and (3) gave: (3a) b. p. 82—150° (1 g.), (3b) b. p. 150°/760 mm. (3 g.) (Found: C, 47·8; H, 7·1. Calc. for $C_6H_{11}O_2Cl$: C, 47·8; H, 7·3%).

(B) *Rate measurements.* A reaction mixture (100 c.c.), containing 30 g. of anhydrous calcium chloroacetate, was made up as described in section (1) (B), and the reaction was followed as before. In this case there was a slight complication due to the slow removal of chloride ion from calcium chloroacetate in formic acid. The rate of this reaction was determined separately and a small correction was applied to the results of the experiments with *tert.*-butyl chloride. In Table III, a and x have their previous significance [section (1) (B)], and are expressed in equivalent c.c. of 0·100N-silver nitrate per 5 c.c. sample. Owing to the above-mentioned disturbance, x_∞ could not be determined accurately, and the constants (k_1, sec.$^{-1}$) were therefore calculated from the equation for a simple first-order reaction, $k_1 = (1/t)\log_e\{a/(a - x)\}$.

TABLE III.

$a = 7·07$.

t	378	870	1500	2340	3360	4860
x	0·54	1·09	1·73	2·54	3·44	4·26
10^4k_1	2·10	1·92	1·87	1·90	1·99	1·90

(5) *Reaction of* tert.-*Butyl Alcohol with Wet Formic Acid and Calcium Chloroacetate.*—*tert.*-Butyl alcohol (19 g.), " Kahlbaum " formic acid (200 c.c.), and calcium chloroacetate (42 g.) were left for 1 day at room temperature. The usual methods of separation gave 4 g. of *tert.*-butyl formate, but no *tert.*-butyl chloroacetate could be isolated.

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