

# Oxygen Exchange into 2-Butanol and Hydration of 1-Butene Do Not Proceed through a Common Carbocation Intermediate<sup>1</sup>

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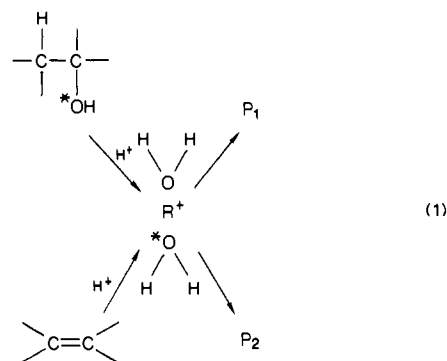
**Abstract:** The acid-catalyzed isomerization of the 4-methyl group of 1,1,1,2,3,3-hexadeuteriated 2-butanol between the 1- and 4-positions occurs faster than dehydration to 2-butene, as measured by hydrogen incorporation from water into the 3-position of 2-butanol. The rate constants for these processes are  $k_{\text{isom}} = 1.1 \times 10^{-6} \text{ s}^{-1}$  and  $k_{\text{hyd}} = 5.6 \times 10^{-7} \text{ s}^{-1}$ , respectively, in 0.55 M  $\text{HClO}_4$  at 100 °C. These results require that isomerization occurs by hydride transfer from C-3 to C-2, as well as by the formation and hydration of 2-butene. The 6% initial yield of isomerized product in the acid-catalyzed hydration of  $[4\text{-}^{14}\text{C}]\text{-1-butene}$ , before there is significant accumulation of 2-butene (Manassen, J.; Klein, F. *J. Chem. Soc.* **1960**, 4023), shows that hydride transfer is also significant in this reaction. Comparison of the product yields from 1-butene and the rate constants for isomerization and oxygen exchange of  $[4\text{-}^{14}\text{C}]\text{-2-butanol}$  in the earlier work shows that the two reactions do not occur through a common carbocation intermediate. The preferential formation of *cis*-2-butene from 1-butene and *trans*-2-butene from 2-butanol confirms this conclusion.

The identification of short-lived intermediates is a particularly difficult problem in the diagnosis of reaction mechanisms. The diagnosis of an  $\text{S}_{\text{N}}1$ , or  $\text{D}_{\text{N}} + \text{A}_{\text{N}}$ ,<sup>2</sup> mechanism is often made from the appearance of the transition state, as indicated by structure-reactivity correlations, isotope effects, and other criteria, but a number of reactions with carbocation-like transition states have been shown to proceed through concerted  $\text{S}_{\text{N}}2$ , or  $\text{A}_{\text{N}}\text{D}_{\text{N}}$ ,<sup>2</sup> mechanisms with no intermediate.<sup>3,4</sup>

A rigorous requirement for a common carbocation intermediate is that it must partition between different reaction paths in the same way when it is formed from different reactants. However, it is not usually possible to apply this criterion to very unstable carbocation intermediates that are formed in solvolysis reactions because the intermediates can react with solvent before the leaving group has diffused away. The leaving group can influence the reactions of a carbocation, so that different partitioning ratios may be found with different leaving groups. This is the case for the solvolysis of simple secondary substrates if an intermediate is formed in these reactions, because the observed inversion of configuration<sup>5</sup> shows that if there is an intermediate it reacts with solvent before it rotates or diffuses into the bulk solvent.

However, the acid-catalyzed exchange of isotopically labeled oxygen between secondary alcohols and water provides an exception to this generalization because the leaving and entering groups are the same, except for the isotopic label. A putative carbocation intermediate can also be generated from an olefin, so that the same intermediate can be generated from two different reactants in the same solvent environment. Such an intermediate,  $\text{R}^+$ , should partition to products in the same way when it is generated from the two different reactants (eq 1).

Manassen and Klein have reported an elegant series of experiments in which a possible carbocation intermediate was generated from  $[4\text{-}^{14}\text{C}]\text{butan-2-}[^{18}\text{O}]\text{ol}$  and from isotopically labeled 1-butene in water. From the measured rates of oxygen



exchange and isomerization it was concluded that if a carbocation intermediate is formed, it can react with either of two equivalent surrounding water molecules.<sup>6</sup> More recently, Herlihy has carried out similar experiments on 1,2-propanediol and prop-2-en-1-ol and reported results that are consistent with a common carbocation intermediate.<sup>7,8</sup>

We report here that the reactions of 2-butanol are more complex than previously assumed and involve a significant amount of hydride migration. Reexamination of the earlier data shows that the product partitioning ratios from 2-butanol and 1-butene are different if hydride migration and products arising from 2-butene are considered. We conclude that these reactions do not proceed through a common carbocation intermediate. The data are consistent with reactions that occur through parallel pathways that have similar, carbocation-like, transition states. It is possible that the reaction mechanisms are concerted because simple secondary carbocations do not have a significant lifetime in the presence of water.

## Experimental Section

**Materials.** 1,1,1,2,3,3-Hexadeuteriated 2-butanol was prepared from 5 g of 2-butanone that was stirred in 50 mL of  $\text{D}_2\text{O}$  containing 2.5 g of  $\text{K}_2\text{CO}_3$  for 12 h. The fraction boiling from 72 to 76 °C was collected, and the procedure was repeated. Fractional distillation collecting the fraction boiling between 70 and 74 °C yielded 4 g of the deuteriated ketone. Analysis of the product by NMR showed complete deuteration of the 1- and 3-positions. The deuteriated 2-butanone (4 g) was dissolved in 18 mL of diethyl ether, dried with  $\text{MgSO}_4$ , and filtered. The solution was added slowly to a solution of 1.1 g of  $\text{LiAlD}_4$  in 20 mL of diethyl ether in a 100-mL round-bottom flask equipped with a reflux condenser. After the mixture stirred for 2 h, water was added slowly to decompose any remaining  $\text{LiAlD}_4$ , and the solution was neutralized to pH 6 with 10%  $\text{H}_2\text{SO}_4$  and extracted twice with 10 mL of ethyl ether. After the

(1) Supported in part by grants from the National Institutes of Health (GM 20888) and the National Science Foundation (PCM 81-17816) and a USPHS fellowship to Paul E. Dietze from the National Cancer Institute (1-F32-CA07832-01).

