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# H−D Exchange in Pinacolone by Deuterium Oxide at High Temperature and Pressure

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The rates of deuteration of pinacolone in pure deuterium oxide at 225 °C and 370 psia of (autogenic) pressure were studied. No novel pathways appear to operate in this $D_2O$-catalyzed process under these conditions. Pseudo-first-order kinetics suggest that the reaction proceeds *via* classical enolization with an observed first-order rate constant of $8.8 \times 10^{-3}$ min$^{-1}$, determined at three concentrations.

Recent studies of organic reactions in liquid water at high temperatures and pressures have demonstrated the potential for aqueous organic chemistry. Higher solubility of organic compounds, a consequence of the decreasing dielectric constant of water as a function of temperature,[1] renders superheated water an effective medium for organic transformations. At 300 °C, water exhibits a density and polarity similar to those of acetone at room temperature.[2] Increased self-dissociation of water and thereby greater capability for acid/base catalysis is realized at high temperature. For example, at 250 °C the ion product of water is 11 and of deuterium oxide 12, compared to 14 and 15, respectively, at 20 °C.[3,4] These changes in the physicochemical properties of water and their useful application to organic chemistry are being explored extensively.

Numerous workers have made contributions to aqueous organic chemistry in both superheated and supercritical water, particularly in geochemistry, fossil fuels, and waste disposal.[5,6] The aqueous environment at 250 to 350 °C supports ionic cleavage, hydrolysis, and condensation reactions.[7] Yet, relatively few detailed mechanistic and kinetic studies on these processes in pure water are available. In one such study, Baliga and Whalley determined mechanisms and rates of alkene hydrations in high temperature water (170−190 °C and 1500−45000 psi), however, in the presence of added acid.[8] Several kinetic studies in supercritical water (albeit with added catalysts) of alcohol dehydrations[9] and oxidations,[10] as well as investigations of substituent and solvent effects[11] and transition-state structures,[12] have been reported. However, supercritical fluids exhibit unique sensitivity to small variations in temperature and pressure.[13] This sensitivity is particularly evident in the extreme effects on density, which cause facile transitions from liquid- to gas- (dense fluid) like behavior and thus changes in solvent properties and reactivities. Fluctuations between the liquid and gaseous state concomitant with significant changes in, for example, dielectric constants, ionic strengths, and hydrogen-bonding capacity do not occur at the reaction conditions of 225 °C and 370 psia applied in the studies described here, in which a constant water density of 0.8 g/mL was maintained. Further, the high sensitivity of reaction rates to changes in dielectric constant (as a result of the related pressure variations) in supercritical water is not a factor in subcritical liquid water. Transition-state volumes in the hydration of ethylene at 180 °C and 100 bars (1450 psia) of −15.5 ± 1.5 cc/mol and of propylene at 100 °C and 100 bars of −9.6 ± 1 cc/mol, as determined by Baliga and Whalley,[8] are within the range of usually encountered activation volumes of ±30 cc/mol for liquid solutions. In contrast, an activation volume of −1200 cc/mol was reported by Narayan and Antal for the dehydration of 1-propanol at the supercritical temperature and pressure of water (374 °C, 3200 psia).[9] Therefore, under the reaction conditions of the present study we assume near-

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[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1994.

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normal activation volumes and thus, most importantly, expect the rate constants not to fluctuate with pressure to the extent associated with supercritical conditions.

Acid- or base-catalyzed organic reactions that take place in pure superheated water appear to follow classical pathways but we know of no directly relevant kinetic studies of this mechanistic question which identify the role of water in the transformations. Unexpectedly rapid conversions occurred with the slate of reactants in our initial studies, in which highly selective and quantitative reactions were observed within 30 min at 200 to 300 °C.[14] Deuterium exchange of the α-methyl protons of pinacolone, however, occurred at suitable rates under these conditions, and the study of this process in pure deuterium oxide at 225 °C and autogenic pressure is presented here.

