47. *Mechanism of Substitution at a Saturated Carbon Atom. Part XXIX. The Rôle of Steric Hindrance. (Section D) The Mechanism of the Reaction of* neo*Pentyl Bromide with Aqueous Ethyl Alcohol.*

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The work described in the foregoing papers gave an indication that the reaction of *neo*pentyl bromide in aqueous ethyl alcohol involved a preliminary, rate-determining ionisation of the halide (cf. especially, the preceding paper). Since the ionisation mechanism had not previously been observed with certainty in primary halide structures, and the rate of ionisation of *neo*pentyl bromide was of particular interest in connection with the general investigation described in this group of papers (see Abstract on p. 157), we have investigated the mechanism of the solvolytic reaction of this halide in some detail. An ionisation mechanism is confirmed by experiments demonstrating the insensitivity of the rate to the presence of alkali and a characteristic sensitivity to changes in the composition of the mixed solvent—these being diagnostic features shown by the solvolytic reactions of certain other halides (*e.g.*, *tert.*-butyl halides), for which a rate-determining ionisation has been established. Furthermore, the products exhibit rearranged structures—a fact which, when taken in conjunction with the work of Whitmore and others, would also imply the prior formation of a carbonium ion.

In general, the first-order solvolysis of alkyl halides in water–alcohol media may be of the unimolecular type, *e.g.*,

$$\left.\begin{array}{l} \mathrm{R{-}X} \xrightarrow{\text{(slow)}} \overset{+}{\mathrm{R}} + \overset{-}{\mathrm{X}} \\ \overset{+}{\mathrm{R}} + \mathrm{H_2O} \xrightarrow{\text{(fast)}} \mathrm{R{-}OH} + \overset{+}{\mathrm{H}} \end{array}\right\} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (S_N1)$$

or of the bimolecular type, *e.g.*,

$$\mathrm{H_2O} + \mathrm{R{-}X} \longrightarrow \mathrm{R{-}OH} + \overset{+}{\mathrm{H}} + \overset{-}{\mathrm{X}} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (S_N2)$$

In previous papers in this series (cf. especially, Bateman, Cooper, Hughes, and Ingold, J., 1940, 925) it has been shown that, although secondary and tertiary halides respectively show a moderate and a well-developed tendency to follow the unimolecular mechanism, yet the common primary halides exhibit such a strong preference for the bimolecular process as to render the unimolecular reaction extremely difficult to isolate.

In Parts XXVI and XXVII (this vol., pp. 157, 161) it was shown that, in *neo*pentyl bromide, reactivity by the bimolecular mechanism is greatly reduced. Since this halide shows considerable reactivity in solvolysis with aqueous alcohol (preceding paper), the hypothesis was entertained that we have here conditions favourable to an ionisation mechanism in a primary halide structure. This hypothesis is now supported by a detailed investigation of the reaction mechanism.

Our evidence of mechanism falls under three heads, (*a*) the effect on reaction rate of the addition of a much stronger nucleophilic reagent than the solvent, (*b*) the effect on reaction rate of increasing the ionising capacity of the solvent, (*c*) the nature of the reaction products. These points will now be discussed.

(*a*) *The Effect of Added Sodium Hydroxide.*—In discussions relating to the various methods available for determining the mechanism of solvolytic reactions for which the reaction order is not itself informative,* we have stressed the importance of the method which depends on the effect on reaction rate of changes in the reagent, and especially on the behaviour of reagents which are much more nucleophilic than the solvent (see, especially, Hughes and Ingold, J., 1935, 244; Bateman, Cooper, Hughes, and Ingold, *loc. cit.*; Hughes, *Trans. Faraday Soc.*, 1938, **34**, 185; 1941, **37**, 603). The simplest and the most conclusive result obtains if these powerful reagents do not influence the rate; it is then inconceivable that the comparatively weakly nucleophilic solvent molecules should function as reagents in the rate-determining process, and the possibility that a bimolecular mechanism may be in operation is thus eliminated for such cases.

