Mechanism of Substitution at a Saturated Carbon Atom. Part XXXVIII. Menschutkin Reactions of Some Simple Alkyl Halides in Sulphur Dioxide Solution.*

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The reaction between methyl iodide and pyridine in sulphur dioxide to form methylpyridinium iodide is of second order, and is evidently a bimolecular nucleophilic substitution. Similar reactions of ethyl iodide and of *iso*propyl bromide with pyridine were too slow for kinetic observation. That of *tert.*-butyl bromide with pyridine to form *iso*butylene and pyridinium bromide has the kinetic characteristics of a unimolecular reaction; in particular, it shows a strong common-ion retardation. However, the rate depends slightly on the reagent concentration; and comparison with the similarly unimolecular reaction of *tert.*-butyl bromide with fluoride ion shows that the rate depends appreciably on the nature of the reagent, and that this dependence is but little influenced by the concentration of the latter. These relations are similar to those observed in the unimolecular substitutions of *m*-chlorobenzhydryl chloride in sulphur dioxide, and are thought to indicate that, when the solvent has not the large margin of ionising power required to support unimolecular mechanisms in their limiting and simplest forms, then at least some of the individual molecular acts of conversion follow paths in which the reagent assists the ionising solvent to varying degrees.

We report here a study of some reactions of simple alkyl halides with pyridine in solvent sulphur dioxide. As in other kinetic studies with that solvent, we have followed the progress of reaction by the associated changes in electrical conductance.

Our first step was to make a qualitative survey of the behaviour of methyl iodide, ethyl iodide, *iso*propyl bromide, and *tert.*-butyl bromide, towards pyridine in sulphur dioxide within the temperature interval, −20° to +15°, to which (see preceding paper) we were limited by our apparatus. Methyl iodide underwent a reaction which was somewhat slow, but nevertheless fast enough to permit determination of initial rates. The reactions of ethyl iodide and of *iso*propyl bromide were too slow to be observed: they must have been slower than the reaction of methyl iodide by at least one order of magnitude. *tert.*-Butyl bromide, on the other hand, underwent a reaction which was somewhat rapid, though its rate could be measured near the lower end of the available temperature range.

In the light of our general knowledge of nucleophilic substitution and elimination, these observations strongly suggest that the reaction of methyl iodide with pyridine is bimolecular, whilst that of *tert.*-butyl bromide with pyridine is unimolecular. For on ascending the homologous series of alkyl groups, we expect bimolecular rates to fall; and therefore, after methyl, for which the rate is already small, it is very likely to become too small for measurement. Concurrently, the unimolecular rates are expected to rise by large ratios along the series; but it is apparent that only with the last member, *tert.*-butyl bromide, does the rate ascend into the observable range of magnitudes.

Kinetic examination of the reactions of methyl iodide and of *tert.*-butyl bromide with pyridine in sulphur dioxide confirmed this preliminary diagnosis. It also disclosed that the reaction of *tert.*-butyl bromide, whilst it has in well-developed form the main kinetic characteristics of the unimolecular mechanism, shows quantitative peculiarities, which are generally similar to those, described in Part XXXVI (*J.*, 1954, 634), of the reaction of *m*-chlorobenzhydryl chloride with amines, and are thought to represent an appreciable limitation to the preference of the solvent for creating ions without accepting help from strongly nucleophilic solutes.

The present kinetic work has been done at −15·03°, the temperature of the experiments, described in the preceding paper, on the reaction of *tert.*-butyl bromide with fluoride ion.

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* Part XXXVII, preceding paper.

It was found a convenient enough temperature for initial rate measurements on the reaction of methyl iodide with pyridine; and, by using it for the reaction of *tert.*-butyl bromide with pyridine, we could compare the rates of reaction of this alkyl halide with the two reagents. This comparison is of significance in the discussion of the mechanisms of these processes.

Kinetics of the Reaction of Methyl Iodide with Pyridine.—As explained in Part XXXVI, the circumstance that our conductivity cells could not easily be made gas-tight limited the duration of kinetic runs to periods of about a working day. In that time, the proportional progress of the reaction between methyl iodide and pyridine was only of the order of 1%. Thus we were restricted to the measurement of initial rates. Our observed conductance–time curves were straight lines, whose slopes gave initial rates, and, when divided by the initial concentration of the methyl iodide, measured specific rates, as recorded in Table 1.

TABLE I. *Initial rates of reaction of methyl iodide with pyridine in sulphur dioxide at* $-15{\cdot}03°$ *as measured by the change in the electrical conductance.*

(The specific conductance κ is in ohm^{-1} cm.$^{-1}$, the concentrations a and c are in mole/l., and the time t is in sec.)