## Results and Discussion

The formation of pinacolone *via* rearrangement of pinacol was quantitative and not reversible; no deuterium incorporation into the *tert*-butyl methyl groups was observed. Thus, the *tert*-butyl resonance served as an internal standard in the measurements of deuterium incorporation at the α-methyl position by $^1$H NMR. We found, though, that $^1$H NMR spectra of aqueous ($D_2O$) solutions of pinacolone acquired at room temperature with a standard proton pulse delay of 1 s yielded integrations of the α-methyl and *tert*-butyl methyl resonances which did not relate in the expected 1:3 ratio. A relative deficiency of 18% in the peak area of the α-methyl protons indicated clearly that in water these protons relaxed considerably more slowly than those of the *tert*-butyl group. To achieve full relaxation of all protons, and thus accurate calculations of residual α protons, a pulse delay of 57 s combined with an acquisition time of 3.2 s at constant temperature (VT setting of 30 °C) was applied.

Rates of reaction at pinacolone concentrations of 0.30, 0.50, and 0.71 M were examined. The reactions occurred at a constant autogenic pressure of 370 psi which was generated by expansion of the reaction medium. Reaction rates as a function of pressure via pre-pressurization of the reaction vessels with an inert gas were not investigated in this study. The water solubility of pinacolone at approximately 100 °C was determined to exceed 1 M; thus, the required miscibility at 225 °C was assured. The homogeneity of (supersaturated) product solutions permitted direct NMR observations of aliquots at room temperature. The percentage of residual α protons was measured by presetting the area of the *tert*-butyl proton peak to 3 (or 300). Thus, in the absence of hydrogen exchange, the relative integration of the α proton resonance ($A_i$) was 1 (or 100), and any decrease in this value indicated the extent of deuteration as $1 - A_f$ ($A_f$ denotes the relative peak area of the partially or completely deuterated α-methyl group). The reproducibility of the integration values was verified to be ±2% by several independently acquired spectra of the same samples.

Data for the reaction at 225 °C and 370 psi and 0.50 M were plotted in first-order format, $\ln(A_f/A_i)$ vs time, as shown in Figure 1. A pseudo-first-order reaction was indicated by the linearity of the plot ($R^2 = 0.95$). The rate constant was $(8.9 \pm 0.5) \times 10^{-3}$ min$^{-1}$. A plot (Figure 2) of $\ln(A_f/A_i)$ vs time ($R^2 = 0.89$) at 0.71 M yielded a rate constant of $(9.4 \pm 0.64) \times 10^{-3}$ min$^{-1}$. Calculations predict the second half-lives ($t_{1/4}$; 75% conversion) to occur within approximately 145 to 155 min of reaction time. In good agreement, deuteration proceeded to 69% at 0.71 M and to 77% at 0.50 M during 135 min, lending support to the concentration independence and thus the first order of the reaction over extended reaction times. A rate constant of $7.1 \times 10^{-3}$ min$^{-1}$ (Figure 3) and a half-life of 91 min were determined for the reaction at 0.30 M.

