

Rates of the Acid-Catalyzed Interconversions among Propylene and the Propyl Alcohols by N.m.r. Anti-Markovnikov vs. Normal Propylene Protonation¹

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A direct estimation of the comparative rates for anti-Markovnikov and Markovnikov hydration of propylene in D₂SO₄-D₂O has been made from a study of the rate of disappearance of the tertiary isopropyl alcohol proton by n.m.r. The rate constant ratio $k_{AM}/k_M < 4 \times 10^{-4}$ for the reactions at 60° in ~55% D₂SO₄ by weight; its central measure estimate is 4×10^{-5} . Predictions of this ratio based upon hyperconjugative models and upon the linear free energy equation for olefin undergoing rate-determining protonation are both encompassed by the range of experimental values obtained. The experiment also yielded information on the rate of exchange of protons from the isopropyl alcohol methyl groups which could be interpreted in terms of the dehydration of this alcohol. The rate of dehydration, the β -secondary isotope effect upon dehydration, i.e., the effect of D vs. H in the methyl groups, and the primary isotope effect in the loss of D or H from carbonium ion-like intermediates could all be extracted from the exchange kinetic data. These are all found to be consistent with an olefin-alcohol interconversion mechanism having a reactive intermediate and/or a transition state with considerable carbonium ion character.

Introduction

In a recent publication² theoretical considerations were made of the possible effects of hyperconjugation (HCJ) on the rates of reactions involving carbonium ion-like transition states. The acid-catalyzed hydration reactions of olefins to produce alcohols were chosen as typical cases. It was argued that despite certain controversial details concerning the nature of pretransition state intermediates,³ the transition states are most probably hydrated alkyl carbonium ions formed by σ -complex protonation of the reactant olefins. Computation of the LCAO-MO electronic energy differences between the olefins and carbonium ions, coupled with the assumed proportionality of the latter to free energies of activation, produced a number of interesting results.

Among these were theoretical affirmation of the Markovnikov and Saytzev-Wagner rules for polar additions to olefins, consistency of the Baker-Nathan order in terms of electron release by HCJ, and the approximate additivity of C-H and C-C bond effects to the electronic energies and, hence, to the free energies of activation. All these results are of a qualitative or semiquantitative nature and were derived from models

which assume HCJ as the sole electronic effect exercised by the substituent alkyl groups.

Results of a more quantitative nature were also obtained. Included principally among these were theoretical estimations of quantities corresponding to the Taft h_H/h_C hyperconjugation ratios⁴ and the prediction that anti-Markovnikov protonation of an unsymmetrical olefin would be less favorable energetically than protonation of the corresponding olefin not bearing the asymmetry-causing alkyl group.⁵ Theoretical values of 1.3 were obtained for h_H/h_C for the olefin hydration systems, identical with the theoretical values computed for aromatic molecule protonation reactions, i.e., for alkylbenzene-alkylbenzenium ion equilibria. In contrast, Taft and Lewis have found values of ~2 for a few olefin and olefin-like molecule reactions, vs. ~1.3 for a large variety of reactions involving alkyl-substituted aromatics. At the same time, the relative rate predictions for anti-Markovnikov additions seem, intuitively, to be underestimated by the HCJ models.

Both discrepancies, it was suggested, likely reside in the choice of inductive and resonance effects postulated to stabilize the carbonium ions relative to the reactant states. In order to test directly the anti-Markovnikov addition rate prediction, a scheme for actual measurement of this rate for propylene was devised. How much of an effect due to induction (I) must be added to the estimated HCJ to reproduce this rate was the question of paramount interest. By the same token, this rate could then, hopefully, be used to test the linear free energy equation separation of I and HCJ effects, and thereby indirectly to reexamine whether the h_H/h_C values derived by theoretical and empirical means are truly at variance with each other.

The experimental scheme by which the rate of anti-Markovnikov addition to propylene was examined allowed, as a bonus, estimations of various rates and deuterium isotope effects for steps in the more rapidly occurring alcohol dehydration and normal (Markovnikov) addition to olefin sequences. Presentation of these results and some discussion of their significance will also be included.

Reaction Processes and Kinetics

Isopropyl alcohol dissolved in an aqueous acid medium undergoes slow dehydration to form propylene, which upon normal proton addition rehydrates to isopropyl alcohol. While most of the olefin is re-

(1) Research performed under the auspices of the U. S. Atomic Energy Commission.

(2) S. Ehrenson, *J. Am. Chem. Soc.*, **86**, 847 (1964).

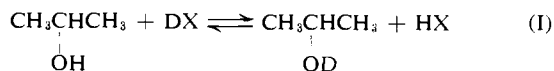
(3) Cf. R. H. Boyd, R. W. Taft, Jr., A. P. Wolf, and D. Christman, *ibid.*, **82**, 4729 (1960).

(4) R. W. Taft, Jr., and I. C. Lewis, *Tetrahedron*, **5**, 210 (1959).

(5) Viz., the reaction, $\text{CH}_3\text{CH}=\text{CH}_2 \xrightarrow{\text{H}^+, \text{H}_2\text{O}} \text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ is predicted to be 2 to 5 kcal./mole less favorable (in ΔF^\ddagger) than the reaction $\text{CH}_2=\text{CH}_2 \rightarrow \text{CH}_3\text{CH}_2\text{OH}$ under the same conditions.

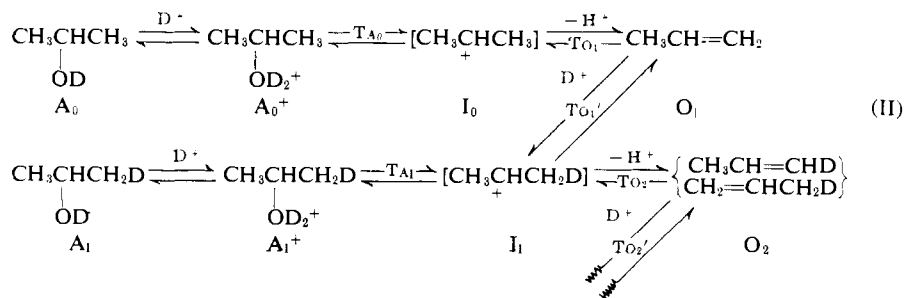
turned to alcohol by this path, some small fraction undergoes abnormal (anti-Markovnikov) protonation to yield *n*-propyl alcohol.

If a deuteronic rather than a protonic medium is employed, *e.g.*, a D₂SO₄-D₂O mixture, three types of D-H exchange occur, two of which are useful in following the alcohol-olefin interconversions. First, most rapid, and not pertinent to the interconversions is



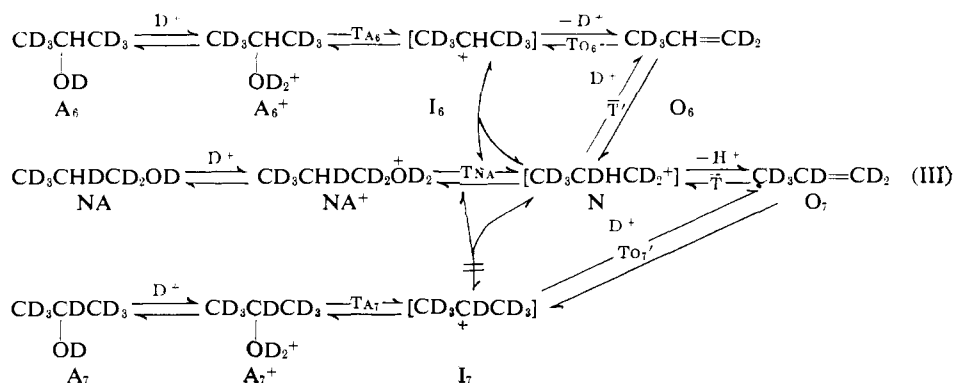
Here, X represents all medium species bearing available deuterium.