No.	a, [MeI]	c, [C_5H_5N]	$10^4\frac{d\kappa}{dt}$	$10^3\frac{d\kappa}{dt}/a$	No.	a, [MeI]	c, [C_5H_5N]	$10^4\frac{d\kappa}{dt}$	$10^3\frac{d\kappa}{dt}/a$
87	0·0376	0·0734	0·183	0·49	85	0·0619	0·1029	0·422	0·68
88	0·0863	0·0870	0·552	0·64	91	0·0811	0·2187	1·23	1·51
89	0·0751	0·1017	0·472	0·63	90	0·0809	0·4581	2·37	2·93

These initial specific rates of increase of conductance are really first-order rate constants in non-standard units, differing from the conventional constants only by a uniform factor of calibration, which we did not determine for this reaction, because we had no other reaction of the same kinetic form with which we wanted to compare it with respect to rate. Plotting the initial specific rates against the concentration of pyridine gave a straight line which passed through the origin (see Fig. 1). This presents a striking contrast to the two given below for reactions of *tert.*-butyl bromide, and to three given in Part XXXVI for substitutions of *m*-chlorobenzhydryl chloride. It demonstrates that the reaction of methyl iodide with pyridine in sulphur dioxide is a second-order process.

We conclude that this reaction, the product of which was shown to be methylpyridinium iodide, is a bimolecular nucleophilic substitution in solvent sulphur dioxide:

$$\mathrm{MeI} + C_5H_5N \longrightarrow \mathrm{MeNC_5H_5}^+ + \mathrm{I}^- \quad . \; . \; . \; . \; . \; . \; . \; . \quad (S_N2)$$

Kinetics of the Reaction of tert.*-Butyl Bromide with Pyridine.*—Although the rates of the reactions of pyridine and of fluoride ion with methyl iodide are of different orders of magnitude, that of the latter being unobservably small, the rates of the reactions of these two reagents with *tert.*-butyl bromide are similar; but they are not identical. If we compare the initial specific rates of reaction of *tert.*-butyl bromide with pyridine (see Table 2) with the corresponding quantities for the reaction of this bromide with fluoride ion (see Table 1 of the preceding paper, p. 634), we see that the pyridine rates are 2—3 times the fluoride-ion rates. Here, the solvent and temperature are the same; and although there is a difference of ionic strength, this cannot be held responsible for the rate difference, since its direction is such as would reduce the observed difference.

TABLE 2. *Some initial specific rates* (k_0 *in sec.*$^{-1}$) *of reaction of* tert.*-butyl bromide with pyridine in sulphur dioxide at* $-15{\cdot}03°$.

No.	[Bu^{t}Br]	[C_5H_5N]	10^5k_0	No.	[Bu^{t}Br]	[C_5H_5N]	10^5k_0
102	0·0336	0·0091	17·5	108	0·0429	0·0420	24·0
103	0·0396	0·0173	20·0	106	0·0334	0·0432	21·5
97	0·0526	0·0414	22·0	107	0·0360	0·0438	23·5

In the graphical comparison in Fig. 2, we observe, first, that the rate of the pyridine reaction appears to increase with the pyridine concentration. The increase is too much to be understood as an ionic-strength effect, since initial ionic strengths in this reaction are quite low. But it is much too small to represent a unit of kinetic order with respect to pyridine. We see also that, whilst the rates of the pyridine and fluoride-ion reactions are different, the difference does not tend to zero as the reagent concentration is diminished over the range of our experiments.

The pyridine reaction, even when it starts rapidly, is soon going relatively slowly, usually at considerably less than one-fifth of its initial rate after one-fifth of its realisable course. Such strong retardations must signify back-conversion of a low-concentration intermediate by an accumulating final product, in our case back-conversion of the *tert.*-butyl carbonium ion by the formed bromide ion. This identification of the effect as the common-ion retardation characteristic of the unimolecular mechanism, was confirmed by experiments in which bromide ions were introduced initially as tetramethylammonium bromide: the initial rates were then strongly reduced; while further retardation of the continuing reaction became milder than the retardations observed in the absence of added bromide ion.