(2) A and D refer to associative and dissociative processes, respectively, and N refers to a nucleophilic or nucleofugic process. A + sign and a \* refer to stepwise processes in which the intermediate does or does not exist long enough to become diffusively equilibrated with the solvent, respectively, while the absence of punctuation refers to a concerted process with no intermediate. (Commission on Physical Organic Chemistry, IUPAC, *Pure Appl. Chem.*, in preparation).

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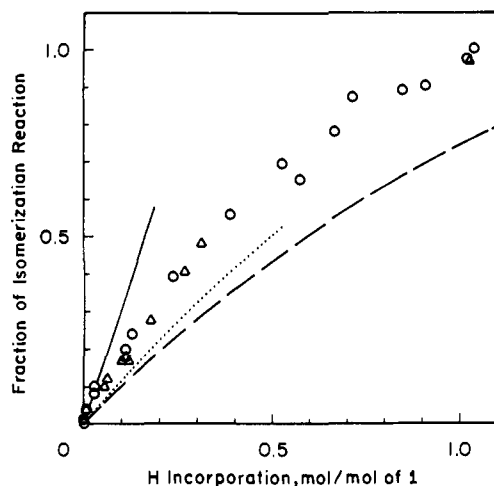
(4) Dietz, P. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 4549-4555.

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**Figure 1.** Plot of the fraction of the isomerization reaction against moles of hydrogen incorporated per mole of 2-butanol for the reaction of 1,1,1,2,3,3-hexadeuteriated 2-butanol at 100 °C in 0.55 M HClO<sub>4</sub>, O, and in 0.82 M HClO<sub>4</sub>, Δ. The solid line represents the initial slope for the points obtained in 0.55 M HClO<sub>4</sub>. The dashed line is calculated for isomerization through 2-butene, assuming no β-deuterium isotope effect on the protonation of 2-butene, and the dotted line is calculated assuming a β-deuterium isotope effect of 1.3, as described in the text.

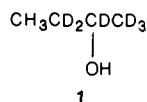
mixture dried over MgSO<sub>4</sub> the ether was allowed to evaporate slowly at room temperature to yield 1.75 g of the deuteriated alcohol.

**Kinetics.** Aliquots of 1.0 mL of a solution of 1.75 g of the deuteriated 2-butanol in 30 mL of 0.55 M HClO<sub>4</sub> were placed in 1-mL ampules, and the ampules were sealed under reduced pressure after freezing in liquid nitrogen. The ampules were placed in a boiling water bath, removed at appropriate times, and opened after quenching in ice. The contents were poured into 1 mL of CDCl<sub>3</sub> and shaken. The chloroform layer was removed, dried with MgSO<sub>4</sub>, and filtered through glass wool into an NMR tube containing a drop of D<sub>2</sub>O to exchange with the alcohol protons. The NMR spectrum was recorded on a Varian 300-MHz spectrometer, and peak areas were carefully integrated. All the peaks of 2-butanol were clearly separated with the 4-methyl signal at 0.9 ppm, the 1-methyl signal at 1.2 ppm, the 3-methylene signal at 1.4 ppm, and the 2-CH signal at 3.7 ppm. Peak areas were standardized by using the total area of the methyl protons as an internal standard.

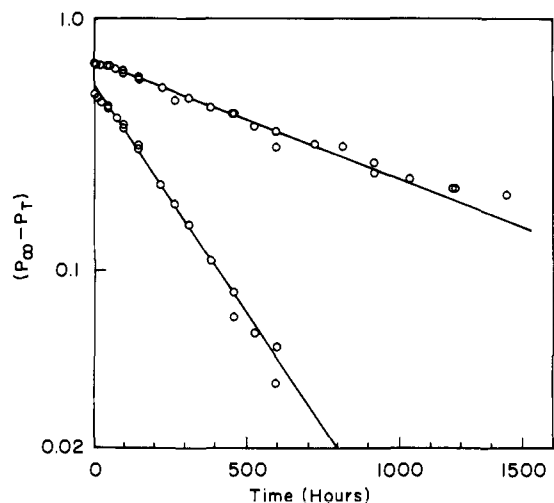
The rate constant for isomerization was obtained from a plot of  $\log(P_\infty - P_t)$  against time, in which  $P_t$  is the area of the 1-methyl signal divided by the total methyl area at time  $t$  and  $P_\infty = 0.5$  is the value at infinite time. The rate constant for hydrogen incorporation was obtained from a plot of  $\log(P_\infty - P_t)$  against time, in which  $P_t$  is the area of the NMR signal corresponding to the 3-methylene group of 2-butanol divided by the total methyl area at time  $t$  and  $P_\infty = 0.66$  is the value of the same ratio at infinite time.