The isopropyl alcohol methyl hydrogens will also exchange but much more slowly



Represented in reaction II are the first isopropyl alcohol dehydration and subsequent propylene rehydration steps which, assuming an infinite available [D]/[H] ratio, will eventually lead to complete exchange of the methyl protons. Transition states are symbolized by T in breached arrows; the subscripts on T indicate the variously deuterated alcohols and olefins undergoing interconversion. The transition states representing deuteration, as opposed to protonation, of the olefin are further distinguished by a prime on T. The bracketed species are isopropylcarbonium ions, which are assumed, for convenience here and consistency with the theoretical models of ref. 3, to be reactive intermediates.

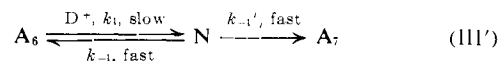
Finally, and even more slowly, the tertiary hydrogen is expected to undergo exchange



Here we have assumed that the anti-Markovnikov process is so slow that all methyl hydrogens have undergone prior exchange. This assumption will subsequently be shown to be justified. $\bar{\text{T}}'$ represents a transition state for anti-Markovnikov deuteration of the olefin CD₃CH=CD₂. (Not shown in this scheme is the abnormal deuteration of O₇ to yield perdeuterio-*n*-propyl alcohol. As will soon become apparent,

this step, similar to the conversion of O₆ to N, is extraneous to the reaction system as observed.)

1. *Kinetics for Anti-Markovnikov Addition.* Reaction III may be simplified, in the essential absence of [H⁺] which precludes the abnormal addition to O₇, to



The slow step with rate constant k_1 is a composite of a dehydration and the abnormal deuteration step: the former is reversible and rapid compared with the latter. Therefore, k_1 is equal to k_{AM} , the rate constant for the latter addition, times the equilibrium constant, K , between the alcohol A₆ and the olefin O₆. As detailed in III, k_{AM} is really the rate constant for abnormal

addition of D⁺ to O₆ to form N directly, plus the product of the rate constant for 1,2-shift of D⁺ in I₆ to form N and the equilibrium constant between O₆ and I₆ (assuming that I₆ really exists as an intermediate). The *n*-propyl-type carbonium ion, N, formed by this process then undergoes rehydration, presumably mainly by relatively rapid intramolecular proton or deuterium shift to the isopropyl ion isomers, I₆ or I₇, followed by fast addition of D₂O.⁶

Therefore

$$-\frac{d[\text{A}_6]}{dt} = k_1[\text{A}_6] - k_{-1}[\text{N}] \quad (1)$$

$$-\frac{d[\text{N}]}{dt} = -k_1[\text{A}_6] + (k_{-1} + k_{-1}')[\text{N}] \quad (2)$$

which, under the steady-state assumption for the re-

(6) V. Gold and R. S. Satchell, *J. Chem. Soc.*, 1938 (1963), argue convincingly for this intramolecular (really intramolecular) shift from rate studies on the conversion of *n*- to isopropyl alcohol. However, whether or not this is the primary mechanism for conversion does not affect the kinetics of interest here. It should be noted as well that the curved arrow from N to I₇, representing this type of shift for hydrogen, is broken, indicating an intermediate rapid exchange of this hydrogen for deuterium once it is on the methyl group.

active intermediate, N, recalling that $k_1 = k_{AM}K$ and upon combination, yields

$$\ln ([A_6]_0/[A_6]) = (k_{AM}kKk_{-1}'/(k_{-1} + k_{-1}'))t \quad (3)$$

If we now designate the ratio k_{-1}/k_{-1}' as i_R , the isotope effect for the interionic shift of D vs. H, and take K in terms of its constituent rate constants, k_{dehyd}/k_M for the isopropyl alcohol-propylene interconversion, then

$$k_{AM}/k_M = 2.303(1 + i_R)S_{AM}/k_{Dehyd} \quad (4)$$

where S_{AM} is the slope of the linear plot of $\log ([A_6]_0/[A_6])$ vs. time. The rate constant, k_M , is, of course, for normal deuteration of O_6 .

Equation 3 is derived under the assumption that the $[H]/[D]$ ratio in the solvent medium is infinitesimal. Since in the present experiments prior exchange of the methyl protons has occurred, this assumption is not correct. If one allows for abnormal protonation of O_6 and reconversion of A_7 by protonation, correction terms to eq. 3 for small $[H]/[D]$ values are obtained

$$\ln ([A_6]_0/[A_6]) = k_0t/(1 + \gamma'[C]) + \frac{i_R(\gamma'[C])^2}{(1 + i_R)} \left\{ \left(\frac{k_0t}{1 + i_R} \right)^2 + \left(\frac{k_0t}{1 + i_R} \right)^3 + \dots \right\} \quad (5)$$

Here, k_0 is $k_{AM}K/(1 + i_R)$, which is the same t coefficient as in eq. 3. The term $\gamma'[C]$ corrects for abnormal protonation: γ' , the isotope effect (k_H/k_D) times a thermodynamic term which expresses the availability of H^+ vs. D^+ from a mixed H-D medium, is for the rate of appearance of $CD_3CH_2CD_2^+$ vs. $CD_3CHDCD_2^+$ from O_6 , which should be equal to the effect for formation of $CD_3CHDCD_2^+$ vs. $CD_3CD_2CD_2^+$ from O_7 .^{7,8} $[C]$ is the ratio of available protium to deuterium in the medium. Since, however, both $\gamma'[C]$ and (k_0t) are always much smaller than unity in the experiments to be described, the correction term in curly brackets is ignored. Therefore

$$k_{AM}/k_M = 2.303(1 + i_R)(1 + \gamma'[C])S_{AM}/k_{Dehyd} \quad (6)$$

The kinetic expression of interest is therefore pseudo-first order in tertiary isopropyl alcohol hydrogen at a given medium acid concentration and requires no further comment at this time.

2. *Kinetics for Methyl Hydrogen Exchange.* From reaction II with neglect for the moment of the return reactions catalyzed by protium, the following kinetic expressions apply (eq. 7)

(7) V. Gold and M. A. Kessick, *Pure Appl. Chem.*, **8**, 421 (1964) have obtained a value for γ (3.9 ± 0.5) for the normal hydration reaction of isobutene. We thank Professor Gold for communication of this value prior to publication. We here assume that the same value within the quoted uncertainty applies to both normal and abnormal hydration of propylene.

