

# Deuteration of Extremely Weak Organic Acids by Enhanced Acid–Base Reactivity in Supercritical Deuterioxide Solution

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**Abstract:** The dramatic changes which occur in the properties of water upon exceeding its critical point lead to dramatic differences in the behavior of dissolved organic solutes. In this paper, the large decreases in the self-ionization and dielectric constants of deuterium oxide which accompany exceeding the critical temperature lead to large increases in the equilibrium constants for the reactions of very weak organic acids with deuterioxide ion. The enhanced acid–base reaction is monitored by the incorporation of deuterium into the organic molecules *via* reaction with deuterioxide ion. Successful deuterium exchange is demonstrated for a variety of organic substance having  $pK_a$  values up to 50. Nearly quantitative exchange of hydrogen isotopes is obtained by reaction with 0.016 M NaOD solution for 10 min at 400 °C at approximately 300 bar pressure for molecules having  $pK_a$ 's up to approximately 43 while longer heating times and more concentrated base solutions allow deuteration of acids having  $pK_a$ 's up to 50. The terminal methyl group is found to be the most acidic carbon of a typical alkyl chain and an unexpected alternation of acid strength along the alkyl chain of dibutylamine is observed.

The reactivity of organic compounds in heated and supercritical water has recently been the subject of some interest.<sup>1–14</sup> This interest has been driven by the potential for environmentally benign toxic waste disposal *via* air oxidation in supercritical water and by fundamental interest in understanding and utilizing chemical reactivity under these unusual reaction conditions. Because most organic compounds are miscible with supercritical water while most inorganic salts are insoluble, it is a potentially important new reaction medium for organic chemistry.<sup>1</sup> Early interest in this area was expressed by those dealing with toxic waste clean-up and was driven by the observation that essentially complete air combustion of a wide variety of organic matter with little or no toxic emissions was possible under supercritical water conditions with air as the oxidant.<sup>15,16</sup>

The bulk of the studies on reactivity in superheated and supercritical water have focused on reactions in which hydroly-

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sis, oxidation, or thermolysis occur at enhanced rates either because of the high temperatures involved or because of the enhanced reactivity of the water. For example, the increased self-ionization constant at 300 °C leads to more rapid acid- and base-catalyzed reaction rates.<sup>10</sup> Numerous examples of complete air oxidation to carbon dioxide, water, and salts have been reported by workers interested in destruction of toxic wastes.<sup>1–3,15–22</sup> Recently several groups have reported on various examples of the nondestructive reactivity of a variety of organic molecules in superheated (200–300 °C, 75 bar) water.<sup>8–14</sup> While these conditions are quite vigorous compared to typical chemical reaction conditions, they are less severe than supercritical conditions ( $T > 375$  °C,  $P > 218$  bar) and, because of large property changes that occur when the critical temperature is exceeded, one can anticipate significant differences between superheated and supercritical reaction conditions.<sup>1,23,24</sup>

In this paper, the results of a study of the reactions of deuterioxide ion with a number of organic compounds in supercritical deuterium oxide are reported. These conditions differ from the superheated conditions mentioned above in that complete miscibility of the organic and aqueous phases is obtained and the self-ionization constant of water is smaller ( $pK_w \sim 15$  for <sup>1</sup>H<sub>2</sub>O and  $\sim 16$  for <sup>2</sup>H<sub>2</sub>O) than room temperature values.<sup>23,25</sup> This latter property is quite different from that of Kuhlmann et al. in which the self-ionization of water was significantly increased ( $pK_w \sim 11$ ) relative to room temperature conditions.<sup>10</sup> Thus, there is approximately a 5 order of

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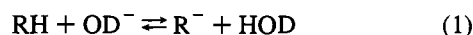
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magnitude difference in the self-ionization constant between the conditions employed by Kuhlmann et al. and this study. This difference would lead to a 2.5 order of magnitude difference for the equilibrium concentration of each ion. These differences arise quite rapidly as the temperature is raised to values above the critical temperature.<sup>1,23</sup> In the temperature and pressure region examined in the work reported here, the water self-ionization constant ( $pK_w$ ) is highly dependent upon solvent density (or pressure) as well as temperature. Variation of 9 orders of magnitude ( $pK_a$  from  $\sim 11$  to  $\sim 20$ ) occurs when the pressure varies from 750 to 250 bars (this pressure variation corresponds with a density change from 0.65 to 0.16 g/mL). Beyond the critical temperature,  $pK_w$  increases, at constant pressure, as the temperatures increases.<sup>23</sup> Below the critical temperature, the variation of  $pK_w$  with pressure is in the opposite direction.<sup>23</sup> The significance of the low value of the self-ionization constant can be illustrated by the general acid-base reaction below:



