

73. *Tracer Studies in Alcohols. Part III.* Intermediates in the Pinacol-Pinacone Rearrangement.*

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The rate of the acid-catalysed rearrangement of pinacol to pinacone is proportional to Hammett's acidity function, h_0 . Pinacol, isolated after incomplete reaction, has partially exchanged its oxygen atoms with those of the solvent ^{18}O -containing water, and comparison between the relative rates of this exchange and of rearrangement can give information on the fate of the carbonium-ion intermediate. At low concentration of acid, *ca.* 70% of the carbonium ions are captured by the solvent water to regenerate pinacol enriched in ^{18}O . This proportion decreases with increasing acidity. The nature of the intermediates is discussed.

WE sought evidence on the mechanism of the pinacol-pinacone rearrangement, and in particular to determine the nature of the carbonium-ion intermediate,¹ choosing the simplest possible system, namely the sulphuric acid-catalysed rearrangement of pinacol in water. Preliminary details have been given elsewhere.²

The pinacol rearrangement is faster in deuterium oxide than in water,^{3,4} so the slow step of the reaction must be the decomposition of the conjugate acid (I) formed in a rapid reversible step. There is much chemical evidence to show that the migration of the alkyl group is intramolecular,¹ and it seems likely that the necessary intermediate for rearrangements in water is a carbonium ion. An epoxide has been isolated from the partial rearrangement of benzopinacol in moist acetic acid,⁵ and appears to be an intermediate under these conditions, but as an epoxide cannot be an intermediate in the rearrangement of some 1 : 2-diols in aqueous solvents^{1,3,3a} its presence in this rearrangement is probably due to special properties of the system.

* Part II, *J.*, 1957, 3402.

¹ Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons Ltd., London, 1953.

² Bunton, Hadwick, Llewellyn, and Pocker, *Chem. and Ind.*, 1956, 547.

³ Ley and Vernon, *J.*, 1957, 2987, 3256; *Chem. and Ind.*, 1956, 146.

^{3a} Meerburg, *Rec. Trav. chim.*, 1905, 24, 131; 1909, 28, 267, 270.

⁴ Duncan and Lynn, *Austral. J. Chem.*, 1957, 10, 1.

⁵ Gebhart and Adams, *J. Amer. Chem. Soc.*, 1954, 76, 3925.

The evidence relevant to the rôle of the solvent comes largely from observations on the dependence of rate upon acid concentration. Uni- and bi-molecular acid-catalysed solvolyses can often be differentiated provided that the reaction is followed at a concentration of acid sufficiently high for the protonating power of the solution (as measured by the Hammett acidity function, h_0) to be greater than the stoichiometric concentration of hydrogen ions, $[H_3O^+]$. By the Zucker-Hammett hypothesis⁶ the rate of a unimolecular reaction should follow h_0 whereas that of a bimolecular reaction should follow $[H_3O^+]$.

This test has been applied to a number of pinacol-pinacone rearrangements, with benzopinacol in moist acetic acid,⁵ and with aliphatic glycols in aqueous acids.^{2,3,7} In all cases the rate of rearrangement has increased with a high power of the acid concentration, but has been closely proportional to the Hammett acidity function, h_0 .

Kinetic evidence on the molecularity of a reaction does not necessarily reveal the detailed mechanism. The rate of disappearance of pinacol, for rearrangement in aqueous acid, is the same as the rate of formation of pinacolone,^{7*} so the intermediate does not build up. The evidence on the rearrangement in water is consistent with the view that a carbonium ion is formed slowly from the conjugate acid of the glycol (I) and this then decomposes to the products. Strong confirmation is provided by a comparison of the products of rearrangement of 2-methylpropane-1:2-diol and its ethers with those of other reactions which go through a carbonium ion.³