(8) For the purpose of making this correction, we have assumed all N is formed by direct abnormal deuteration of O_6 . Abnormal protonation of O_6 completely precludes formation of N. On the other hand, if N is also formed by interionic shift, normal protonation of O_6 to I_8 may be followed by interionic shift to form an n -propyl ion which can quickly convert to N. Therefore, to the extent the interionic shift path contributes, the correction factor must be decreased. We here choose the maximum correction, consistent with our attempt to estimate an upper limit for k_{AM}/k_M .

$$\left. \begin{aligned} -\frac{d[A_0]}{dt} &= k[A_0] \\ -\frac{d[A_1]}{dt} &= -k[A_0] + k\beta[A_1]\left(\frac{5X}{5X+1}\right) \\ -\frac{d[A_2]}{dt} &= -k\beta[A_1]\left(\frac{5X}{5X+1}\right) + k\beta^2[A_2]\left(\frac{4X}{4X+2}\right) \\ &\vdots \\ -\frac{d[A_3]}{dt} &= -k\beta^4[A_4]\left(\frac{2X}{2X+4}\right) + k\beta^5[A_5]\left(\frac{X}{X+5}\right) \end{aligned} \right\} \quad (7)$$

Implicit in these equations is the understanding that the rate of dehydration of isopropyl alcohol is much slower than the corresponding rate of propylene hydration at the acid concentration of interest.⁹ The rate constant, k , here refers to the dehydration of the alcohol with six methyl hydrogens,¹⁰ β is the β -secondary isotope effect per deuterium atom, and X is the primary isotope effect for loss of a methyl hydrogen rather than deuterium from the carbonium ion. If deuterium is lost from these ions, the over-all exchange process is, in essence, reversed.

To be completely precise, X is a mixed primary and secondary effect. The primary effect is accompanied by a secondary α -deuterium effect, *i.e.*, a rate decrease is to be expected when D is substituted for H on the carbon atom from which a group (here a proton or deuteron) is removed. This effect usually amounts to $\sim 15\%$,¹¹ which if applicable here would require X to vary with extent of reaction. However, we expect a much smaller effect in the cases of present interest because of little progress in C-H rupture at the transition state for dehydration (*vide infra*). The rates of removal of H or D from carbon bearing a stationary D will be diminished, to a good approximation,¹² by equal factors so as to cancel the α -effect in X . Furthermore, in certain species, *e.g.*, A_1 where loss of H from the CH_3 group is expected to proceed at a faster rate than from the CH_2D group, the α -effect is further washed out since we view only the average rate of exchange for these molecules. Therefore, the parenthesized functions of X , where the integers are statistical factors, are much less affected by the second-

(9) R. R. Beishline, Ph.D. Thesis, Pennsylvania State University, 1962, pp. 44, 77, reports $K([i\text{-PrOH}]/P_{olefin}) = 3.2 M^{-1} \text{ atm}^{-1}$ or $K([i\text{-PrOH}]/[olefin]) > 300$, as long as h , the distribution coefficient of olefin between the solution and gas phases, is less than 10^{-3} , which is almost certainly the case.

(10) We may precisely identify the rate of deuterium exchange in the alcohol with its dehydration rate as long as only one H-D exchange occurs per dehydration. This appears to be the case here; under the very similar reaction conditions, 53% perchloric acid at 60°, Beishline (ref. 9, p. 74) was able to find no deuterium incorporation in propylene after approximately one half-life for propylene hydration in a medium 0.452 mole fraction of D. We conclude from a kinetic analysis of his system that less than 10% extra D can be introduced per dehydration in the present case. This result is to be contrasted with that obtained by J. Manassen and F. S. Klein, *J. Chem. Soc.*, 4203 (1960), for n -butenes under very different conditions (0.55 N $HClO_4$ at 100°) where it appears that roughly three deuterium exchanges occur per two alcohol dehydrations.

(11) S. Seltzer, *J. Am. Chem. Soc.*, **83**, 2625 (1961).

(12) J. Bigeleisen, *J. Chem. Phys.*, **23**, 2264 (1955).

dary effects than X itself. The α -effects were ignored for these reasons.

The rate expression for total methyl hydrogen concentration is, then

$$-\frac{d\tau_H}{dt} = -\sum_{j=0}^5 (6-j) \frac{d[A_j]}{dt} = \quad (8)$$

$$k \sum_{j=0}^5 \beta^j \left\{ \frac{(6-j)X}{(6-j)X+j} \right\} [A_j] \quad (9)$$

Upon integration, most easily accomplished by successively integrating eq. 7, one finds

$$(\tau_H/\tau_{H_0}) = \frac{1}{6_j} \sum_{j=0}^5 \left\{ (6-j) \beta^{j(j-1)/2} p_j^{-1} \times \prod_{l=0}^j p_l \sum_{m=0}^j \frac{\exp(-\beta^l p_l k t)}{\prod_{m=0}^j (p_m \beta^m - p_l \beta^l)} \right\} \quad (10)$$

Here, $p_j = (6-j)X/[(6-j)X+j]$, and the prime on the denominator product term indicates $m \neq l$.

Allowing for return reactions, in the presence of H^+ , eq. 7 may be reformulated as

$$\begin{aligned} -\frac{d[A_0]}{dt} &= kd_0[A_0] - k\beta h_0 \left(\frac{1}{5X+1} \right) [A_1] \\ -\frac{d[A_1]}{dt} &= -kd_1[A_1] + k\beta h_1 \left(\frac{1}{5X+1} \right) [A_1] + \\ &\quad k\beta d_1 \left(\frac{5X}{5X+1} \right) [A_1] - k\beta^2 h_1 \left(\frac{2}{4X+2} \right) [A_2] \\ &\quad \vdots \\ -\frac{d[A_5]}{dt} &= -k\beta^4 d_4 \left(\frac{2X}{2X+4} \right) [A_4] + \\ &\quad k\beta^3 h_4 \left(\frac{5}{5X+1} \right) [A_5] + k\beta^5 d_5 \left(\frac{X}{X+5} \right) [A_5] - \\ &\quad k\beta^6 h_5 [A_6] \quad (11) \end{aligned}$$

All symbols with the exception of d_j and h_j have previously been defined. The latter are

$$d_j = \frac{k_{D_i}[D^+]}{k_{D_i}[D^+] + k_{D_i}[H^+]} \quad (12a)$$

and

$$h_j = \frac{k_{H_i}[H^+]}{k_{D_i}[D^+] + k_{H_i}[H^+]} \quad (12b)$$

where k_{D_i} and k_{H_i} are respectively the rates of formation of the appropriate isopropylcarbonium ions upon deuteration and protonation of olefin, O_{j+1} . These terms may be rewritten for convenience as, recalling the convention adopted in formulating eq. 5 and 6

$$d_j = (1 + \gamma_j[C])^{-1} \quad (13a)$$

and

$$h_j = \gamma_j[C](1 + \gamma_j[C])^{-1} \quad (13b)$$

[C] is again the ratio of available protium and deuterium in the solvent and γ_j is k_{H_i}/k_{D_i} times the thermodynamic term for availability of H^+ vs. D^+ . Assuming that γ_j is to a very good approximation independent of j (i.e., that the k ratio for proton vs. deuterium addi-

tion to olefin is not changed by change in the relative protium-deuterium content of the olefin), even though the constituent k values themselves doubtlessly are, then

$$-\frac{d\tau_H}{dt} = k \sum_{j=0}^5 \beta^j \left\{ \frac{(6-j)Xd - jh}{(6-j)X+j} \right\} [A_j] = \quad (14)$$

$$k \sum_{j=0}^5 \beta^j \left\{ \frac{(6-j)X - j\gamma[C]}{(1 + \gamma[C])(6-j)X+j} \right\} [A_j] - k\beta^6 \left(\frac{\gamma[C]}{1 + \gamma[C]} \right) [A_6] \quad (15)$$