## Results

We have measured the rate of solvent hydrogen incorporation from water into the 3-position of partially deuteriated 2-butanol, **1**, and the rate of approach to equilibrium for isomerization of the methyl group between the 1- and 4-positions of **1** in 0.55 M perchloric acid at 100 °C. Isomerization that proceeds through

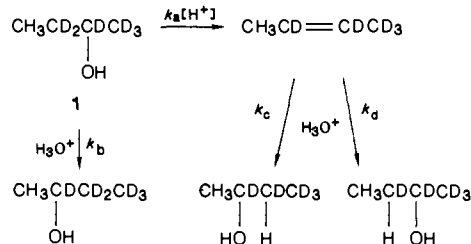


dehydration to 2-butene and rehydration gives H incorporation into the 3-position of the product and would give an initial slope of 1.0 in a plot of hydrogen incorporation against the fraction of isomerization. However, the solid line in Figure 1 shows that the initial rate of isomerization is faster than the initial rate of H incorporation. The slope of the solid line was obtained from a linear plot of  $\log x$  against  $y$ , from the data of Figure 1. A second H is incorporated into the 3-position after isomerization has occurred so that hydrogen incorporation will become larger than isomerization through 2-butene after the initial phase of the reaction. The dashed line shows the theoretical curve for isomerization and H incorporation through 2-butene, taking account of



**Figure 2.** Semilogarithmic plots for the isomerization of the 4-methyl group (lower line) and the incorporation of hydrogen into the 3-methylene position (upper line) of 1,1,1,2,3,3-hexadeuteriated 2-butanol in 0.55 M HClO<sub>4</sub> at 100 °C, measured by NMR integration as described in the Experimental Section.

## Scheme I



this additional incorporation. The additional incorporation was obtained from the difference between first-order plots for the incorporation of 2H (total incorporation) and 1H (isomerization). The dotted line shows the expected ratio of isomerization to hydrogen incorporation, assuming a β-secondary deuterium isotope effect of 1.3 that favors the addition of water to 2-butene at the position that gives the isomerized product. The triangles in Figure 1 show that similar results were obtained from an experiment in 0.82 M perchloric acid at 100 °C that was followed for a shorter time.

The plots in Figure 2 give first-order constants for isomerization approaching equilibrium of  $1.1 \times 10^{-6} \text{ s}^{-1}$  and for incorporation of two protons into the 3-position of  $2.8 \times 10^{-7} \text{ s}^{-1}$  in 0.55 M perchloric acid. This gives a rate constant for the incorporation of one proton,  $k_{\text{hyd}}$ , of  $5.6 \times 10^{-7} \text{ s}^{-1}$ . Only the incorporation of the first proton in the first turnover of **1** is relevant for isomerization that proceeds through 2-butene. The observed rate of H incorporation into the 3-position will be decreased in the second turnover because of isomerization of H from the 3- to the 2-position; however, this decrease will be partially offset by α- and β-secondary deuterium isotope effects that increase the reaction rate of the protium-containing species. The first few points for H incorporation show a small negative deviation that may reflect approach to the steady-state concentration of 2-butene; the approach to the steady state is complete in 35 h for [4-<sup>14</sup>C]butan-2-[<sup>18</sup>O]ol.<sup>6</sup> The experiment in 0.82 M HClO<sub>4</sub> at 100 °C gave  $k_{\text{isom}} = 1.9 \times 10^{-6} \text{ s}^{-1}$  and  $k_{\text{hyd}} = 5.3 \times 10^{-7} \text{ s}^{-1}$  (data not shown). The errors in rate constants are estimated to be ≤15%.

## Discussion

The fact that solvent protons are incorporated into **1** shows that a significant amount of reaction occurs through the formation of 2-butene, in agreement with previous results.<sup>6</sup> When 2-butene is formed it is protonated to give alcohol that is either isomerized or not isomerized, each incorporating a solvent proton with the rate constants  $k_c$  and  $k_d$  of Scheme I. Formation of the isomerized

alcohol ( $k_c$ ) will be favored by a  $\beta$ -deuterium isotope effect.

If isomerization occurred entirely through 2-butene, with no hydride migration and no  $\beta$ -deuterium isotope effect, each dehydration would give an isomerized mixture of products upon rehydration, and a plot of the fraction of isomerization against hydrogen incorporation would have an initial slope of 1.0, as described in the Results section. In fact, the initial slope of this ratio is 3, as shown by the solid line in Figure 1. The dashed line shows the expected relationship of isomerization and H incorporation in the absence of a  $\beta$ -deuterium isotope effect on the rehydration reaction, and the dotted line shows the initial slope if a  $\beta$ -deuterium isotope effect of  $k_H/k_D = 1.3$  favors hydration to give the isomerized product.

The ratio  $k_c/k_d = 1.3$  is based on a maximum  $\beta$ -deuterium isotope effect of 1.1 for each  $\beta$ -D. The value of 1.1 was calculated from an observed kinetic isotope effect of 1.14 per  $\beta$ -D for the solvolysis of 2-propyl naphthalenesulfonate in hexafluoro-2-propanol<sup>9</sup> by correcting for the fractionation factors (relative to acetylene) 1.324 and 1.362 for  $\text{CH}_3\text{CH}_2\text{CH}_2\text{D}$  and  $\text{CH}_2=\text{CHCH}_2\text{D}$ , respectively.<sup>10</sup> A value of 1.1 per  $\beta$ -D has also been calculated for the equilibrium formation of the 2-propyl cation.<sup>11</sup>

The large initial ratio of isomerization to hydrogen incorporation requires that isomerization must also occur by a mechanism that does not involve hydrogen incorporation. This additional isomerization can be accounted for by a pathway involving hydride migration,  $k_b$  in Scheme I, which may or may not involve incorporation of a solvent water molecule.