In the present application we investigated the effect of various concentrations of sodium hydroxide on the rate of reaction of *neo*pentyl bromide in 70% aqueous ethyl alcohol at 95°; the results are given in Table I.

Table I.

Rates of reaction of neo*pentyl bromide in aqueous ethyl alcohol containing varying concentrations of sodium hydroxide.*

Initially, [RBr] ~0·05N; k_1 is the first-order rate constant (first order with respect to the alkyl halide) in sec.$^{-1}$.

Initial [NaOH], N	0·015	0·075	0·200
$k_1 \times 10^7$	1·54	1·54	1·53

The rate is obviously independent of the concentration of hydroxide ions. These ions, and, *a fortiori*, the solvent molecules, do not function as reagents in the rate-determining stage of the reaction; in short, the results exclude a bimolecular mechanism. The evidence is further strengthened by more detailed reference to

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* Since the solvent is in large excess, the reaction will be of the first order irrespective of mechanism, *i.e.*, independently of whether or not the solvent molecules function as reagents in the rate-determining stage of the reaction. Significant departures from first-order kinetics are not to be expected in the case now under investigation (cf. Bateman, Hughes, and Ingold, J., 1940, 960).

the first experiment summarised in the table ([NaOH] = 0·015N). In this instance, the hydroxide ion concentration was not sufficient to maintain the solution alkaline, and it became acidic during the course of the measurements; nevertheless, the calculated first-order rate coefficients were approximately constant throughout the measured range of reaction (cf. experimental section). Good first-order constants were also obtained in the other experiments.

(*b*) *The Effect of Increasing the Water Content of the Medium.*—The effect of solvent variation is, in some respects, not so critical and conclusive as the effect described above, but it provides useful auxiliary evidence of mechanism. Both mechanisms should be facilitated by passing to a more aqueous solvent, but a unimolecular reaction, depending, as it does, on a preliminary rate-determining ionisation of the alkyl halide, should be more strongly influenced by solvation factors than should a bimolecular reaction, wherein solvent molecules participate as effective reagents in the rate-determining process (Bateman, Cooper, Hughes, and Ingold, *loc. cit.*). The difference in the quantitative nature of the effects may be illustrated by reference to available data relating to the methyl, ethyl, *iso*propyl and *tert.*-butyl halides. We give here the approximate ratios of the first-order rate constants in "60%" and "80%" aqueous ethyl alcohol ($k_{60\%}/k_{80\%}$) for the solvolytic reactions of the bromides of this series at 25° *: MeBr 2, EtBr 2, $Pr^{\beta}Br$ 3, $Bu^{\gamma}Br$ 10. There is independent evidence here for the conclusion that a predominantly bimolecular reaction in the case of the first two compounds gives way to a unimolecular reaction in the last, the case of the *iso*propyl halide being of intermediate type (see, especially, Bateman *et al.*, *loc. cit.*). With *neo*pentyl bromide, it will be seen from the figures given in the experimental section that a change from "70%" to "50%" aqueous ethyl alcohol produces a six-fold increase of rate at 95°. For a change from 80% alcohol to 60% the factor is likely to be larger, in fact, about 10.† The effect is thus very similar to that for *tert.*-butyl bromide, and this fact may be regarded as evidence in favour of an ionisation mechanism in the case of *neo*pentyl bromide.

(*c*) *The Reaction Products.*—In general, the reaction of an alkyl halide with a reactive solvent gives rise to the same products independently of whether the mechanism is a one-stage bimolecular process or a two-stage unimolecular process involving a preliminary ionisation. Exceptions may, however, arise in the following way: In the bimolecular mechanism, the direct attachment of the reagent, proceeding synchronously with the expulsion of the replaced group, invariably gives rise to a product in which the alkyl group is the same as in the reactant. When an intermediate carbon cation is formed, however, it may in special cases undergo rearrangement, so that the products formed in a subsequent reaction with the solvent may contain an alkyl group structurally distinct from that of the reactant. A study of the reaction products may thus afford a useful criterion of the mechanism of the reaction by which halogen is eliminated from certain alkyl halides, and the *neo*pentyl structure, because of its well-known tendency to undergo rearrangement to give *tert.*-amyl derivatives, is a good case for such a study.