In reaction media where [C] is very small, the last term of eq. 15 will be unimportant until the exchange reaction approaches completion. If this term is ignored, the identity of form of eq. 9 and 15 is apparent, where p_j is now $[(6-j)X - j\gamma[C]]/[(1 - \gamma[C])(6-j)X + j]$. The fact that p_j is now time dependent *via* the time dependence of [C], through formation of H and depletion of D as the exchange progresses, provides no difficulty. [H]/[D] values are easily computed at any time from knowledge of the initial concentrations of these species and from the measured value τ_H .

$$\begin{aligned} [H] &= [H]_0 + 6[i\text{-PrOH}]_0(\tau_{H_0} - \tau_H)/\tau_H \\ [D] &= [D]_0 - 6[i\text{-PrOH}]_0(\tau_{H_0} - \tau_H)/\tau_H \quad (16) \end{aligned}$$

Included in $[H]_0$ are contributions both from the solvent and from the readily exchanged alcohol hydroxyl proton; because of the approximate linearity of τ_H vs. t , *vide infra*, the value of [H] entered in the integrated equation was the average of $[H]_t$ and $[H]_0$.

It is therefore possible to determine statistically, at least in principle, all the reaction parameters in this exchange, k , β , X , and γ from measured values of τ_H as a function of time by the nonlinear, least-squares fit of these data to eq. 10 as modified in eq. 15. In practice, a slightly less demanding procedure could be followed. The value of γ for the related and substantially similar hydration reaction of isobutene⁷ was adopted. With a good estimate of k , obtained from the instantaneous slope of eq. 10 by a zero-limit expansion, *i.e.*

$$\tau_H/\tau_{H_0} = (6 - ktd)/6 \quad (17)$$

and a fair guess of β , the best values of k and β could be computed for specified X values. Repetition of the fitting accompanying ordered removal of points, starting with the last, was carried out to ensure that the term ignored in eq. 15 would not materially affect the final parameter results. [Note well, this should be a reasonably sensitive test since $[A_6]$ varies roughly as $(\Delta\tau_H/\tau_{H_0})^6$.] Best values of k , β , and X could then be readily obtained from the grids of k , β , and goodness-of-fit over the grid variables X and the number of data points. Several further details of the procedure are to be found in the Appendix.

Experimental

Reagents. Baker reagent grade 2-propanol, Matheson Spectrograde dioxane, and D_2O from the Savannah River Plant were used. D_2SO_4 was prepared by refluxing previously distilled SO_2Cl_2 with a little more than 2 equiv. of D_2O until a single phase was obtained.¹³

(13) J. H. Freeman and C. E. C. Richards, Report AERE GP/R, 2479, 1958.

The sulfuric acid was then boiled until a negative test for Cl^- resulted. The solution was diluted with D_2O to about 55% and then titrated to get the actual weight per cent of the acid.

Kinetic Measurements. Kinetic experiments were carried out by measuring the integrated areas of the methyl and tertiary proton n.m.r. peaks vs. the proton peaks of dioxane as an internal standard, all as a function of time using a Varian A-60 spectrometer. A premixed solution of known weights of isopropyl alcohol and dioxane in a known weight of 57.2% sulfuric acid- d_2 - D_2O solution was pipetted into an n.m.r. tube (0.5-mm. wall) and sealed off after the solution was completely degassed under high vacuum. All tubes were inserted in blackened polyethylene for protection against light and placed in a 60° thermostated bath. At appropriate times, the tubes were withdrawn from the bath, cooled under running tap water, and their integrated spectra were taken. In a preliminary run involving exchange in the methyl group and in runs A and B, concerned with exchange of the tertiary hydrogen, the spectra were recorded at about 27°. In run C where the quantitative results for methyl hydrogen exchange were obtained, the tube was maintained at 10° to preclude exchange during measurement. Each kinetic point was integrated in each direction consecutively for a total of 16 times; the average values and deviations were obtained in the usual manner.

Initial integrations of methyl vs. dioxane protons agreed well with the relative concentrations from the known weights of isopropyl alcohol and dioxane added; the ratio of tertiary proton to dioxane, however, was smaller than the true concentration. This was suspected to be due to the large difference in peak widths between the split tertiary proton and sharp dioxane peaks.¹⁴ After substantial exchange in the methyl groups, it was noticed that the ratio of tertiary proton to dioxane proton peak areas was different for scanning in the two directions. It appeared that the relaxation time for the tertiary proton had increased and, therefore, 2.5 min. was allowed between sweeps. The various spectrometer controls were set as follows: radiofrequency field, 1.2 mgauss; filter bandwidth, 1.0; integral amplitude, 80; sweep time, 25 sec. The spectrum amplitude varied during the course of the run; it was always chosen so that the sum of the two integrals, dioxane and methyl or dioxane and tertiary proton, was ~ 0.75 the vertical height of the chart.

Sample Composition. Runs A and B were conducted with samples 0.386 *M* in isopropyl alcohol and 0.066 *M* in dioxane which were 56.2% D_2SO_4 by weight. The acid medium had essentially no protium prior to addition of the organic compounds since freshly prepared acid was employed. In run C, a sample 0.486 *M* in isopropyl alcohol and 0.177 *M* in dioxane which was 54.9% D_2SO_4 by weight was used. This sample was determined by n.m.r. to be 2.7 *N* in free protium immediately after mixing, of which 2.2 *N* was assumed due to hygroscopic water contamination of the original acid sample, stored for 3 months in the cold but not under rigid desiccation. For comparison this sample was 81.4 *N* in total deuterium.

(14) Cf. J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 77.

Product Studies. After about 3400 hr. at 60°, a tube containing sample D, [*i*-PrOH] ~ 0.2 *M*, [dioxane] ~ 0.04 *M* in $\sim 57\%$ D_2SO_4 , was opened and some isopropyl ether was added. The n.m.r. spectrum showed the center of the septet of the tertiary protons of isopropyl ether to be displaced ~ 16 c.p.s. upfield from the center of the broad tertiary proton peak of exchanged isopropyl alcohol.

The n.m.r. tube with contents was cooled in ice and slowly neutralized with ~ 10 *N* NaOH. The aqueous phase was extracted with 1 ml. of isopropyl ether and the organic phase was dried over Na_2SO_4 overnight. The organic solution was vapor phase chromatographed on a dibenzyl ether column at 77°, He = 15 p.s.i., in a Perkin-Elmer vapor fractometer. The ether appeared 4.1 min. after the air peak, followed by the isopropyl alcohol peak (9.2 min. after air). In a known mixture of 10 ml. of isopropyl ether and 5 drops of isopropyl alcohol, the elution times after air were ether, 4.1 min. and alcohol, 8.9 min. In another experiment, the tube containing sample B was opened after ~ 3000 hr. at 60° and neutralized by NaOH as above. The precipitated Na_2SO_4 was washed twice with water so that the total aqueous fraction was ~ 6 ml. The organic materials were extracted from this aqueous solution with 1 ml. of diethyl ether and dried with Na_2SO_4 for 1 hr. This fraction was also chromatographed on a dibenzyl ether column to give two peaks with areas in the approximate ratio of 4:1 at 8.9 and 38.8 min., respectively. The first is undoubtedly isopropyl alcohol and the second is probably dioxane.