The same conclusion is reached by comparison of the first-order rate constants for hydrogen incorporation and isomerization (Figure 2). The rate constants for isomerization and hydrogen incorporation into **1** that occurs through 2-butene are given by eq 2 and 3. The rate constant for the formation of rearranged

$$k_{\text{hyd}} = k_a \quad (2)$$

$$k_{\text{isom}} = \frac{2k_a k_c}{k_c + k_d} \quad (3)$$

alcohol is multiplied by 2 in eq 3 because the first-order rate constant for approach to equilibrium in the isomerization reaction is equal to the sum of the forward and reverse rate constants, which are essentially equal in this reaction.<sup>6</sup> In the absence of a  $\beta$ -deuterium isotope effect on hydration, each formation and hydration of 2-butene would give isomerization with  $k_c = k_d$  and  $k_{\text{isom}} = k_{\text{hyd}}$  (the rate of isomerization is twice the rate of hydration to give rearranged product, but only half of the reactions give rearranged product).

The observed rate constants  $k_{\text{isom}} = 1.1 \times 10^{-6} \text{ s}^{-1}$  and  $k_{\text{hyd}} = 0.56 \times 10^{-6} \text{ s}^{-1}$  are inconsistent with this prediction and require an additional pathway for isomerization. A  $\beta$ -deuterium isotope effect that favors hydration to give the isomerized product with  $k_c = 1.3k_d$  gives  $k_{\text{isom}}/k_{\text{hyd}} = 1.13$  from eq 2 and 3, which is much smaller than the observed ratio  $k_{\text{isom}}/k_{\text{hyd}} = 1.9$ . The observed ratio of 1.9 would require a  $\beta$ -deuterium isotope effect of  $k_c/k_d = 19$ . The rate constant for incorporation of the second H may be decreased, as noted above, but the rate of incorporation of the first H from the initial slope of the first-order plot for H incorporation in Figure 2 provides an accurate measure of 2-butene formation and hydration.

The rate constant for isomerization through both butene formation and hydride transfer (Scheme I) is given by eq 4. The

$$k_{\text{isom}} = \frac{2k_a k_c}{k_c + k_d} + 2k_b \quad (4)$$

rate constant for hydride transfer is multiplied by 2 because each

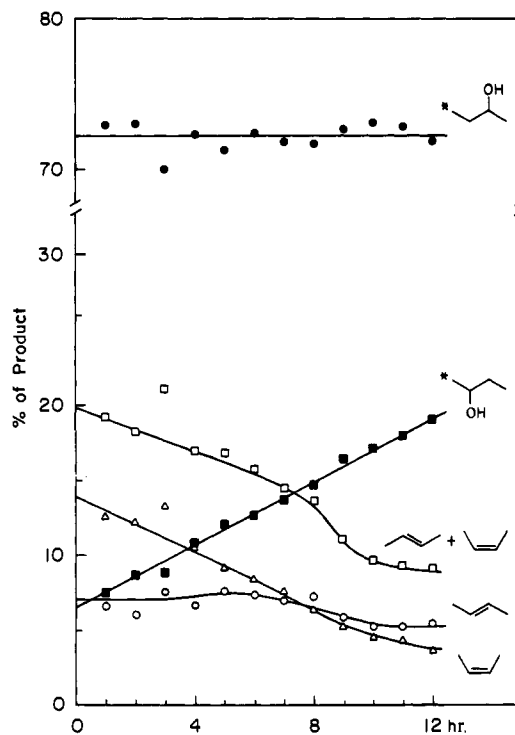
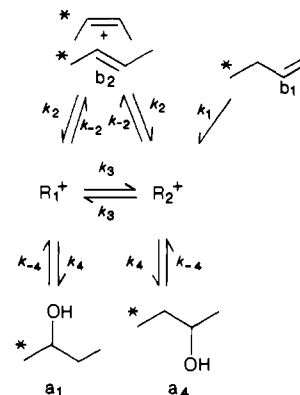


Figure 3. Plot of the fraction of total products against time for the reaction of  $[4\text{-}^{14}\text{C}]\text{-1-butene}$  in  $0.55 \text{ M HClO}_4$  at  $100^\circ\text{C}$ :  $\text{cis-2-butene}$ ,  $\Delta$ ;  $\text{trans-2-butene}$ ,  $\circ$ ;  $\text{cis- and trans-butene}$ ,  $\square$ ;  $[1\text{-}^{14}\text{C}]\text{-2-butanol}$ ,  $\blacksquare$ ;  $[4\text{-}^{14}\text{C}]\text{-2-butanol}$ ,  $\bullet$ .<sup>6</sup>

#### Scheme II



hydride transfer gives rearranged alcohol, not an equilibrium mixture of products. Taking a  $\beta$ -deuterium isotope effect on hydration of  $k_c/k_d = 1.3$ , the observed ratio  $k_{\text{isom}}/k_{\text{hyd}} = 1.9$  gives  $k_a/k_b = 2.6$ , from eq 2 and 4. This corresponds to 72% isomerization by dehydration to 2-butene, followed by rehydration, and 28% isomerization by hydride transfer.

The difference between the rate constant  $k_{\text{isom}} = 1.1 \times 10^{-6} \text{ s}^{-1}$  for **1** and  $k_{\text{isom}} = 5.2 \times 10^{-6} \text{ s}^{-1}$  for  $[4\text{-}^{14}\text{C}]\text{-2-butanol}$  at  $101.4^\circ\text{C}$  in  $0.555 \text{ M HClO}_4$ <sup>6</sup> may be accounted for by  $\alpha$ - and  $\beta$ -secondary deuterium isotope effects and primary isotope effects for deprotonation and hydride transfer, in addition to a small contribution from the difference in temperature; however, we have not attempted a quantitative analysis of these isotope effects.