FIG. 1. *Reaction of methyl iodide with pyridine in sulphur dioxide at* $-15{\cdot}03°$: *initial specific rates, expressed in terms of the electrical conductance, plotted against the concentrations of pyridine.*

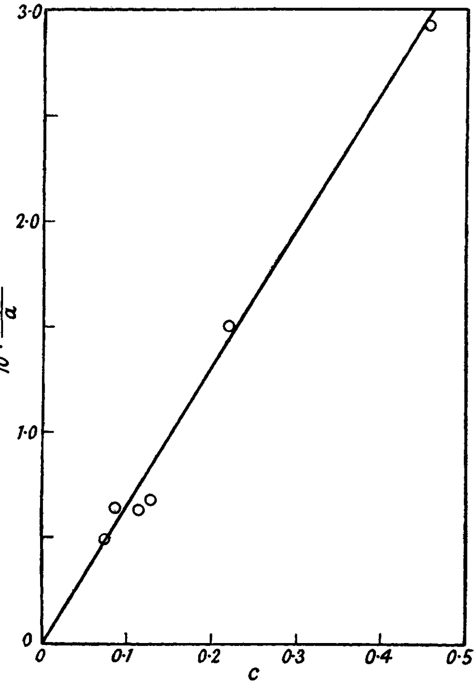
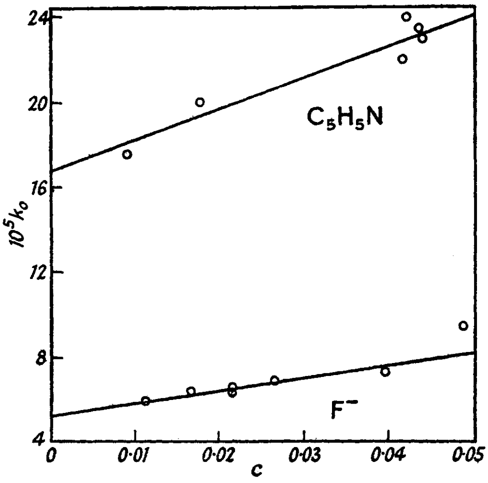


FIG. 2. *Reactions of* tert.*-butyl bromide with fluoride ion and with pyridine in sulphur dioxide at* $-15{\cdot}03°$: *initial specific rates* (k_0 *in sec.*$^{-1}$) *of reaction of the alkyl halide plotted against the concentration* (*c in mole/l.*) *of the reagent.*



The definite result obtained in this most highly diagnostic of known tests for the unimolecular mechanism justifies us in regarding the reaction of *tert.*-butyl bromide with pyridine in sulphur dioxide as essentially unimolecular, even though we may later add qualifications of detail to our description:

$$\mathrm{Bu^tBr} + \mathrm{C_5H_5N} \underset{(2)}{\overset{(1)}{\rightleftharpoons}} \mathrm{Bu^{t+}} + \mathrm{Br^-} + \mathrm{C_5H_5N} \begin{cases} \xrightarrow{(3)} \mathrm{Bu^tNC_5H_5^+} + \mathrm{Br^-} \quad . \quad . \quad . \quad (S_N1) \\ \xrightarrow{(3')} \mathrm{C_4H_8} + \mathrm{HNC_5H_5^+} + \mathrm{Br^-} \quad . \quad (E1) \end{cases}$$

In this formulation, allowance is made for both substitution and elimination, since both are obviously possible. Actually the only final products which we could find were those of the elimination process; but the possibility is not excluded that they may have arisen by a final fast elimination from a previously formed substitution product, the *tert.*-butylpyridinium ion. In any event the rate would be controlled by step (1). We formed the impression that the overall reaction was reversible, and appreciably incomplete in our conditions, but, for the reasons mentioned in Part XXXVI, we were not able to determine equilibrium constants.

The initial specific rates of some runs in which tetramethylammonium bromide was initially added are given in Table 3. The factors f, by which the rate is reduced by the added salt, when present in a concentration ρ times that of the pyridine, allow us to estimate, by means of the equation $\alpha = (f^{-1} - 1)/\rho$, the retardation constant α, that is, the ratio of the specific rate of step (2) of the reaction scheme written above, to the sum of the specific rates of steps (3) and (3′). From these figures, and the analogous results recorded in Table 2 of the preceding paper (p. 645), we may conclude that the rates with which fluoride ion, bromide ion, and pyridine combine with the pre-formed *tert.*-butyl carbonium ion in sulphur dioxide diminish in the order of naming, and for our conditions stand to one another as the reciprocals of the numbers, 0·30, 1·0, and 25 respectively.

TABLE 3. *Initial specific rates* ($k_0^{(b)}$ *in* sec.$^{-1}$) *of reaction of* tert.*-butyl bromide with pyridine in the presence of tetramethylammonium bromide in sulphur dioxide at* −15·03°.