Results and Discussion

Figure 1 presents the results obtained from runs A and B where both the rates of disappearance of the methyl and tertiary isopropyl alcohol hydrogens were followed. At the left, with the scale given on the left ordinate, are the fractions of methyl hydrogen remaining in the alcohol as a function of time. The curve constructed for these points is sight drawn. The much more rapid exchange of these hydrogens than those in the tertiary position, recorded in the main body of the plot, is quite striking. The latter are displayed exactly as read in the experiment, *i.e.*, as the ratios of integrated tertiary isopropyl alcohol to dioxane proton peak areas. The ordinate on the right of Figure 1 is scaled directly for these ratios, and the flags indicate the experimental average deviations for each point from the 16 determinations made per point.

At 60°, with alcohol 0.386 *M* and in the presence of 56% by weight D_2SO_4 in D_2O , which constitute optimum conditions for observing the abnormal addition,¹⁵ it is apparent that less than 5% of the tertiary alcohol protons have exchanged in 7 months. In contrast, just about complete methyl hydrogen exchange occurred in less than 1 month.

Table I contains the parameter values obtained by least-squares analysis of the $[\text{A}_t]/[\text{dioxane}]$ data fitted to eq. 5, truncated as explained, and with these results

(15) These were judged to be optimum conditions from two points of view. The first concerned achievement of the most rapid rates of interconversion without promoting side reactions as noted by Gold and Satchell⁹ at 100° in 8 *M* HClO_4 . The other related to the availability of complementary data on the system, *i.e.*, even though the rate of dehydration of isopropyl alcohol was to be measured here, *vide infra*, the value for $\text{H}_2\text{O}-\text{H}_2\text{SO}_4$ media at this temperature was of interest for basic comparisons.

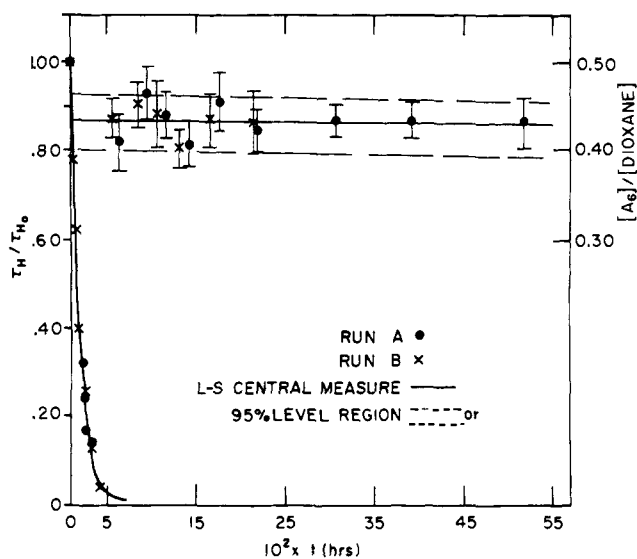


Figure 1. Exchange of isopropyl alcohol methyl protons (left ordinate) and tertiary proton (right ordinate) as functions of time in 56.2% D_2SO_4 - D_2O at 60°.

employed in eq. 6. Considerably more quantitative estimates of just how slow anti-Markovnikov addition is compared to the normal process may now be drawn from these results.

Table I. Rate Data and Statistics for the Anti-Markovnikov Hydration of Propylene in 56.2% D_2SO_4 at 60°

Statistical measure	Weighting procedure ^a			
	[Av. dev.] ⁻¹		[Av. dev.] ⁻²	
$10^6 S_{AM}$ (hr. ⁻¹)	0.50		0.21	
Std. dev., δ				
$10^6 \delta$ (S_{AM})	1.73		2.67	
(Points) ^b	0.016		0.015	
$([A_6]/[dioxane])_0$	0.432		0.431	
Isotope effect, $i_R =$	$1/2$	$1/4$	$1/2$	$1/4$
$10^4 k_{AM}/k_M^c$				
Central measure	0.34	0.28	0.14	0.12
95% confidence level maximum	2.68	2.23	3.76	3.13

^a Each point weighted as reciprocal of its average deviation or square of average deviation obtained from 16 measurements to get each point. ^b In log units. ^c With $\gamma[C] = 1/9$ and $k_{dehyd} = 6.6 \times 10^{-3}$ hr.⁻¹ (0.975)⁶ for $CD_3CHODCD_3$ in D_2SO_4 - D_2O as determined below. Compare 3.36×10^{-2} hr.⁻¹ extrapolated from H_2SO_4 - H_2O value for $CH_3CHOHCH_3$ at 60° in 54.8% H_2SO_4 - H_2O by assuming same rate dependence as in $HClO_4$ - H_2O (see ref. 9).

To the 95% confidence level, *i.e.*, allowing two standard deviations from the central measure, $k_{AM} < 4 \times 10^{-4} k_M$, essentially independent of the choice of i_R ¹⁶ and whether the measured points are weighted as the reciprocals or reciprocals squared of the average deviations.¹⁷ This estimate, understandably 10 times

(16) Of the two values of i_R chosen for quantitative application in Table I, the value of $1/2$ is probably to be preferred. *Cf.*, for isotope effects in intramolecular hydrogen shifts, C. Jambon, Ph.D. Thesis, University of Paris, Paris, France, 1962.

(17) (a) The latter corresponds more closely to the statistical process for determining maximum reliability of an estimate from multiple measurements on a given observable. (b) If in the propanol isomerization studies carried out by Gold and Satchell, ref. 6, Table V, one assumes equilibrium has been established and K_{equil} for $[i-PrOH]/[n-PrOH] \sim 100$, neglecting reactant impurities and side reactions, a rough value of k_{AM}/k_M may be estimated. For the reactions in 8 M

larger than the central measure estimates because of the considerable uncertainty in experimental points and the small degree of reaction completed, represents an upper relative rate limit for the abnormal process. The upper limit judgment, it should be noted, is based both on the statistical aspects of the treatment and from the product studies described. In the latter, while it has been clearly ascertained that the tertiary hydrogen seen by n.m.r. must belong to isopropyl alcohol (see Experimental) and thereby be potentially exchangeable, one cannot conclusively rule out the possibility that other processes besides the abnormal hydration have contributed to the slight decrease in $[A_6]$ observed. Included in Figure 1 are the reciprocal average deviation weighted central measure and 95% confidence level least-squares curves. These appear almost linear over the small degree of reaction completed.