From the bimolecular (S_N2) reaction of *neo*pentyl bromide with sodium ethoxide in dry ethyl alcohol, only ethyl *neo*pentyl ether could be isolated (this vol., p. 157). For the solvolytic reaction with 50% aqueous ethyl alcohol, however, a study of the reaction products under the conditions of our kinetic experiments (at 125°, and in the presence of excess alkali) gave evidence of the formation of ethyl *tert.*-amyl ether and olefin (see experimental section). The yield of olefin thus obtained (36%) is roughly that to be expected on the assumption of the formation of the *tert.*-amyl cation.‡ Under the conditions of our experiments (alkaline medium), it is inconceivable that these products could arise from a bimolecular reaction of the halide with the solvent (to give *neo*pentyl derivatives) followed by subsequent rearrangement. Hence the possibility that the halogen may be eliminated by a bimolecular mechanism is again excluded, and the results are consistent with the assumption of a rate-determining ionisation of the alkyl halide.

The mechanism of this change will be discussed in more detail in Part XXXII, where it will be shown that rearrangement is definitely diagnostic of the setting free of a group with an incomplete carbon octet—in this case, obviously, the *neo*pentyl cation. The rearrangement of this to the *tert.*-amyl cation is subsequent; it will be shown, in another example in which evidence from optical activity is available, that rearrangement follows, rather than accompanies, ionisation, and is therefore a consequence of ionisation, rather than a contributory cause. Thus the measured rate is essentially an ionisation rate, and it is consistent that it is of the order of magnitude we had predicted by extrapolating to primary bromides the ionisation rates of

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* Calculated from the results of Hughes, Ingold, *et al.* (J., 1936, 225; 1940, 925) and Taylor (J., 1937, 992). The expression "x%" aqueous ethyl alcohol means a mixture made from x vols. of anhydrous ethyl alcohol and $100 - x$ vols. of water.

† For *tert.*-butyl chloride, for example, the conversion factor ($k_{60\%}/k_{80\%} \div k_{50\%}/k_{70\%}$) is 1·5 (Hughes, J., 1935, 255).

‡ A comparable figure for the ratio in which the *tert.*-amyl cation, formed as an intermediate in the solvolysis of *tert.*-amyl bromide, is partitioned between olefin elimination and hydrolytic substitution is not available, but it may be roughly deduced in the following way: The unimolecular solvolysis of *tert.*-amyl bromide in "100%," "80%," and "60%" alcohol at 25° gave 36, 26, and 20% olefin (Hughes and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 657). In "50%" alcohol at 25° the figure might therefore be about 18%. The effect of increasing the temperature can be assessed from the results of Hughes and MacNulty (J., 1937, 1283) for the influence of temperature variation on the rate constants of elimination and substitution in the unimolecular solvolysis of *tert.*-amyl chloride in "80%" aqueous ethyl alcohol. Assuming that the partitioning of the *tert.*-amyl cation between elimination and substitution is similarly influenced by temperature when the original reactant is *tert.*-amyl bromide and the solvent "50%" aqueous ethyl alcohol, it can be shown that the olefin obtainable from the reaction of the bromide with the "50%" alcohol solvent at 125° should account for about 40% of the total reaction—a figure which is in reasonably good agreement with the value (36%) for the yield of olefin formed from *neo*pentyl bromide under these conditions.

tertiary and secondary bromides; and that in another solvent (Part XXXI) it is of the order of magnitude of the measured rates for other primary bromides, which, in that solvent, we believe to be undergoing unimolecular solvolysis.