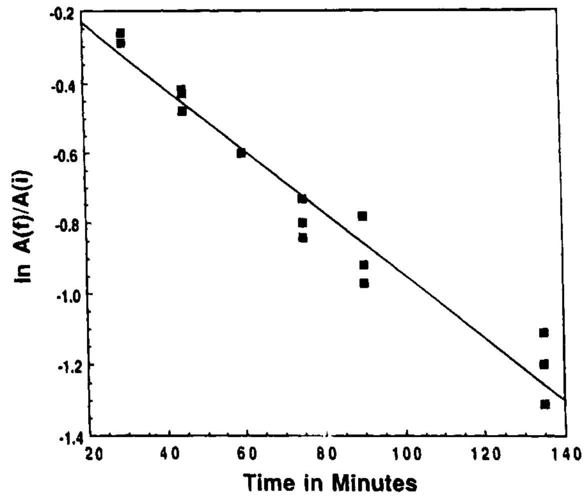

**Figure 1.** Pinacolone; H/D exchange at 0.50 M, 225 °C.

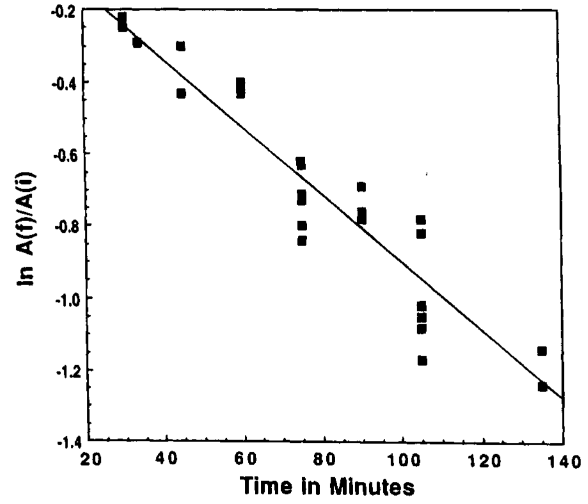

**Figure 2.** Pinacolone; H/D exchange at 0.71 M, 225 °C.

Even though these values differ from those at higher concentration, we do not attribute this to a concentration dependence of the reaction rate. Solvent−solute and solute−solute clustering undoubtedly occur under our reaction conditions to a great extent, even though at different extents relative to conventional conditions, considering the hydrogen-bonding capacity of both pinacolone and water. We do, however, expect these interactions, particularly those involving the bulk solvent, to be independent of substrate concentrations and thus not to influence the reaction rate as a function of concentration. We are confident in assigning a first-order designation to the reaction because a rate constant of $(8.9 \pm 0.36) \times 10^{-3}$ min$^{-1}$ and a $t_{1/2}$ of 78 min, extracted from the combined data at all three concentrations, indicate maximum errors associated with these reaction param-

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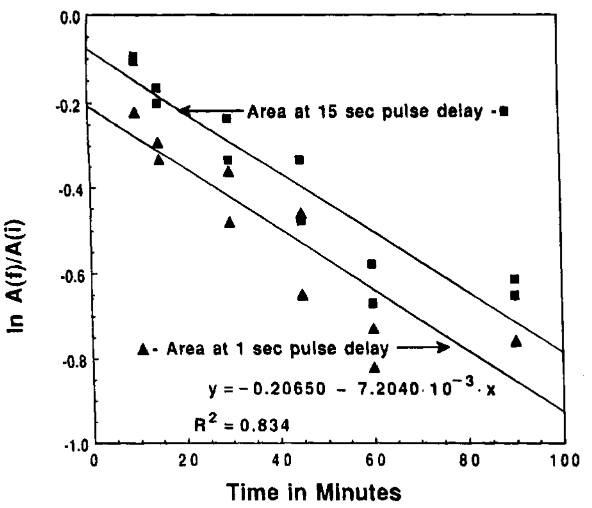


**Figure 3.** Pinacolone; H/D exchange at 0.30 M, 225 °C.

eters of 20% and 15%, respectively, which are considered within acceptable margins. The extent of deuteration in the series of experiments at 0.30 M was measured with a pulse delay of only 15 rather than 57 s (data obtained with a delay of 1 s yielded a rate constant of $7.2 \times 10^{-3}$ min$^{-1}$; Figure 3). The good agreement between rate constants at 0.50 M calculated from integrations of spectra acquired with a pulse delay of 1 s ($k = 10 \times 10^{-3}$ min$^{-1}$) and 57 s ($k = 8.9 \times 10^{-3}$ min$^{-1}$) confirms the validity of the value of $k$ at 0.30 M. Although measurements of the absolute extent of deuteration are different in the presence of residual saturated protons, the slope of the line defined by the data is unchanged.