With these results in hand, it is of some interest to compare them with the Taft linear free energy equation estimations of k_{AM}/k_M . All parameters are not available for the latter but some seemingly sensible analogies will allow estimates. Taking the reference olefin to be ethylene with hydration rate constant, k^0

$$\log k_M/k^0 = \rho^*(2\sigma_{Me^*} - \sigma_{Me^*}) + 2R_{Me} - R_{Me} \quad (18)$$

and

$$\log k_{AM}/k^0 = \rho^*(\sigma_{Et^*} - \sigma_{Me^*}) + R_{Et} - R_{Me} \quad (19)$$

Here, the carbon atoms invested with the positive charge in the carbonium ions formed from ethylene, and from propylene by normal and abnormal addition are stabilized, respectively, by one and two methyl and one ethyl group. The σ^* values are on the hydrogen standard scale. Since $R_{Me} = 3h_H$ and $R_{Et} = 2h_H + h_C$, where h_H and h_C are the hyperconjugation parameters, respectively, for C-H and C-C bonds, and assuming that the h values for the similar acetal and ketal hydrolysis reactions apply, then¹⁸

$$\log k_M/k^0 = -3.5(-0.49) + 3(0.62) = 3.58$$

$$\log k_{AM}/k^0 = -3.5(-0.10) + 0.24 - 0.62 = -0.03$$

Combination of these results reveals $k_{AM}/k_M \approx 2 \times 10^{-4}$, just inside the upper limit obtained in the work described here. At the same time, a considerably smaller ratio corresponding to, or somewhat less than, the central measure estimate is necessary to yield agreement with the theoretical k_{AM}/k_M . With a μ -value of 0.62,² the two-dimensional HCJ models predict $k_{AM}/k_M = 10^{-5}$ - 10^{-6} .

In summary, it is clear that the present results do not bring us substantially closer to resolution of the paramount issue, *i.e.*, what is the relative importance of induction vs. hyperconjugation in reactions where alkyl carbonium ions are formed. Assuming the h_H and h_C values employed do apply, their use predicts k_{AM}/k_M to be considerably greater than what HCJ theory predicts, and they also yield an anomalously

$HClO_4$ at 100°, this ratio is $\sim 6 \times 10^{-3}$. Considering the experimental uncertainties, especially in the latter, this and the values reported here are in satisfactory agreement.

(18) σ^* values from R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 619. $\rho^* = -3.5^9$ (originally from unpublished work of R. W. Taft and T. Hall). Acetal and ketal hydrolysis h values.¹ For the latter reactions, presumably also involving neutral ground and carbonium ion transition states, $\rho^* = -3.6$.

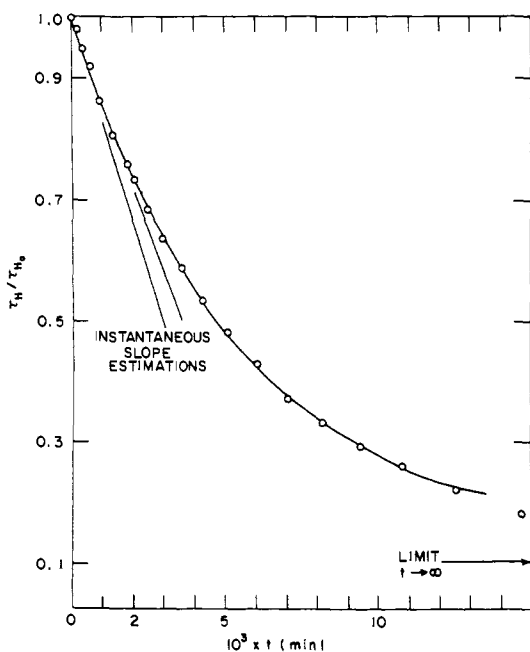


Figure 2. Exchange of isopropyl alcohol methyl protons in run C as a function of time: 54.9% D_2SO_4 at 60° .

high h_H/h_C quotient (~ 2.6) compared both to theory and to experimental results for aromatic reaction systems (~ 1.3). Both predictions are encompassed by the experimental result, that from the linear free energy equation only in the extreme, however.

In Figure 2, the results of run C are displayed. The 20 τ_H/τ_{H_0} vs. time points measured, plus a convergence-tested estimate of the equilibrium value of this ratio, are shown along with estimated upper and lower limits for the instantaneous slope, $[d(\tau_H/\tau_{H_0})/dt]_{t=0}$. Uncertainty flags are not shown; for only one point is the uncertainty as large as 3% of the measured value while for most it is on the order of 1%. With $\gamma = 3.9 \pm 0.5$ and from the known concentrations of H and D, $k_{inst} = (1.05 \pm 0.10) \times 10^{-3} \text{ min.}^{-1}$.

Starting at or around these values of k , with $\beta = 0.9$ – 1.0 , these parameters were refined within eq. 10 as modified in eq. 15. In Figure 3 a typical plot obtained by fitting the first 19 data points is given. Goodness-of-fit,¹⁹ for the best fit obtained for the data, is plotted as a function of X for several values of γ centered about 4.0. The refined values of k and β corresponding to the minima of these curves are also shown. It is immediately apparent that although discrimination of the best γ -value on the basis of goodness-of-fit is not possible, the best values of β and k vary very little over the range of γ . The best value of X is, however, rather strongly coupled with choice of γ which is not surprising when p_j of eq. 15 is examined; *i.e.*, the numerator of this term indicates an increased X for an increase in γ necessary to hold p_j near constancy.

In Figure 4, GOF is plotted vs. X for the 20, 19, 18, and 17 point sets obtained by successive removal of later points, with $\gamma = 4.0$. Further removal, as checked

(19) Goodness-of-fit (GOF) is a useful statistical measure which resembles the conventional standard deviation but includes dependence upon the excess number of data to be fit over the number of parameters to be determined, *i.e.*, where $\text{std. dev.} = (\sum X^2/n_D)^{1/2}$, $\text{GOF} = \sum X^2/(n_D - n_p)$.

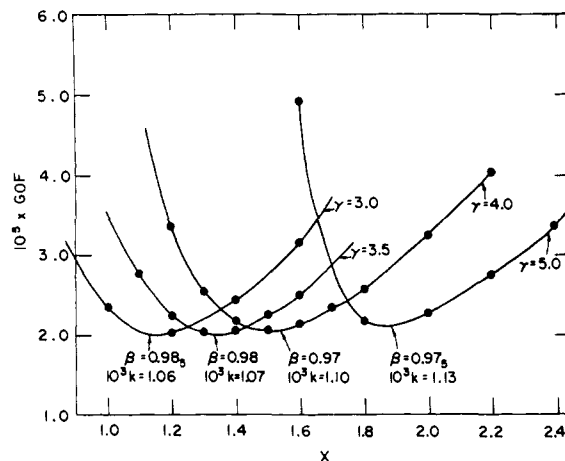


Figure 3. Fitting curves for 19 point set with various values of γ .