EXPERIMENTAL.

Materials.—*neo*Pentyl bromide was prepared and purified as previously described (this vol., p. 157). The " 70% " aqueous ethyl alcohol was obtained by mixing, at room temperature, 70 vols. of dry ethyl alcohol (cf. this vol., p. 160) with 30 vols. of distilled water, and " 50% " aqueous alcohol was similarly prepared from equal volumes of the constituents. Appropriate quantities of sodium hydroxide were dissolved in the media, and the alkali concentration determined by titration against standard acid.

Kinetic Measurements.—A weighed quantity of the halide, sufficient to yield an approximately 0·05N-solution, was made up to 100 ml. at 0° with alkaline solvent. Portions of 5 ml. were then enclosed in small sealed tubes, which were immersed in the thermostat for known times, and the halide ion content determined as previously described (this vol., p. 160).

The selection of detailed experiments in Table II illustrates the nature of the results from which the rate coefficients are obtained. The first-order constants are calculated by means of the equation, $k_1 = (1/t) \log_e C_0/C_t$, where C_0 and C_t are the concentrations of the alkyl halide at zero time and after t seconds, respectively, and are expressed in ml. of 0·010N-silver nitrate per 5 ml. sample.

TABLE II.

A. *Medium " 70% " Aqueous Ethyl Alcohol. Temp.* 95·0°.

(*a*) Initially, [NaOH] = 0·0153N.

t (hrs.)	0	69	144	288	310·5	359	405	503	572	624	672 *
[RBr]	25·57	24·58	25·53	21·82	21·54	21·03	20·50	19·43	18·79	18·13	17·76
$k_1 \times 10^7$	—	1·60	1·60	1·53	1·53	1·52	1·52	1·52	1·50	1·53	1·51

(*b*) Initially, [NaOH] = 0·200N.

t (hrs.)	0	46	118	170	244	337·5	412	556	771
[RBr]	24·23	23·60	22·66	22·02	21·27	20·17	19·37	17·96	15·94
$k_1 \times 10^7$	—	1·58	1·57	1·56	1·49	1·51	1·51	1·49	1·51

B. *Medium " 50% " Aqueous Ethyl Alcohol. Temp.* 95·15°.

Initially, [NaOH] = 0·075N.

t (hrs.)	0	38·5	86·5	135·5	167·5	215·5	260·75	312·5
[RBr]	23·61	20·74	17·53	14·72	13·32	11·62	9·88	8·47
$k_1 \times 10^7$	—	9·35	9·58	9·58	9·50	9·15	9·30	9·15

C. *Medium " 50% " Aqueous Ethyl Alcohol. Temp.* 125·15°.

Initially, [NaOH] = 0·075N.

t (hrs.)	0	2	2·8	4·2	5·0	6·0	7·0	8·0	9·0	17·2	18·2
[RBr]	23·28	20·23	19·32	17·77	16·53	15·65	14·49	13·84	12·90	6·95	6·61
$k_1 \times 10^5$	—	1·95	1·85	1·79	1·90	1·84	1·88	1·81	1·83	1·95	1·92
t (hrs.)	19·2	20·2	21·25								
[RBr]	6·09	5·95	5·40								
$k_1 \times 10^5$	1·94	1·88	1·93								

* The solution had become acidic at this point. Owing to the slowness of the hydrolysis, the solvent reacts appreciably with hydrobromic acid during the time required for a completed run, and we were thus prevented from conducting experiments in more strongly acidic media.

Arrhenius Parameters.—From the rate constants in " 50% " aqueous ethyl alcohol at 95·15° (mean $k_1 = 9{\cdot}37 \times 10^{-7}$ sec.$^{-1}$) and 125·15° (mean $k_1 = 1{\cdot}88 \times 10^{-5}$ sec.$^{-1}$), the parameters B and E of the Arrhenius equation, $k = Be^{-E/RT}$, are found to be $1{\cdot}5 \times 10^{11}$ (sec.$^{-1}$) and 29·0 (kg.-cals.) respectively.