**Isomerization and Oxygen Incorporation of 1-Butene and 2-Butanol.** We now examine the hypothesis that the reactions of  $[4\text{-}^{14}\text{C}]\text{-labeled 1-butene}$  and 2-butanol in  $0.55 \text{ M perchloric acid}$  at  $101.4^\circ\text{C}$  that were examined by Manassen and Klein proceed through a common carbocation intermediate,  $\text{R}^+$ . The reactions may be described by Scheme II, which is the same as that proposed previously<sup>6</sup> except for the addition of the hydride-transfer pathway with the rate constant  $k_3$ .

Figure 3 shows the fractional yields as a function of time for the reaction of  $[4\text{-}^{14}\text{C}]\text{-1-butene}$  to give  $[4\text{-}^{14}\text{C}]\text{-2-butanol}$  ( $a_4$ ),

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(10) *Isotope Effects on Enzyme Catalyzed Reactions*; Cleland, W. W., O'Leary, M. H., Northrop, D. B., Eds.; University Park Press: Baltimore, 1976; p 11.

(11) Williams, I. H. *J. Chem. Soc., Chem. Commun.* **1985**, 510-511.

[1-<sup>14</sup>C]-2-butanol ( $a_1$ ), and *cis*- and *trans*-2-butene ( $b_2$ ).<sup>6</sup> The major product is unrearranged 2-butanol ( $a_4$ ), which is formed in a yield of approximately 73% that is independent of the time of reaction. The initial yield of 2-butene is 20%, with a 2:1 preference for the *cis* isomer; this is followed by isomerization to give an excess of the thermodynamically favored *trans* isomer. The important result is that the rearranged [1-<sup>14</sup>C]-2-butanol ( $a_1$ ) is formed with no induction period and an initial yield of 6% (solid squares, Figure 3). This is followed by a slow increase in yield as 2-butene is hydrated to 2-butanol ( $a_1$  and  $a_4$ ). The 6% yield of  $a_1$  at zero time represents the formation of rearranged 2-butanol in the initial reaction, before a pool of 2-butene has been formed, and must represent isomerization by hydride transfer in a carbocation intermediate ( $k_3$  in Scheme II) or in a concerted reaction upon protonation of 1-butene. It is known that the acid-catalyzed reaction of 1-hexene in trifluoroacetic acid gives 10% hydride transfer.<sup>12</sup> The solvolysis of 3-methyl-2-butyl *p*-toluenesulfonate in acetic acid proceeds with hydride transfer, and the deuterium isotope effect of  $k_H/k_D = 2.2$  on the observed rate constant is consistent with assistance to solvolysis by a hydride transfer in a concerted reaction mechanism.<sup>13</sup>

The initial relative yields of products from the reaction of 1-butene through an intermediate carbocation according to Scheme II are given by eq 5-7;<sup>14</sup> the initial observed yields (Figure 3) are also shown. Solving eq 5-7 simultaneously gives relative values of the rate constants for partitioning of the carbocation intermediate  $R_4^+$  of 0.74, 0.18, and 0.08 for  $k_4$ ,  $k_{-2}$ , and  $k_3$ , respectively, and a partitioning ratio  $k_{-2}/k_4 = 0.24$ .

$$k_{a4} = k_4 = 0.73 \quad (5)$$

$$k_{b2} = k_{-2} + \frac{k_3 k_{-2}}{k_3 + k_{-2} + k_4} = 0.20 \quad (6)$$

$$k_{a1} = \frac{k_3 k_4}{k_3 + k_{-2} + k_4} = 0.06 \quad (7)$$

The rate constant for isomerization of [4-<sup>14</sup>C]-2-butanol to an equilibrium mixture of  $a_4$  and  $a_1$  through a carbocation intermediate according to Scheme II is given by eq 8. The rate

$$k_{\text{isom}} = k_{-4} \left( \frac{k_{-2} + \frac{2k_3 k_4}{k_{-2} + k_3 + k_4} + \frac{k_3 k_{-2}}{k_{-2} + k_3 + k_4}}{k_{-2} + k_3 + k_4} \right) \quad (8)$$

$$k_{\text{ex}} = k_{-4} \left( \frac{k_{-2} + 0.5k_4 + k_3}{k_{-2} + k_3 + k_4} \right) \quad (9)$$

constants  $k_3$ ,  $k_{-2}$ , and  $k_4$  describe the fractions of reaction of  $R_2^+$  to give  $R_1^+$ , 2-butene, and 2-butanol, respectively. Rate constants for the formation of isomerized alcohol are multiplied by 2 because  $k_{\text{isom}}$ , the rate constant for approach to equilibrium, is the sum of the forward and reverse rate constants; however, the rate constants for reaction through 2-butene are equal to the contribution of butene formation to isomerization, as described above, so that  $k_2$  is equal to  $k_{\text{isom}}$  for this reaction path.<sup>6</sup> The  $k_3 k_4$  term describes formation of isomerized alcohol by hydride transfer, and the  $k_3 k_{-2}$  term describes formation of 2-butene after hydride transfer.

The rate constant for oxygen exchange between 2-butanol and the solvent is given by eq 9 if hydride transfer ( $k_3$ ) is accompanied by incorporation of oxygen from the solvent and by eq 10 if hydride

$$k_{\text{ex}} = k_{-4} \left( \frac{k_{-2} + 0.5k_4}{k_{-2} + k_3 + k_4} \right) \quad (10)$$

transfer is accompanied by oxygen migration, without exchange with solvent.<sup>14</sup> Note that oxygen exchange occurs from deprotonation ( $k_{-2}$ ) and rehydration, as well as by return of  $R^+$  to 2-butanol ( $0.5k_4$ ; the 0.5 is based on the assumption that the carbocation in this and related reactions can react with either of two water molecules, only one of which is isotopically labeled<sup>6,15</sup>).

