# KINETIC HYDROGEN ISOTOPE EFFECTS IN THE HYDRATION OF ISOBUTENE

V. Gold and M. A. Kessick

King's College, University of London, London U.K.

Kinetic isotope effects can be measured either by the direct comparison of reaction velocities or by the observation of relative isotopic abundances in the product (or in the unchanged starting material)[1]. For practical reasons the first method is generally restricted to primary protium–deuterium isotope effects.

The work, of which this paper is a preliminary summary, deals with the application of both methods to the hydration of isobutene (2-methylpropene) in aqueous solutions of perchloric acid

$$(CH_3)_2C{=}CH_2 + H_2O \rightarrow (CH_3)_3C{\cdot}OH$$
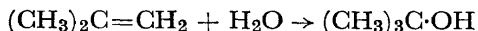
The isotope effects studied arise from the use of different hydrogen isotopes as constituents of the reaction medium. In this way one obtains from ordinary isobutene an alcohol containing isotopic label in one of its nine C–H bonds, and the product experiments are concerned with the isotopic abundance of the carbon-bound hydrogen. The rate comparisons were based on measurements of the concentration of olefin as a function of time, in protium oxide, deuterium oxide, and their mixtures as solvents.

It was noted some time ago[2] that some acid-catalysed addition reactions of olefins are apparently characterized by an isotope effect close to unity, whereas in others formation of C–H is favoured relative to C–D or C–T. Explanations of this dichotomy were based on differences in the nature of the acid (or medium) from which the added hydrogen nucleus is derived[2], or on a difference between olefins[3] giving rise to secondary alcohols and those yielding tertiary alcohols. It was, however, pointed out[2] that the only results indicating a small isotope effect were based on a direct rate comparison in isotopically different media, whereas all others were derived from determinations of the isotopic composition of the product. It therefore seemed important to establish whether the size of the isotope effect is in fact determined by the method of measurement.

Previous work on isobutene[4] had shown that its reaction velocity would be convenient for measurements. Our own experiments[5] established that the product (t-butyl alcohol, 2-methylpropan-2-ol) does not exchange C–H bonds at a sufficient speed to vitiate the determination of kinetic isotope effects by isotope assay of the product.

The following blocks of experiments were accordingly performed:

(1) The rate of disappearance of olefin from solutions of isobutene in aqueous perchloric acid was observed at a series of acid concentrations, using either ordinary water or deuterium oxide (>97.7 per cent D) as solvent. A vapour-free reaction vessel was used. It was also confirmed that

the initial concentration of olefin in solution agrees with the final concentration of t-butyl alcohol, so as to exclude the possibility of spurious effects due to mechanical escape of olefin or side reactions. As noted by earlier workers, the reaction velocity increases with acid concentration slightly more rapidly than required by first-order dependence on the acid concentration[4]. Over the entire range of concentrations of perchloric acid (0·1–0·5M) the isotope effect remains sensibly constant, the reaction in protium oxide being faster than that in deuterium oxide containing the same molar concentration of acid by a factor of 1·45, but the limited precision of the measurements (± 2 per cent) would not exclude a slight trend with concentration. (Although small, this isotope effect is somewhat larger than that found in the hydration of 2-methylbut-2-ene and 1-methylcyclopentene in a two-phase system)[6].

(2) Analogous measurements were carried out using H_2O–D_2O mixtures at a fixed acid concentration (0·434M). The rate constant decreases roughly linearly with increasing atom fraction of deuterium (n) in the solvent. These results clearly do not obey the predictions of the Gross–Butler treatment (with modern constants[7, 8]) for reactions in which the transition state of the reaction has the composition substrate + proton (deuteron). With the extreme rate ratio (k_{H_2O}/k_{D_2O}) of 1·45 this theory predicts the reaction velocity to pass through a maximum. Our finding is at variance with conclusions reached by Purlee and Taft[6] for their compounds.