Reaction Products.—A study of the reaction products was made under the conditions of the kinetic experiments in " 50% " aqueous ethyl alcohol at 125°.

Olefin estimations, carried out as described in Part XXVI (this vol., p. 161), showed that olefin formation accounted for 36% of the total reaction.

Owing to the small quantities of products available, a special technique was devised for characterising and estimating the other compounds formed. The method is based on comparisons of colour intensities produced when certain alcohols (not ethyl alcohol) are heated with sulphuric acid and an aromatic aldehyde. The original procedure of Penniman (*Ind. Eng. Chem. Anal.*, 1937, **9**, 91) and Coles (*ibid.*, 1942, **14**, 20) was found, for our purpose, to be too sensitive, and lacking in discrimination between the various products which might be present. The following method was finally adopted: The sample (5 ml.) is diluted to 50 ml. with distilled water, and 5 ml. portions of the dilute solution are placed in boiling-tubes, cooled in ice, and mixed with 25 ml. of 65% sulphuric acid and 2 ml. of a solution containing 1·75 g. of vanillin in 100 ml. of absolute ethyl alcohol. The mixture is then heated on a boiling water-bath for 20 minutes, cooled, and the colour density produced measured by means of a "Hilger Spekker Absorptiometer" against a blank similarly obtained from 5 ml. of alkaline (0·075N) "50%" aqueous ethyl alcohol. In general 6—8 samples were treated simultaneously under the same conditions, one being the blank, while two or more contained solutions of *tert.*-amyl alcohol for comparison. A calibration curve was constructed using a series of standard solutions of *tert.*-amyl alcohol (concentrations = 0·005—0·050M) in the solvent employed in the kinetic studies, but this curve was used only in the preliminary estimation of the products; for increased reliability, the unknown sample was compared with two standard solutions of *tert.*-amyl alcohol, one slightly stronger and one slightly weaker than the test sample.

Preliminary experiments were carried out in order to compare the intensity of the coloration produced when 5-ml. samples of standard solutions (always in the solvent employed in the kinetic runs) of *neo*pentyl alcohol, trimethylethylene, ethyl *tert.*-amyl ether and *tert.*-amyl alcohol were treated as described above. The results are set out below:

Solution tested.	Colour density relative to blank (drum readings).
0·020M-*tert.*-Amyl alcohol	0·35, 0·35, 0·35
0·020M-Ethyl *tert.*-amyl ether	0·30, 0·30, 0·30
0·017M-Olefin	0·05, 0·05, 0·03
0·07M-*neo*Pentyl alcohol	0·03, 0·03, 0·03

Thus, by comparison with *tert.*-amyl alcohol and ethyl *tert.*-amyl ether, which produce very similar results, *neo*pentyl alcohol and trimethylethylene give almost negligible colorations under the conditions used. Further tests, and the use of the calibration curve, showed that a reaction solution (originally containing *neo*pentyl bromide) contained, after completion of the solvolysis, *tert.*-amyl alcohol and *tert.*-amyl ether (taken collectively) in about 0·28M concentration. Five tubes containing the reaction products, together with two standard solutions of *tert.*-amyl alcohol (0·025M and 0·030M) were then similarly treated and tested. By interpolation from the comparisons, assuming linearity in the calibration curve for this narrow region of concentration change, the combined concentrations of *tert.*-amyl alcohol and ether in the samples (neglecting a small correction due to the presence of olefin and treating the alcohol and ether as equivalent in intensity) were thus found to be 0·028, 0·029, 0·030, 0·027 and 0·029M; mean = 0·028$_6$M. The bromide-ion concentration in the reaction tubes was 0·0455M; the results therefore indicate that the *tert.*-amyl substitution products accounted for about 63% of the total reaction.

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