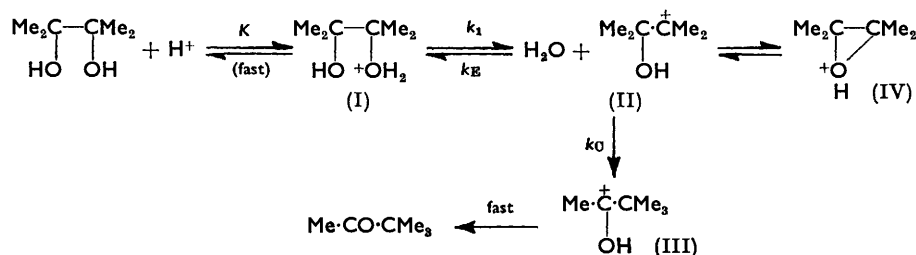
Discussion.—The nature of the acid catalysis of the rearrangement of pinacol is shown by comparisons of the rate in deuterium oxide and water,⁴ and the molecularity is given by the plots of $\log k$ against $-H_0$ being straight lines of near unit slope (Table 1). The

TABLE 1. Rate of rearrangement of pinacol in aqueous sulphuric acid at 72.9° and at 100°.

At 72.9°							
$[H_2SO_4]$ (m)	0.055	0.108	1.33	1.85	2.46	2.83	3.37
$10^4 k$ (sec. ⁻¹)	0.0086	0.016	0.386	0.737	1.26	1.67	2.80
$-H_0$	—	—	0.42	0.67	0.98	1.15	1.37
At 100°							
$[H_2SO_4]$ (m)	0.437	0.920	1.50	2.43			
$10^4 k$ (sec. ⁻¹)	3.30	6.98	13.2	29.2			

At both temperatures the slope of $\log k$ against $-H_0 = 0.90$. The rates calc. for 1.5m- H_2SO_4 fit the equation $k = 10^{10.7} \exp(-33,700/RT)$ (sec.⁻¹).

unchanged pinacol, isolated after partial reaction, has partially exchanged its oxygen atoms with the solvent water. This exchange is acid-catalysed, and its rate-dependence upon acid concentration is similar to, but not identical with, that of rearrangement. We conclude that both exchange and rearrangement go through a common carbonium-ion intermediate.



The amount of oxygen exchange between the unchanged pinacol and water measures the extent to which the carbonium ion (II) is captured by the water molecules to regenerate

* Olefins are formed under certain conditions.^{7*}

⁶ Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791.

⁷ Duncan and Lynn, *J.*, 1956, 3512.

^{7a} Fieser, "Experiments in Organic Chemistry," Heath, New York, 1941, 100.

pinacol. The amount of rearrangement measures the extent to which the carbonium ion (II) rearranges to give (III), which then decomposes rapidly to give pinacone. (We mention later why we believe that the last stage would be fast.) The rate of capture of the carbonium ions (II) by water will probably depend upon some function of the concentration, or perhaps the activity of water. The tendency for water to capture this carbonium ion will, therefore, decrease with increasing acidity (and decreasing water content) of the solution. On the other hand, the rate of rearrangement of the carbonium ion (II) \rightarrow (III) should not depend much upon the water content of the solvent. The simplest series of reactions for this conversion is that shown; the methyl group migrates intramolecularly, (II) \rightarrow (III), and the hydrogen attached to the oxygen atom is lost very rapidly as a proton, so playing no particular kinetic part in this partitioning of the carbonium ion but making the conversion (II) \rightarrow (III) irreversible.

The relative rate constants, k_E and k_O , of these reactions of the carbonium ion (II) are given by:

$$\frac{\text{Rate of exchange}}{\text{Rate of rearrangement}} = \frac{k_E}{k_O} \propto [\text{H}_2\text{O}] \cdot \frac{f_{\text{H}_2\text{O}} \cdot f_{\text{R}^+}}{f_{\text{ROH}_2^+}}$$

In formulating this equation we assume that the transition states for exchange and rearrangement will be akin to the conjugate acid (I) and the carbonium ion (II) respectively and denote their activity coefficients as $f_{\text{ROH}_2^+}$ and f_{R^+} respectively.

Various obvious simplifications can be made to this equation. If the whole activity-coefficient term is neglected we can predict a linear dependence of k_E/k_O on the stoichiometric concentration of water. Alternatively, neglect of the term $f_{\text{R}^+}/f_{\text{ROH}_2^+}$ predicts dependence upon the activity of water. In fact the results fit reasonably well with either hypothesis. However, the overall changes in the ratio k_E/k_O (Table 2), and in the water content of the solvent, are comparatively small, so the experimental uncertainty is not

TABLE 2. Oxygen exchange in aqueous sulphuric acid at 72.9°.