(3) The hydration was carried out under similar conditions as in the previous experiments but using in the medium a tracer concentration of tritium. The product was extracted from the final solution by equilibration with inactive t-butyl alcohol. Hydroxylic tritium was removed from the alcohol by washing. The radioactivity of this alcohol (now due to C–T bonds alone) was compared with that of the medium. It was found that the activity of the alcohol (per mole) was 6·9 times smaller than the activity of tritium in protium oxide solvent (per g-atom exchangeable hydrogen). Analogous measurements using H_2O–D_2O mixtures with tracer tritium indicate that this ratio declines (by a factor of ca. 3) as the atom fraction of deuterium increases from 0 to 1. This trend agrees with the expectation that deuterium competes less effectively than protium with tritium.

(4) The hydration was performed in a two-phase system by hydration of gaseous isobutene using protium oxide with a tracer concentration of tritium. The alcohol was then isolated without use of diluent. The radioactivity assay carried out as above again showed the alcohol to be 6·9 times less active than the medium. The agreement of this result and that of the preceding experiment confirms that the use of the two-phase system does not make any essential difference.

(5) A similar experimental arrangement was used to isolate alcohol from experiments using H_2O–D_2O mixtures as solvent. The deuterium content of the carbon–hydrogen bonds of the alcohol was determined by infrared spectrometry. For values of n in the range 0·1–0·9, the concentration of deuterium (per mole of alcohol) was consistently lower than that of the medium (per g-atom of exchangeable hydrogen). The ratio $n(1 - m)/m(1 - n)$ (n being the atom fraction of deuterium in the solvent and m the mole fraction of t-butyl-d_1 alcohol in the isolated alcohol) changes

only slowly with composition, with a mean value of $3 \cdot 9 \pm 0 \cdot 5$ (the limits being extreme values). This ratio is in good agreement with the value of $6 \cdot 9$ of the preceding experiments by application of Schaad's formula[9] ($6 \cdot 9^{1/1 \cdot 442} = 3 \cdot 8$).

DISCUSSION

The results of experiments clearly establish the existence of an isotope effect in this reaction, as a result of which the entry of lighter hydrogen isotopes is favoured relative to heavier ones. It remains to decide with what stage or stages of the reaction the isotope effect is associated.

The mechanism of the hydration of olefins is still a much-debated problem. Although superficially a very simple reaction, the mechanistic schemes proposed for it include some of considerable complexity[3, 10]. The features of the reaction which seem most significant *and* are not based on controversial criteria of mechanism are (*i*) the occurrence of specific hydrogen ion catalysis, and (*ii*) the fact that oxygen exchange in secondary or tertiary alcohols is a faster reaction than hydrogen exchange. The first of these facts implies that the transition state has the composition {olefin, $H^+ \pm x H_2O$}; the second one indicates that formation of the C–H bond involves a higher energy barrier than formation of the C–OH bond.[11] Accordingly we look on the rate-controlling step of the reaction essentially as a "slow proton transfer" (the term being used in a broad sense) in which a proton from the hydrogen ion loses its equivalence with the two other hydrogen nuclei of the hydroxonium ion on entering the transition state of the reaction. The attainment of this transition state need not occur in a single stage. Since the reaction shows specific hydrogen ion catalysis[4] the process is likely to involve complete severance of the H–O bond of the transferred proton, but it is possible that water molecules are nevertheless included in the transition state of the reaction by attachment elsewhere. This is the kind of pseudo-equilibrium

$$H_3O^+ + S + x H_2O \rightleftharpoons \{SH^+ \ldots x H_2O\}^{\ddagger}$$
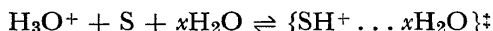
to which the Gross–Butler theory, governing the isotopic fractionation between H_3O^+ and SH^+ in an isotopically mixed solvent, should be applicable[8].