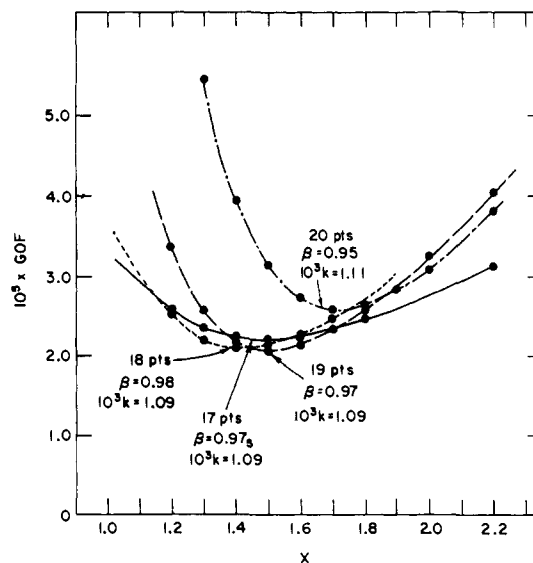


Figure 4. Fitting curves for 17–20 point sets with $\gamma = 4.0$.

for the 16 and 15 point sets not shown, does not result in any further shifting of the curves although the flattening trend continues. One may conclude, then, that after removal of data point 20, the refined parameters k , β , and X (graphically) do not change noticeably with further depletion of the set and that, consequently, the term ignored in eq. 15 is unimportant. If this term was important, the sets of 19, 18, ... points should have been characterized by a continued shifting as the points were removed. The jump from the 20 to 19 point sets is, most likely, due to error in point 20.

Table II summarizes the statistical results over all degrees of freedom. It seems entirely reasonable on these bases, with the value of $\gamma = 3.9 \pm 0.5$, to derive the following parameter values and probable uncertainties. The pseudo-first-order rate constant of dehydration of $CH_3CH(OD)CH_3$ is $k = (1.10 \pm 0.05) \times 10^{-3} \text{ min.}^{-1}$; this value is quite insensitive to γ and the size of the data set. The secondary isotope effect (D to H) in this dehydration, $\beta = 0.975 \pm 0.015$, is somewhat more sensitive to the above variables, but only in the sense of how different it, β , is from unity. Finally, there is the primary isotope effect for loss of a methyl hydrogen rather than a deuterium from the

Table II. Refined Values of β , k , and X for the Methyl Hydrogen Exchange Reactions of Isopropyl Alcohol

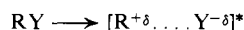
No. of points	$\beta, 10^3k \text{ (min.}^{-1}), X [10^5 \text{ GOF}]^a$			
	3.0	3.5	4.0	5.0
20	0.965, 1.07, 1.4 [2.1]	0.96, 1.09, 1.5 [1.9]	0.95, 1.11, 1.7 [2.5]	0.94, 1.14, 2.1 [2.6]
19	0.985, 1.06, 1.2 [1.9]	0.98, 1.07, 1.3 [1.9]	0.97, 1.10, 1.5 [1.9]	0.965, 1.13, 1.9 [1.9]
18	0.985, 1.06, 1.2 [1.9]	0.985, 1.07, 1.3 [1.9]	0.98, 1.09, 1.4 [2.0]	0.97, 1.12, 1.7 [1.9]
17	0.985, 1.06, 1.2 [2.0]	0.98, 1.07, 1.3 [2.0]	0.975, 1.09, 1.5 [2.1]	0.97, 1.13, 1.8 [2.1]
16	0.985, 1.06, 1.2 [2.1]	0.985, 1.07, 1.3 [2.1]	0.98, 1.08, 1.4 [2.2]	0.975, 1.12, 1.7 [2.2]

^a Interpolated minima of GOF from curves as exemplified by Figures 3 and 4.

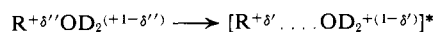
carbonium ion, $X = 1.6 \pm 0.4$, which is quite sensitive to the choice of γ . A representative curve with $k = 1.10 \times 10^{-3} \text{ min.}^{-1}$, $\beta = 0.973$, $X = 1.5$, and $\gamma = 4.0$ is drawn through the points in Figure 2 for illustration of the fitting.

It is of interest to examine these results in terms of the mechanistic and medium conditions which produce them and to draw comparisons with effects noted in similar systems. The β -value quoted corresponds, in the more conventional notation, k_H/k_D , to 1.026 ± 0.016 , which upon cursory examination seems rather small for a β -secondary isotope effect. For example, Robertson and co-workers²⁰ have found 1.07 and 1.05 per β -deuterium atom, respectively, for SN1 solvolysis of isopropyl tosylates and bromides. However, when the ground-to-transition state differences are examined, this result appears not at all unreasonable.

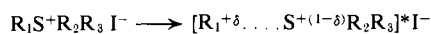
For the SN1 solvolysis reactions



an essentially neutral ground state must be compared to a transition state where at least some positive charge is established on R, which may be delocalized by hyperconjugation to the terminal alkyl groups. The magnitude of this charge separation depends, of course, for a given R, on the nature of Y and the medium. On the other hand, in the dehydration where the acidity of the medium is as high as in the experiments described, essentially all the alcohol exists as ROD_2^+ , and the rate-determining step for reaction is²¹



It seems entirely reasonable here that in both the starting and transition states, both formally positively charged, some delocalization of the charge on R occurs. Therefore, in a simplified symbolic sense, even though $\delta' > \delta''$, $(\delta' - \delta'') < \delta$. Accepting this interpretation, a more pertinent comparison may be had from the reaction system



where the isotope effect is on the order of 3% (per β -D atom in R_1) when $R_1 = t\text{-amyl}$.²²

Two seemingly significant implications accompany this analysis. The first suggests the transition state for

(20) K. T. Leffek, R. E. Robertson, and S. E. Sugamori, *Can. J. Chem.*, **39**, 1989 (1961).

(21) According to E. N. Arnett and J. N. Anderson, *J. Am. Chem. Soc.*, **85**, 1542 (1963), secondary alcohols such as isopropyl alcohol should be $\sim 95\%$ protonated in 55% by weight H_2SO_4 .

(22) S. Asperger, N. Ilakovac, and D. Pavlovic, *Croat. Chem. Acta*, **34**, 7 (1962).

dehydration rather strongly resembles the starting state, whereas in hydration the carbonium ion-like transition state accompanying protonation is quite different from the starting state olefin. The second concerns the isotope effect which is to be expected for the equilibrium between alcohol and protonated alcohol, *i.e.*, for the rapid and reversible step preceding dehydration. If the small value of β may be rationalized, then an isotope effect of 2–4% may be expected for the alcohol protonation equilibrium since some carbonium ion character is postulated for R in ROD_2^+ .

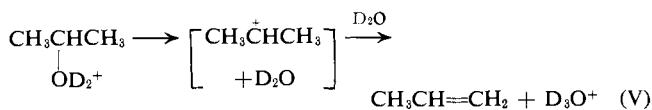
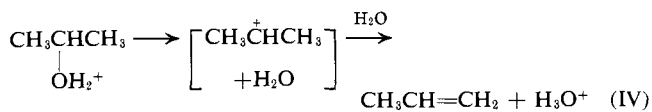
That the rate constant for dehydration measured here, *i.e.*, $k = 6.6 \times 10^{-2} \text{ hr.}^{-1}$, is just about twice the value reported by Beishline for an $H_2SO_4-H_2O$ medium of approximately the same acidity and at the same temperature (See Table I, footnote c, and ref. 9), is also of interest. Correlations of relative rates of acid-catalyzed reactions in H_2O and D_2O have been made previously by Long and Bigeleisen.²³ In mechanisms with specific hydrogen ion catalysis in an equilibrium prior to the slow step, rates in D_2O are often 2.5–3 times faster than rates in H_2O . The factor that is usually responsible for this rate enhancement is the ratio of dissociation constants for the protonated vs. the deuterated substrate, *i.e.*, $K_{SH^+}/K_{SD^+} \approx 3$, where S is the substrate.²³ This cannot be responsible for the rate increase observed here because at the level of acidity employed the alcohol is better than 95% protonated; we estimate the concentration of ROH_2^+ in water to differ from that of ROD_2^+ in D_2O by $\sim 1\%$ for equal concentrations of acid near the 55% by weight region.