No.	[Bu^{t}Br]	[C_5H_5N]	[NMe_4Br]	ρ	$10^5 k_0^{(b)}$	f	α
109	0·0314	0·0417	0·0088	0·231	3·1	0·135	27
110	0·0348	0·0434	0·0217	0·500	2·1	0·091	20
111	0·0339	0·0438	0·0015	0·034	12·0	0·52	27
112	0·0340	0·0862	0·0063	0·073	6·5	0·35	25
						Mean =	25

Just as for the reactions of pyridine and triethylamine with *m*-chlorobenzhydryl chloride (Part XXXVI), so for that of pyridine with *tert.*-butyl bromide, it appears that the observed kinetic form is described fairly well, though not quite exactly, by the equation of the unimolecular mechanism (*loc. cit.*). This is illustrated in Table 4 below. The small deviations may be due either to unreality in the idealisations of theory, or, conceivably, to some systematic experimental error.

To summarise, the reaction of *tert.*-butyl bromide with pyridine in sulphur dioxide is kinetically quite unlike the corresponding reaction of methyl iodide, but is very similar to that of *m*-chlorobenzhydryl chloride. The common-ion retardation, characteristic of the unimolecular mechanism, is pronounced. Yet the absolute rate depends slightly on the concentration, and appreciably on the nature of the reagent; and the dependence of the rate on the nature of the reagent is only slightly sensitive to the concentration of the latter. This is a paradoxical situation for single or simultaneous reactions composed exclusively of steps of integral kinetic order; and the suggestion, made in Part XXXVI, may apply here, namely, that, when the unimolecular mechanism is nearly breaking down for lack in the solvent of a sufficiently outstanding power of solvation, then many individual molecular acts of conversion are assisted in varying degrees by the presence of the reagent, though few if any may employ that intimate and specific co-operation which is associated with the bimolecular mechanism.

EXPERIMENTAL

In general, the procedure described in Part XXXVI was followed, and it is therefore necessary only to mention the differences. In the reaction of methyl iodide, the conductance readings were not calibrated to give concentrations. In the reaction of *tert.*-butyl bromide, they were so calibrated, on the assumption that pyridinium bromide was the only reaction product which caused the changes of conductance. In constructing calibration curves, the pyridinium bromide was introduced directly in concentrations determined by weighing. The values of the conversion factor $\Delta x/\Delta\kappa$ varied from 11·5 mole ohm cm.$^{-1}$ at the dilute end of our concentration range to more than twice that value at our highest concentrations.

The initial specific rates of the reaction of methyl iodide with pyridine are in Table 1, and those of the reaction of *tert.*-butyl bromide with pyridine are in Tables 2 and 3. The proportions of the methyl iodide reaction which could be followed were so small that the conductance–time curves were straight lines, which need not be illustrated. The corresponding graphs for the *tert.*-butyl bromide reaction were strongly curved, especially near the beginning of reaction. The course of one of these runs is recorded in Table 4, from which a diagram could be constructed, having the same general appearance as Fig. 2 of Part XXXVI (p. 639), except that now the experimental points run slightly off the unimolecular curve toward its concave, instead of its convex, side. The Table itself illustrates the much stronger curvature in these reactions than, for example, in second-order reactions, by the column of calculated second-order rate constants, which drop to one-half of their initial value after 10% of reaction; calculated first-order rate constants would, of course, drop faster. The moderate success of the general unimolecular equation in describing these reactions is illustrated in the last column of the Table by the rate-constants calculated on this basis.

TABLE 4. *Illustrating the kinetic course of the reaction of* tert.*-butyl bromide with pyridine in sulphur dioxide at* −15·03° (*run* 106).

Initially, $a = [\mathrm{Bu^tBr}] =$ 0·0324 and $c = [\mathrm{C_5H_5N}] =$ 0·0432. The product concentration is x (M) at time t (sec.). The second-order constants (k_2 in sec.$^{-1}$ mole^{-1} l.) are the calculated values of $\{1/t(c - a)\} \ln \{a(c - x)/c(a - x)\}$, whilst the unimolecular constants (k_1 in sec.$^{-1}$) are computed with $\alpha = 25$ from the equation given on p. 635 of Part XXXVI.

t	10^4x	$10^2x/a$	10^4k_2	10^5k_1
101	6·4	1·9	47	21·8
130	8·0	2·4	46	22·6
164	8·8	2·6	41	21·0
180	10·1	3·0	41	21·2
243	12·1	3·6	40	20·8
300	14·0	4·2	35	19·7
420	16·5	5·0	30	18·4
600	22·0	6·6	28	18·8
900	28·0	8·4	24	18·3
1200	34·0	10·2	22	17·7
1500	39·0	10·7	20	17·7
1800	43·0	13·0	19	17·9
2400	51·0	15·3	16	17·9

Mean of first five values = 21·5
Initial value from graph = 23·0

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