Another experimental fact which has to be borne in mind is the pronounced departure from first-order dependence on acid concentration observed even at quite low concentrations. This has been attributed to specific salt effects[4] or to acidity-function behaviour[12], both interpretations implying the importance of specific medium effects.

Accordingly, we attempt to apply the principles of the Gross–Butler theory to those of our results which relate to rate comparisons within the same medium, *i.e.* the product ratios determined in experiments (3)–(5).

Although the theory of the kinetic solvent isotope effect in acid-catalysed reactions has recently received a good deal of attention, the corresponding treatment for product isotope effect does not seem previously to have been given, and the most important equations are now summarized. In view of recent evidence for the adequacy of the formula H_3O^+ for the hydrogen ion [13,14] our treatment is written in terms of this formula. The other

assumptions in the derivation and the symbolism have been explained previously[8]. On this basis the ratio R_n of the tritium activity present at tracer level in a D_2O-H_2O mixture to the activity found in the product is given by

$$R_n = \frac{\text{Activity of water (per g-equiv.)}}{\text{Activity of product (per mole)}}$$

$$= \frac{1 - n + nl^{1+2\alpha} k_D/k_H}{\lambda^{1+2\alpha} k_T/k_H} \tag{1}$$

where k_H, k_D and k_T are rate coefficients for proton, deuteron, triton transfer from the species H_3O^+, D_3O^+, and T_3O^+, respectively. l is the exchange equilibrium constant ($\equiv L^{-1/6}$) for deuterium–protium distribution between hydrogen ions and water, and λ the corresponding constant for tritium and protium. α is the exponent in the Brönsted relation which, in the present case, we shall assume to be unity, in view of the absence of general acid catalysis. When the solvent contains no deuterium oxide ($n = 0$), equation (1) becomes

$$R_0 = \frac{k_H}{\lambda^{1+2\alpha} k_T} \tag{2}$$

For $n = 1$,

$$R_1 = \left(\frac{l}{\lambda}\right)^{1+2\alpha} \frac{k_D}{k_T} \tag{3}$$

For the relative amounts of protium and deuterium in the product, we get

$$r = \frac{n}{1 - n} \times \frac{1 - m}{m} = \frac{k_H}{l^{1+2\alpha} k_D} \tag{4}$$

Simplification is possible if we assume

$$\lambda = l^{1\cdot442} \tag{5}$$

Experimental values for R_0 and r were obtained in the present work and, by substituting these values in equations (2) and (4) (and using equation 5), we obtain the following ratios of rate coefficients applicable to H_2O as solvent,

$$\frac{k_H}{k_D} = 1\cdot14$$

$$\frac{k_H}{k_T} = 1\cdot22$$

These values are quite close to unity, despite the large isotope effect evident in the values of R_0 and r. The low ratio k_H/k_D is much closer to the values of k_{H_2O}/k_{D_2O} obtained by direct rate comparisons ($1\cdot45$) but does not quite agree with it†. We currently inclined to the view that this disagreement is connected with the susceptibility of the reaction to medium effects and

† It should be noted, however, that l is not known very accurately.

likewise the failure of the Gross–Butler treatment for rate measurements in H_2O–D_2O mixtures, but we expect that more reliable values for R_n, which are now being obtained, will allow us to specify the behaviour in mixed solvents more completely.

It is evident from the theoretical analysis that large isotope effects should indeed be associated with measurements of product compositions, in contrast to lower ratios from rate ratios. The fair agreement of this prediction with our results suggests that the rate-controlling step of the reaction is indeed a "slow proton transfer" from H_3O^+. A slightly larger isotope effect has been reported for proton transfer from H_3O^+ to the double bond in an enolate anion[15]. The large isotope effects derived from product experiments are thus due not to a kinetic isotope effect but to the factors $\lambda^{-(1+2\alpha)}$ and $(l/\lambda)^{(1+2\alpha)}$ which are largely thermodynamic isotope effects.

On this view there is no need to ascribe the difference in isotope effects to a difference between rate-limiting and product-controlling steps.

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