[H ₂ SO ₄] (m)	Time (hr.)	N _∞ (atoms % excess)	N _t	Reaction (%)	k _E /k _O
0.053	89	0.784	0.202	20	2.7
1.60	2.5	0.665	0.234	30	2.4
2.12	2.0	0.659	0.273	36	2.4
2.12*	2.0	0.651	0.249	33	2.4
5.35	0.3	0.660	0.257	57	1.2

* [Pinacone] initially present equivalent to *ca.* half [pinacol]. As solutions were made up by weight it is convenient to express [H₂SO₄] in terms of molality.

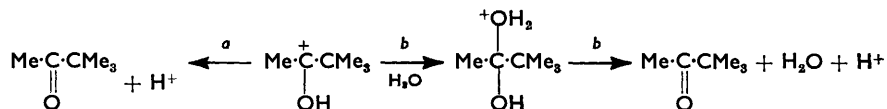
small by comparison with the changes in the ratio k_E/k_O . Further, as the solutions for the exchange experiments contained appreciable amounts of pinacol, we cannot attach any great significance to the exact numerical values of k_E/k_O for various acidities, although the direction of the changes is significant.

The rate of formation of pinacone is not the rate of formation of a carbonium ion from pinacol. It is in fact less than half this at low concentrations of acid. The complete rate equation for the formation of pinacone is: Rate = $Kk_1k_0h_0[\text{ROH}]/(k_E + k_O)$, where [ROH] is the concentration of pinacol. This rate will be equal to that of formation of the carbonium ion $Kk_1k_0[\text{ROH}]$ only if $k_O \gg k_E$. This is obviously not so in the present experiments. However the ratio $k_O/(k_E + k_O)$ will not change much over a large change in acid concentration, and it will be sensibly constant relative to h_0 . In going from 1.6m- to 5.35m-sulphuric acid, the ratio changes by *ca.* 2-fold, but h_0 changes *ca.* 30-fold. We can extrapolate this ratio to higher concentrations of acid, and calculate that in 50% sulphuric acid (w/w) more than 90% of the carbonium ions will rearrange to pinacone. Thus at higher acidities the rate of rearrangement will be the rate of formation of carbonium ions. Attempts were made to test this point, but unfortunately the rate of dissolution of the large amounts of pinacol required for the isotope experiments was slower than its rearrangements at these high acidities. Cases may exist where the partitioning

of the carbonium ion may change so rapidly with acidity that dependence of rate upon h_0 may be lost.

This general picture of the partitioning of the carbonium ion between solvent capture with oxygen exchange and a chemical reaction not requiring direct intervention of water, is very similar to that suggested for the acid-catalysed oxygen exchange and olefin elimination of *sec.*-butyl alcohol (Part II).

The formation of pinacone from the carbonium ion (III) could follow two routes, one a rapid loss of a proton (*a*), the other hydration followed by dehydration (*b*).



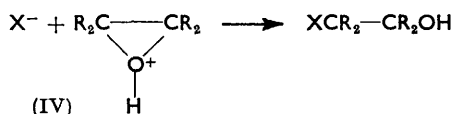
Oxygen exchange between water and ketones is much faster than the pinacol rearrangement, and so an experimental test between these two possibilities based upon isolation of pinacone from a rearrangement in H_2^{18}O cannot be made,⁸ although it might be feasible in other solvents.

We conclude from the exchange results that the conversion of the carbonium ion (II) into pinacone does not involve a water molecule in an activated step. The slow step must be the conversion of (II) into (III), possibly synchronised with proton removal, and if the ion (III) is attacked by water to form the hydrate of pinacone, this attack must be fast compared with the interconversion (II) \rightarrow (III), and can have no kinetic significance on the overall rate of rearrangement or on this rate relative to that of oxygen exchange.