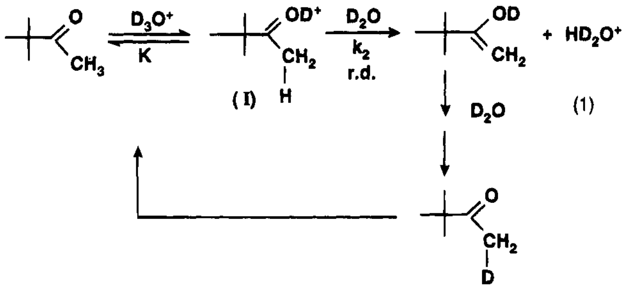
Sources of deviations in $k$ attributable to errors unique to the unconventional reaction setup used here are, for example, the effect on the reaction of small variations in the total solution or reactor volumes. Deviations in headspace occupied by gas (mixed vapors) rather than liquid may cause nonlinear behavior as the result of perturbation of the water–reagent mixture or because of competing gas-phase reactions. Additionally, uncertainties in heat-up times, which exist despite close monitoring of the temperature, lead to imprecision in the determination of the total reaction time since the external and not the internal temperature of the reactor was measured. A difference of as little as 1 min in heat-up time will introduce considerable errors in rate measurements, particularly for short reaction times. Another source of error, fluctuation of the reaction temperature by ±2 °C, results in an uncertainty of $\pm 5 \times 10^{-4}$ in the value of $k$ and contributes to the overall standard errors determined for the rate constants at the three concentrations. We do not consider the effects of adventitious oxygen a significant source of errors since oxygen, at any concentration level, does not enter into the mechanistic pathway of this deuterium exchange reaction and at the trace amount level, may cause only negligible side reactions.

The present results may be compared with a rate constant of $9.72 \times 10^{-4}$ min$^{-1}$ ($1.62 \times 10^{-5}$ s$^{-1}$) determined by Rappe and co-worker for the DCl-catalyzed deuteration of pinacolone in aqueous dioxane at 40 °C.[15] The same workers observed a slightly higher rate ($k = 1.8 \times 10^{-3}$ min$^{-1}$, $3.0 \times 10^{-5}$ s$^{-1}$) when the reaction was catalyzed by base ($Na_2CO_3$) under otherwise identical conditions.[16] Ahmed reported a rate constant of $1.1 \times 10^{-3}$ min$^{-1}$ ($1.9 \times 10^{-5}$ s$^{-1}$), which was also derived from a base ($K_2CO_3$) catalyzed reaction in aqueous dioxane at 30 °C.[17]

In this investigation, an activation energy of about 20 kcal/mol was calculated for reactions at 200 to 250 °C and applied to a temperature-dependent extrapolation of the 225 °C rate constant for calculation of the rate constant at 40 °C. Comparison of this theoretical value ($6 \times 10^{-8}$ min$^{-1}$) to those observed by Rappe indicated that the rate constant observed at 225 °C was approximately 3 to 4 orders of magnitude smaller than expected from the actual rate acceleration caused by the elevated temperature. Thus, the deuteration of pinacolone under our conditions appears to have been subject to factors which retarded the reaction rate. Rate retardation may be caused primarily by the greatly reduced acidity and basicity of the reaction medium. Whereas Rappe's studies utilized acid catalyst concentrations of $4.9 \times 10^{-2}$ M and base catalyst concentrations of $3.9 \times 10^{-3}$, the reactions reported here occur at $10^{-6}$ M for either catalyst based on the reported autoprotolysis constant.[4] If an equilibrium constant, $K$, of at least 1 is assumed for the preequilibrium in the acid-catalyzed reaction, eq 1, then a rate expression for the rate determining step is given by eq 2, where the concentration of the protonated ketone, I, by definition of $K \geq 1$,

$$\text{rate} = k_2[\text{I}] \qquad (2)$$

must be equal to the $D_3O^+$ concentration, i.e., $10^{-6}$. Consequenly, a comparison of the acid concentration employed by Rappe and co-worker ($4.9 \times 10^{-2}$ M) with that in our study ($1 \times 10^{-6}$ M) predicts a rate retardation of approximately 4 orders of magnitude based on pH dependence only. A rate acceleration of approximately $10^5$, however, is expected as a result of the higher temperature. This leads to a postulated overall rate increase by 1 order of magnitude relative to that observed at 40 °C. Thus, a $\Delta k$ of approximately 1 order of magnitude is predicted as well as experimentally determined.