There are two multiplicative effects which can account for the faster rate in D_2O : the secondary isotope effect in the loss of water from the acidified alcohol and the medium effect of D_2O as compared to H_2O . The latter effect would be expected to increase the rate in H_2O over D_2O by about 5% as determined from the work of Robertson²⁴ and Swain²⁵ and their co-workers, and requires no further comment. The other effect enters in the slow step (loss of water) which can be written as follows, proceeding to olefin

(23) F. A. Long and J. Bigeleisen, *Trans. Faraday Soc.*, **55**, 2077 (1959). In a study of deoxymercuration of 1-iodomercuri-2-propanol in dilute acid, $k_{D_2O}/k_{H_2O} = 2.16$ (M. M. Kreevoy, *J. Am. Chem. Soc.*, **81**, 1099 (1959)). The deviation of K_{SH^+}/K_{SD^+} from unity could possibly be the major contributor to the over-all isotope effect in this study.

(24) R. E. Robertson and P. M. Loughton, *Can. J. Chem.*, **35**, 1319 (1957).

(25) C. G. Swain, R. Cardinaud, and A. D. Ketley, *J. Am. Chem. Soc.*, **77**, 934 (1955).



An estimate of the rate effect in going from reactant to the species in brackets can be obtained by considering the following equilibria

$$\frac{(\text{R}^+)(\text{H}_2\text{O})}{(\text{ROH}_2^+)} = K_{1V} \quad \frac{(\text{R}^+)(\text{D}_2\text{O})}{(\text{ROD}_2^+)} = K_V$$

and

$$\frac{(\text{ROD}_2^+)(\text{H}_2\text{O})}{(\text{ROH}_2^+)(\text{D}_2\text{O})} = K_{1V}/K_V$$

The last equation is formally similar to

$$\frac{(\text{HOD}_2^+)(\text{H}_2\text{O})}{(\text{HOH}_2^+)(\text{D}_2\text{O})} = L^{-1/2}$$

where $L = 9.5$ and H , considered here to be distinguishable from the other protons, is the proton being transferred.²⁶ If the assumption that the partition function ratio $Q_{\text{ROD}_2^+}/Q_{\text{ROH}_2^+} = Q_{\text{HOD}_2^+}/Q_{\text{HOH}_2^+}$ is justified, the equilibrium constant $K_{1V}/K_V = 0.47$.²⁷

Now, from the observation of a primary isotope effect, X , in the loss of H or D from carbon in the dehydration step, the transition state should be placed somewhere to the right of the brackets in the above schemes (see eq. III earlier). If for the moment, however, it is placed inside the bracket, the equilibrium constant ratio for the reaction carried out in H_2O and D_2O , $K_{\text{H}_2\text{O}}^*/K_{\text{D}_2\text{O}}^*$ (*i.e.*, the ratio of the equilibrium constants in transition state theory between reactants and transition states), is given by K_{1V}/K_V . As the position of the transition state is hypothetically moved from inside the bracket toward olefin, $K_{\text{H}_2\text{O}}^*/K_{\text{D}_2\text{O}}^*$ is expected to vary from 0.47 toward unity.

Neglecting the small medium effect, the observed rate ratio for dehydration in D_2O vs. H_2O , *i.e.*, about 2, indicates that the actual transition state equilibrium constant ratio $K_{\text{H}_2\text{O}}^*/K_{\text{D}_2\text{O}}^*$ is close to 0.5, which in turn places the transition state of the slow dehydration step at a point where a large amount of C–O bond rupture has taken place but where there is little participation of the second water molecule acting as a base.

(26) E. L. Purlee, *J. Am. Chem. Soc.*, **81**, 263 (1959); for tabulated values of L , see K. Heinzinger and R. E. Weston, Jr., *J. Phys. Chem.*, **68**, 744 (1964).

(27) This assumption has been made previously: C. G. Swain and E. R. Thornton, *J. Am. Chem. Soc.*, **83**, 3884 (1961).

This implies little methyl group C–H rupture, which is in agreement with the small value obtained for X .

We may consider X more directly in terms of the original scheme (III), above, to test the presumed notion of considerable carbonium ion character in the transition state for olefin addition, *e.g.*, T_{O_1} . This transition state was assumed to have considerable ionic character, *i.e.*, to lie closer to the intermediate than to the olefin. Therefore, in the reverse reaction, proceeding from the ion intermediate to the same transition state which is the process which determines X , there should be a relatively small change in electronic structure, and, hence, a small rate difference between loss of D and H.²⁸ Again consistency with the small value of X is noted; the secondary α -effect which contributes a correction to the primary effect should also be very small, relative to "normal" secondary effects, by the same reasoning.

Appendix

Equation 10 as modified in eq. 15 provides the relationship between the observables $\tau_{\text{H}}/\tau_{\text{H}_0}$ and t from which the parameters β and k are to be determined. The parameters X and γ are chosen and held while best values of β and k are computed; X is later determined by finding the best over-all fit to eq. 10 as modified by 15 upon variation of X . Therefore

$$\tau_{\text{H}}/\tau_{\text{H}_0} = f(t; X, \gamma, \beta, k) + \epsilon(t) \quad (\text{A1})$$

The latter may be expanded in a Taylor series where $f^0 = f(t; X, \gamma, \beta^0, k^0)$

$$f = f^0 + \frac{\partial f}{\partial \beta} \Delta \beta + \frac{\partial f}{\partial k} \Delta k + \frac{1}{2!} \left\{ \frac{\partial^2 f}{\partial \beta^2} (\Delta \beta)^2 + \frac{\partial^2 f}{\partial k^2} (\Delta k)^2 + \frac{\partial^2 f}{\partial \beta \partial k} \Delta \beta \Delta k \right\} + \dots \quad (\text{A2})$$

Under the assumption that the guesses for β and k (β^0, k^0) are close to the best values for these parameters, *i.e.*, those for which $\Sigma \epsilon^2$ over all points is a minimum, higher order derivatives than the first are dropped. Equation A2 is thereby linearized; by the Gauss–Newton method²⁹ corrections to β and k are iteratively computed until ($\Sigma \epsilon^2 = \Sigma (f - f^0)^2$) is minimized. This procedure has been programmed for the IBM 7094 with the following convergence criteria: $\Delta \beta$ and $\Delta k < 10^{-3}$ or $\Delta \text{std. dev.} < 0.01 \text{ std. dev.}$ On the order of 100 such runs were made for various X and γ with an average time of ~ 3 sec. per run required. Liberal testing assured that convergence to the same parameters and fitting was accomplished independent of reasonable starting parameter choices.

(28) *Cf.* F. H. Westheimer, *Chem. Rev.*, **60**, 265 (1960).

(29) *Cf.* H. O. Hartley, *Technometrics*, **3**, 269 (1961).