The rate of carbonium-ion formation is the sum of the rates of oxygen exchange and rearrangement, and can be compared with known rates of the unimolecular heterolysis of *tert.*-butyl alcohol in aqueous hydrochloric acid.⁹ The rate of carbonium-ion formation from pinacol is *ca.* 1/50th of that of *tert.*-butyl alcohol (this assumes that the catalysing effects of hydrochloric and sulphuric acids are similar). There is therefore no assistance to bond fission from either the migrating methyl group or the hydroxyl oxygen atom. The decrease of rate has two probable causes: (1) the basicity of pinacol will be less than that of *tert.*-butyl alcohol, because of the increased size of the molecule and the $-I$ effect of the hydroxyl group; and (2) the rate of carbonium-ion formation from the conjugate acid will be decreased by this inductive effect of this hydroxyl group.

There are three alternative routes for oxygen exchange between water and unchanged pinacol other than *via* the formation and capture of a carbonium ion, but we now mention why we believe them to be unimportant.

(i) Oxygen exchange may go *via* the formation and hydrolysis of an epoxide but, as the acid hydrolysis of epoxides is unimolecular with formation of a carbonium ion from the conjugate acid of the epoxide (IV) as the slow stage,¹⁰ such a route would be *via* a carbonium ion which is already involved in the rearrangement, and the rôle of the epoxide would merely be that of a species in equilibrium with the carbonium ion. It would be, for our experiments, equivalent to a temporary form of the carbonium ion, and this would not effect the interpretation of our results. A different situation might arise if the rates of rearrangement and oxygen exchange were compared in solutions containing appreciable amounts of halide ions, X^- . These are powerful nucleophilic reagents and they might attack the conjugate acid of the epoxide in a bimolecular step of the form:



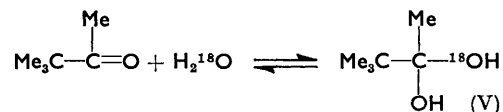
⁸ Winstein and Ingraham, *J. Amer. Chem. Soc.*, 1955, **77**, 1738.

⁹ Dostrovsky and Klein, *J.*, 1955, 791.

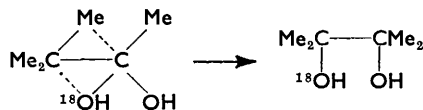
¹⁰ Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2667.

(ii) Oxygen exchange *via* bimolecular attack of a water molecule upon the conjugate acid of pinacol (I) is very unlikely. It would be an S_N2 attack by water upon a tertiary atom of a compound having a highly substituted β -carbon atom, and the steric compressions in such a bimolecular transition state would be very great. Further the kinetic form for the rate of oxygen exchange at various acid concentrations is powerful evidence against such a mechanism of exchange.

(iii) The exchange of oxygen atoms between ketones and water is rapid in acid solution¹¹ and so the oxygen atom of pinacone will be in isotopic equilibrium with the water *via* a reversible hydration:



If this hydrate (V) could rearrange to pinacol



the pinacol so formed would be isotopically enriched. Such a reaction seems unlikely, because the pinacol-pinacone rearrangement is irreversible and goes to completion. It was excluded explicitly by showing that the ratio of the rates of oxygen exchange and rearrangement was almost independent of added pinacone (Table 2). Added pinacone decreased the extents of both oxygen exchange and rearrangement to the same slight extent (*ca.* 10%). This could be because it, like other organic molecules,¹² decreases the acidity as measured by H_0 , and because in the amounts added it formed a separate layer into which some of the pinacol might have been extracted.

Recently this problem of the pinacol rearrangement has been attacked by a study of kinetic isotope effects.¹³ Pinacol was labelled with ^{14}C on either the "methyl" or the "alcoholic" carbon atoms. The ^{14}C -labelled pinacols rearranged less rapidly than the unlabelled compounds above 78° , with concentrations of the catalysing hydrochloric acid $<0.2\text{M}$. The isotope effects were very large, and much greater than those normally observed in bond-breaking processes. They suggest that both the breaking of the carbon-oxygen bond and the migration of the methyl group are activated processes, in agreement with evidence reported here and elsewhere. However, no kinetic isotope effect was observed in an experiment at 60° with 0.995M -hydrochloric acid. The reason for this striking difference is not obvious. The two sets of experiments differ in both temperature and the concentration of the catalysing hydrochloric acid. Formation of the epoxide from a carbonium ion, and its reversion to this ion, would decrease any kinetic isotope effect (by making the distribution of the tracer random); if this occurred at low but not high temperatures the results would be explicable. Another source of uncertainty is that the comparatively high (*ca.* 1M) concentration of the nucleophilic chloride ion might affect some detail of the reaction path.