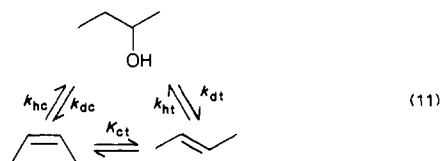
It has been shown that the formation of 1-butene from 2-butanol is not significant.<sup>6</sup> The ratio of  $k_{-2}/k_4$  for partitioning of a carbocation intermediate formed from 2-butanol was calculated from eq 8-10, the ratio of the observed values<sup>6</sup>  $k_{\text{isom}} = (5.18 \pm 0.12) \times 10^{-6} \text{ s}^{-1}$  and  $k_{\text{ex}} = (7.49 \pm 0.16) \times 10^{-6} \text{ s}^{-1}$ , the relationship  $k_4 + k_{-2} + k_3 = 1.0$  for the partitioning of  $R^+$ , and the value  $k_3 = 0.08$  for hydride transfer that was obtained from the partitioning of 1-butene. The partitioning ratio  $k_{-2}/k_4$  is 0.73 if hydride migration is accompanied by oxygen incorporation from solvent (eq 9) and 0.44 if hydride migration occurs without oxygen exchange (eq 10). The difference between these values and the partitioning ratio  $k_{-2}/k_4 = 0.24$  for the reaction of 1-butene is well beyond the estimated errors of the observed rate constants and product yields. In particular, hydration to 2-butanol is preferred over deprotonation to 2-butene for the reaction of 1-butene, whereas deprotonation is of comparable or larger importance compared with hydration for the reaction of 2-butanol.

An analogous calculation, omitting the terms for hydride transfer in eq 8 and 9, gives  $k_{-2}/k_4 = 1.12$ , which differs from the value  $k_{-2}/k_4 = 0.501$  obtained from the reaction of 1-butene by a mechanism that does not involve hydride transfer.<sup>6</sup>

The different partitioning ratios for the acid-catalyzed reactions of 1-butene and 2-butanol show that these reactions do not proceed through a common carbocation intermediate according to Scheme II. This conclusion is confirmed by comparison of the observed ratio  $k_{\text{isom}}/k_{\text{ex}}$  for 2-butanol with the ratio calculated from the product yields in the reaction of 1-butene, according to eq 8-10. The observed product yields give the ratio  $k_{\text{isom}}/k_{\text{ex}} = 0.50$  from eq 8 and 9 and  $k_{\text{isom}}/k_{\text{ex}} = 0.57$  from eq 8 and 10. These are significantly smaller than the experimentally observed ratio  $k_{\text{isom}}/k_{\text{ex}} = 0.692 \pm 0.031$  for [4-<sup>14</sup>C]-2-butanol.<sup>6</sup>

**Stereochemistry of 2-Butene Formation.** Protonation of 1-butene gives an initial yield of *cis*-2-butene that is approximately twofold larger than that of the more stable *trans*-2-butene (Figure 3).<sup>6</sup> The faster decrease in the total percent yield of *cis*-butene than of *trans*-butene (Figure 3)<sup>6</sup> shows that the rate of hydration of the *cis* isomer is faster at 101.4 °C. Direct measurements have shown that hydration of the *cis* isomer is 2.4 times faster than that of the *trans* isomer in water at 25 °C<sup>16</sup> and the *cis* isomer is less stable than the *trans* isomer by  $\Delta H = 0.95 \text{ kcal mol}^{-1}$ ,<sup>17</sup> which corresponds to a factor of 5.0 at 25 °C.

The faster hydration of *cis*-butene compared with *trans*-butene and the greater thermodynamic stability of *trans*-butene require that the rate constant for the dehydration of 2-butanol to *trans*-2-butene be larger than that for dehydration to *cis*-2-butene. The relationships between these rate and equilibrium constants are given by eq 11 and 12. Values of  $K_{\text{ct}} = 5.0$  and  $k_{\text{hc}}/k_{\text{ht}} = 2.4$  give  $k_{\text{dt}}/k_{\text{dc}} = 2.1$ .



$$\frac{k_{\text{dt}}}{k_{\text{dc}}} = K_{\text{ct}} \frac{k_{\text{ht}}}{k_{\text{hc}}} \quad (12)$$

(15) This assumption is supported by the finding that simple secondary substrates undergo solvolysis in solvents of moderate nucleophilicity with complete inversion,<sup>5</sup> so that any carbocation intermediate must react rapidly with a solvent molecule on the opposite side to the leaving group before there is significant diffusion or rotation. A larger fraction than 0.5 would give a larger ratio  $k_{-2}/k_4$ .

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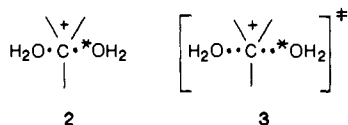
(14) These equations are similar to equations described by Manassen and Klein,<sup>6</sup> with the addition of the  $k_3$  pathway for hydride transfer and the inclusion of oxygen incorporation from 2-butene hydration and from hydride transfer (eq 9).