(1)

Similar arguments when applied to the base-catalyzed mechanism, eq 3, employing a difference in base concentrations of $10^{-3}$ ($1 \times 10^{-6}$ vs $3.9 \times 10^{-3}$), indicate a corresponding rate retardation. From the rate acceleration effected by the higher reaction temperature, an overall increase in rate by $10^2$ is predicted, but an increase by only 1 order of magnitude is observed. This is an acceptable match in light of the approximations and large potential for error described previously for extrapo-

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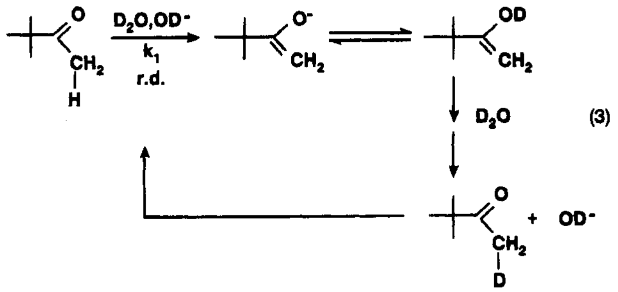

(3)

lations (e.g., the rate acceleration determined from an Arrhenius plot of only two data points separated by 185 °C).

Our present data are generally compatible with either an acid- or a base-catalyzed mechanism although the combined errors do not make the case compeling. Since the reactions are catalyzed by deuterium oxide, both types of catalysis may be operating in this potentially ambicatalytic medium.

## Summary

Hydrogen exchange in pinacolone, catalyzed by superheated deuterium oxide, appears to follow classical pathways eluciated under traditional acid- or base-catalyzed conditions at conventional temperatures. A first-order reaction is realized at rates which agree well with the combined effects of rate acceleration as a function of temperature and of rate retardation as a function of catalyst concentration.

## Experimental Section

Pinacolone (98% pure) was used as received from Aldrich. Deuterium oxide (99.9% pure) was obtained from Cambridge Isotope Laboratories and purged with nitrogen for a minimum of 30 min immediately before transfer to the reactor. The reactors were fashioned from $^3/_4$ in. stainless steel (316 SS) Swagelok plugs and caps available from R. S. Crum. The total volume of the sealed reactor was 4.9 mL. Catalysis of the reaction by either the metal surfaces or dissolved metal species was not anticipated,[17] and no significant concentrations of metallic components were detected by Inductively Coupled Plasma Emission Spectroscopy (ICPES) in deuterium oxide after a 10-day exposure to a new reactor at 300 °C or in reaction mixtures from new and used reactors.

Typically, an appropriate amount of pinacolone (0.30–0.71 M, 0.13–0.30 mL) was measured by syringe into the Swagelok plug followed by addition of $D_2O$ to yield the desired concentration at a total room temperature volume of 3.40 mL. Once the reaction temperature reached 225 °C, expansion of the solution led to nearly 100% filling of the reactor with liquid water. Caution should be exercised to avoid overfill of a closed, pressurized vessel.[19] The Swagelok plug containing the reagents and the cap were purged of oxygen, and the reactor was sealed under nitrogen to avoid potential side (oxidation) reactions. A thermocouple was attached to the exterior wall of the reactor prior to immersion into a Techne constant-temperature fluidized sand bath at 225 °C. Temperature equilibration to ±2 °C was monitored continuously and was reached in less than 5 min. Timing of the reaction commenced once a constant temperature was established. The reactor was immersed in a cold water bath to quench the reaction after the desired reaction time. The homogeneous product solution was examined by $^1H$ NMR using a Bruker AM 360 spectrometer. A minimum of 25 scans (transients) per NMR sample was acquired. The *tert*-butyl methyl resonance served as an internal standard in the determination of α-methyl deuteration via relative integration of the residual α-methyl resonance.

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