EXPERIMENTAL

Materials.—Pinacol (B.D.H.) was recrystallised from water as the hexahydrate, m. p. 46° . Its purity was checked by periodate titration.

Kinetics.—All reactions were followed by periodate titration of unchanged pinacol. At various times sealed tubes, containing aliquot portions of the reaction mixture, were removed from a thermostat, cooled, and broken under an excess of sodium hydrogen carbonate. An

¹¹ Cohn and Urey, *J. Amer. Chem. Soc.*, 1938, **60**, 679.

¹² Long and Paul, *Chem. Rev.*, 1957, **57**, 1.

¹³ Duncan and Lynn, *Austral. J. Chem.*, 1957, **10**, 7.

excess of standardised periodate solution was added and the mixture left overnight at room temperature; the iodine liberated on addition of potassium iodide was estimated by titration against sodium arsenite. The reaction mixtures remained colourless under all the experimental conditions (cf. ref. 7).

The first-order rate coefficients were evaluated graphically. The constants presented agree reasonably well with those given elsewhere.⁷

Isotope Exchange.—Solutions of isotopically normal pinacol, in isotopically enriched water containing sulphuric acid, were heated in sealed ampoules. After a definite time of heating the amount of reaction was determined by periodate titration.

Where comparison was possible (at low acidity), the amount of reaction found was similar to that calculated from the kinetic data. This suggests that the reaction rate is not changed greatly by the comparatively high concentration of pinacol (*ca.* 1M) used for the exchange experiments (Found for reaction for 89 hr. with 0.053M-H₂SO₄ at 72.9°, reaction = 20%. Calc., 22.5%). This difference arises because water, formed from pinacol during the reaction, dilutes the sulphuric acid, and because pinacol probably decreases the acidity, as measured by *H*₀. Comparison between the found and calculated amounts of reaction could not be made for experiments at the higher acidities. For these the times required for solution of the pinacol, and warming of the reaction mixture, are not negligible compared with the total reaction time. For these reasons the amounts of reaction (Table 2) are calculated from direct measurements by periodate titration.

After a suitable time the solutions were cooled; the pinacone separated, and was removed. Crystals of pinacol hydrate separated when the aqueous portion was cooled to 0°. These were washed with a little ice-cold water and dissolved in warm water. The traces of acid in this solution were exactly neutralised with barium carbonate, and the barium sulphate was spun off. Water was removed under reduced pressure until crystals of pinacol hydrate separated. These were dehydrated by azeotropic distillation with benzene at the pressure of a water pump. This reduced losses of pinacol by co-distillation with benzene. The dried pinacol was then distilled under reduced pressure and stored in a desiccator. A portion was pyrolysed to carbon monoxide *in vacuo* on red-hot carbon heated by a radio-frequency induction furnace. The carbon monoxide was analysed mass spectrometrically.

The usual scale of the experiments was 24 g. of pinacol hexahydrate (air dried) dissolved in 100 g. of acidified H₂¹⁸O. In calculating the extent of isotopic exchange, allowance was made for the water of crystallisation of the pinacol.

In all experiments the concentration of pinacol was small relative to that of water, and the relative rates of oxygen exchange and chemical reaction are given by

$$k_E/k_O = [2 \log N_\infty / (N_\infty - N_t)] / \{\log [a/(a - x)]\}$$

where *a* and *a - x* are respectively the concentrations of pinacol initially and at the time of isolation, *t*, and *N*_∞ and *N*_{*t*} are respectively the isotopic abundance of pinacol calculated for complete exchange and found for the isolated material and measured in atoms % excess above normal.

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