An exact quantitative comparison is not possible because of the difference in temperature, but the opposite preferences of  $k_{dt}/k_{dc} = 0.5$  and  $2.1$  for the formation of *trans*- and *cis*-butene from 1-butene and 2-butanol, respectively, show that these two reactions do not proceed through a common carbocation intermediate according to the mechanism of Scheme II. This confirms and extends the conclusion of Monitz and Whiting that no carbocation intermediate with a lifetime of  $\geq 10^{-12}$  s is formed upon protonation of *cis*-4-octene in acetic acid, which gives *trans*-3-octene but no *trans*-4-octene.<sup>18</sup>

The preference for formation of *cis*-2-butene from 1-butene means that there is little or no destabilization from a steric interaction of the 4-methyl group and the developing 1-methyl group of *cis*-butene in the transition state; it suggests that dispersion and hydrophobic interactions may provide a small favorable interaction between these groups. The two methyl groups are attached to  $sp^2$  and developing  $sp^2$ -hybridized carbon atoms and are presumably not yet coplanar in the transition state.<sup>18a</sup> Preferential formation of the *trans* isomer from 2-butanol appears to be reasonable because concerted elimination to form *cis*-butene requires reaction of the unstable *gauche* conformation to form the unstable *cis* product.

Inspection of space-filling molecular models does not suggest that there is significant steric hindrance to nucleophilic attack or proton removal by water that might give different ratios of these reactions in different rotational isomers of carbocations that might be formed from 1-butene and 2-butanol.

**Oxygen Exchange with Solvent.** Bunton and co-workers<sup>19</sup> have reported a ratio of  $k_{rac}/k_{exch} = 2.0$  for the acid-catalyzed racemization and exchange of  $^{18}\text{O}$  with solvent of 2-butanol, and Herlihy has reported the same ratio for propane-1,2-diol.<sup>7</sup> A ratio  $k_{rac}/k_{exch} = 2.0$  is consistent with either the formation of a symmetrically solvated carbocation intermediate, **2**, that collapses the



reactants or products with the same rate constant, faster than the leaving water molecule diffuses away, or a concerted  $S_N2$  displacement with inversion through transition state **3**. In both cases, each event that gives exchange proceeds with inversion and gives a ratio  $k_{rac}/k_{exch} = 2.0$ . The intermediate postulated by Manassen and Klein has partial covalent bonding to the solvating water molecules;<sup>6</sup> it has essentially the same structure as transition state **3**.<sup>3</sup>

The reported ratio  $k_{rac}/k_{exch} = 2.0$  for 2-butanol is difficult to reconcile with the significant fraction of the reaction that proceeds through 2-butene with a ratio  $k_{rac}/k_{exch} = 1.0$ . Formation of 2-butene was observed by Manassen and Klein and accounts for a rapid initial decrease in the total concentration of 2-butanol;<sup>6</sup> it is also required by the observed incorporation of solvent hydrogen in the present and earlier<sup>6</sup> work. Formation of 2-butene gives loss of optical activity whether or not it escapes from the reaction mixture. Hydride transfer is also likely to give oxygen exchange with  $k_{rac}/k_{exch} < 2.0$ . Further work is needed to clarify the relationship of these rate constants. A plot of the reported values<sup>19</sup> of  $\log k$  for racemization and exchange against  $H_0$  appears to be consistent with values of  $k_{rac}/k_{exch}$  in the range 1.8–2.0, and a ratio

$k_{rac}/k_{exch} = 1.8$  has been reported at higher acid concentrations.<sup>20</sup>

Herlihy's ratio  $k_{rac}/k_{exch} = 2.0$  is consistent with concerted substitution with inversion because this reaction does not involve significant elimination.<sup>7</sup> Herlihy has also found the same product ratios in the acid-catalyzed reactions of 1,2-propanediol and prop-2-en-1-ol, based on measured rates of racemization and rearrangement to propanal for propanediol and of product disappearance and 1,2-propanediol formation for prop-2-en-1-ol.<sup>7,8</sup> This result is consistent with reaction through a common intermediate from both reactants,<sup>8</sup> however, it is also consistent with concerted reactions of the two compounds through several different carbocation-like transition states of comparable energy that give the observed product ratios.

Measurements of oxygen exchange and elimination of 2-methyl-2-propanol have shown a considerably smaller ratio of deprotonation to hydration, with  $k_2/k_4 = 0.035$ ,<sup>21</sup> than for 2-butanol, and protonation of 2-methylbut-1-ene and 2-methylbut-2-ene gives alcohol with no measurable deprotonation to the isomeric olefin in aqueous solution.<sup>22</sup> In contrast, tertiary substrates generally give more elimination than secondary substrates upon solvolysis in aqueous-organic solvents.<sup>23</sup> It was this difference that lead Manassen and Klein to suggest that the reactions of secondary substrates and tertiary substrates in water do not proceed through ordinary carbocation intermediates, which would be expected to give similar product ratios for oxygen exchange and for solvolysis, but that 2-butanol reacts through the symmetrical intermediate **3**, which resembles the transition state for bimolecular substitution.<sup>6</sup> An alternative hypothesis is that **3** is a transition state for concerted bimolecular substitution and that there is no common carbocation intermediate.

## Conclusion

The formation of a common carbocation intermediate in the acid-catalyzed reactions of 2-butanol and 2-butene in water is inconsistent with the following.

(1) A common intermediate must partition in the same way to products, but 1-butene and 2-butanol give different ratios of deprotonation and water addition if the same fraction of hydride transfer occurs in the two reactions. (2) Different ratios of *cis/trans*-2-butene are formed from 1-butene and 2-butanol.

It does not appear likely that the different product ratios can be accounted for by different rotational or solvational states of a carbocation intermediate that has a short but significant lifetime. Both reactions occur in the same homogeneous medium, and a reactive intermediate would be surrounded by water; it is likely that the developing positive charge of a cationic intermediate would orient the water dipole into a favorable position for reaction.

We conclude that these reactions do not occur through an intermediate with a significant lifetime in a stepwise reaction mechanism. They must, therefore, occur largely or entirely by parallel concerted mechanisms through transition states that have a large amount of carbocation character and similar Gibbs energies.

If there is no carbocation intermediate in the acid-catalyzed reactions of 2-butanol and 1-butene, it is unlikely that a carbocation exists in the reaction of 1,2-propanediol, which contains more electron-withdrawing substituents.

We do not know if the reactions involve "coupled" or "uncoupled" concerted mechanisms.<sup>24</sup> If they are coupled, the attacking water molecule provides significant nucleophilic assistance and stabilization of the transition state by attacking carbon or hydrogen. If they are uncoupled, there is no such assistance; nucleophilic attack by water occurs further along the reaction coordinate than dehydration or protonation but without a significant additional barrier or a separate reaction step.

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Substitution at simple secondary carbon centers is known to be subject to nucleophilic assistance, and the rate constants for reactions of 1-(4-nitrophenyl)-2-propyl tosylate, iodide, and bromide with solvent components fall on the same Swain-Scott plots as those for reagents that react by second-order nucleophilic substitution.<sup>4</sup> This suggests that oxygen exchange occurs through a coupled concerted mechanism, as suggested for other leaving groups in secondary systems.<sup>3</sup> On the other hand, the absence of a large difference in the ratio of hydride transfer to solvent attack for the protonation of 1-butene in water and 1-hexene in trifluoroacetic acid<sup>13</sup> suggests that there is little nucleophilic assistance for solvent attack in this reaction, so that the 1,2-addition may be uncoupled concerted. It is likely that the solvent is directly involved in proton transfer to and from carbon.

The appearance of the transition state, as indicated by structure-reactivity correlations, isotope effects, and other characteristics, is often used to diagnose the nature of reaction mechanisms. However, the appearance of the transition state does not distinguish between a two-step mechanism and a concerted, one-step mechanism with a transition state that resembles the presumed intermediate. As pointed out by Hammett, different

reactions with similar, carbocation-like transition states can actually occur through parallel pathways of similar energy.<sup>25</sup> The similar response of these different reactions to changing substituents, solvent, temperature, and other variables does not prove that the reactions proceed through a common intermediate; it only shows that the transition states have similar structures.

Reactions that proceed through carbocation intermediates have carbocation-like transition states, and there is a strong tendency in the literature to fit experimental data to the paradigm that reactions with carbocation-like transition states proceed through carbocation intermediates. We suggest that it is time to reject this paradigm and that the conclusion that a reaction proceeds by an S<sub>N</sub>1 (or D<sub>N</sub> + A<sub>N</sub> or D<sub>N</sub>\*A<sub>N</sub>)<sup>2</sup> mechanism should be based on evidence that a carbocation is formed as an intermediate in the reaction.

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## Solvolysis of Benzyl Azoxytosylate and the Effect of Added Bases and Nucleophiles in Aqueous Trifluoroethanol and Aqueous Acetonitrile

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**Abstract:** The rates and products of reaction of benzyl azoxytosylate (**1b**) in 1:1 (v/v) aqueous trifluoroethanol containing sodium perchlorate, sodium thiocyanate, sodium iodide, sodium bromide, sodium chloride, sodium hydroxide, sodium acetate, perchloric acid, and imidazole (buffered and unbuffered) have been measured at 42 °C as part of an investigation into its mechanism of solvolysis. Nonbasic solutes give only small rate effects (some rate enhancing, others rate retarding), but, if nucleophilic, they lead to substitution products—the classic evidence of an S<sub>N</sub>1 reaction mechanism. After the initial rate-determining fragmentation, about half of the total solvolytic reaction proceeds through an electrophilic benzylic intermediate which is sufficiently long-lived to be trapped by nucleophilic solutes such as thiocyanate and the halide anions to give benzyl thiocyanate and benzyl halides. The other half gives the solvent-derived products benzyl alcohol and benzyl trifluoroethyl ether by a route which is not affected by dilute nonbasic solutes. Sodium acetate, which leads to negligible formation of benzyl acetate, and imidazole lead to the formation of trifluoroethyl tosylate; imidazole also produces *N*-tosylimidazole. These two base-induced bimolecular reactions involve nucleophilic attack at the sulfur of the tosyl group and involve electronic polarization of **1b** in the opposite sense from that in the unimolecular fragmentation. One of the minor products in the presence of bases from the trappable intermediate of the solvolysis reaction is benzaldehyde, which suggests that the intermediate is C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>ON<sub>2</sub><sup>+</sup>, a new type of reactive electrophile. It is not yet certain whether the half of the unimolecular fragmentation reaction which does not proceed through the trappable intermediate involves another electrophilic intermediate which is simply too short-lived to be intercepted by dilute nucleophiles or whether about half of the initial fragmentation is followed by a concerted uncoupled capture of the nascent benzyl cation by solvent. Replacing a small proportion of the trifluoroethanol in the reaction medium by the more nucleophilic ethanol does not have a drastic effect upon the overall course of the reaction, and a very similar mechanism also appears to be operative in aqueous acetonitrile.

Alkyl azoxytosylates (**1**) have been known for many years,<sup>1,2</sup> but only recently have they been recognized as solvolytic substrates.<sup>3</sup> Structurally, these compounds relate both to alkyl tosylates (**2**) and to diazo compounds that intervene as intermediates in solvolytic deamination reactions.<sup>3-5</sup> We have already described an investigation into the mechanism of solvolysis of

2-adamantyl azoxytosylate (**1a**).<sup>3,5</sup> The results were interpreted in terms of a rate-determining fragmentation followed by nu-

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