The equilibrium constant for such a reaction is given by  $K_a/K_w$  where  $K_a$  is the acid dissociation constant of the weak acid, RH, and  $K_w$  the self-ionization constant of  $D_2O$ . Since the  $\Delta H$  for weak acid ionizations is usually positive, one would expect that at the high temperatures required to achieve supercritical conditions the  $K_a$ 's of most acids will be significantly greater than the room temperature values. Therefore, there is a reasonable prospect that organic acids that are too weak to react *via* reaction 1 at 25 °C or even 300 °C may react at 400 °C. For example, assuming that  $\Delta S$  is negligible and that  $\Delta H$  is constant, the acid dissociation constant of benzene would be expected to increase from its room temperature value of  $10^{-43}$  ( $pK_a = 43$ ) to approximately  $10^{-19}$  ( $pK_a = 19$ ) at 400 °C.<sup>26</sup> Thus, within the limitations of these approximations, the equilibrium constant for reaction 1, when RH is benzene, should be on the order of  $10^{-3}$  under the experimental conditions employed in this work. Furthermore, because of the high-temperature reaction conditions rapid kinetics are also anticipated, suggesting that rapid turnover by reaction 1 may be a feasible route to isotopic hydrogen exchange.

In the following pages, the successful application of reaction 1 to the deuteration of weakly acidic carbon-hydrogen bonds is demonstrated. The use of this reaction for the qualitative ordering of relative  $pK_a$  values of extremely weak acids as well as its application to the production of deuterated compounds are discussed, and some unusual observations are reported.

## Experimental Section

Reactions were carried out in sealed high-pressure tubes. Samples were contained in tubes made of 316 stainless steel 0.79 cm outside diameter, 0.095 cm wall thickness, and 3.2 cm in length (cell volume  $\sim 1.1$  cm<sup>3</sup> including cap volumes). The tubes were sealed at each end with a two-ferrule design stainless steel Swagelok cap. This arrangement produced leak free seals up to pressures of 700 bar (10 500 psi).

All organic compounds, except 9,9'-spirobifluorene, investigated in this study were obtained from commercial sources in the highest available purity. Their purity was verified by <sup>13</sup>C NMR spectroscopy, and in all cases, no additional purification was necessary. 9,9'-Spirobifluorene was a gift.<sup>27</sup> Deuterium oxide was obtained in 99.9% isotopic purity from Cambridge Isotope Laboratories.

NaOD and KOD solutions used in this investigation were prepared by dissolving the solid bases in deuterium oxide followed by drying in a rotary evaporator and redissolving in deuterium oxide. Although the

**Table 1.** Fractional Deuterations of Various Compounds

compound	conditions	site	percent deuteration
acenaphthene	<i>a</i>	all	> 80%
acetophenone	<i>b</i>	methyl	> 80%
	<i>b</i>	phenyl	none
	<i>c</i>	methyl	> 80%
	<i>c</i>	phenyl	> 80%
benzene	<i>d-f</i>	all	> 80%
benzotrifluoride	<i>c</i>	all	> 80%
4-bromophenyl phenyl ether <sup>g</sup>	<i>c</i>	phenyl ring	$\sim 50\%$
	<i>c</i>	bromo ring	> 80%
	<i>c</i>	1,4,5,8	> 80%
dibenzothiophene	<i>c</i>	3,6	$\sim 50\%$
	<i>c</i>	2,7	$\sim 70\%$
	<i>c</i>	ortho	> 80%
	<i>c</i>	meta, para	$\sim 65\%$
fluorobenzene	<i>c</i>	ortho	> 80%
	<i>c</i>	meta, para	none
2-methylpentane	<i>c</i>	methyls	$\sim 20\%$ <sup>i</sup>
	<i>h</i>	all others	none
nitrobenzene <sup>f</sup>	<i>c</i>	ortho	> 80%
	<i>c</i>	meta	$\sim 70\%$
	<i>c</i>	para	$\sim 50\%$
	<i>c</i>	all	> 80%
pyrazine	<i>c</i>	all	> 80%
pyridine	<i>c</i>	all	> 80%
9,9'-spirobifluorene	<i>c</i>	all	> 80%
toluene	<i>k</i>	methyl	> 80%
	<i>k</i>	ring	none
	<i>l</i>	methyl	> 80%
	<i>l</i>	ring	> 80%

<sup>a</sup>  $\sim 0.016$  M NaOD, 12 min, 500 °C. <sup>b</sup>  $D_2O$ , 10 min, 400 °C. <sup>c</sup>  $\sim 0.016$  M NaOD, 10 min, 400 °C. <sup>d</sup>  $\sim 0.03$  M  $Na_2CO_3$ , 42 min, 400 °C. <sup>e</sup>  $D_2O$ , 3 min, 400 °C. <sup>f</sup>  $\sim 0.16$  M KOD, 30 min, 340 °C. <sup>g</sup> Decomposition noted, see text. <sup>h</sup>  $\sim 0.16$  M KOD, 150 min, 380 °C. <sup>i</sup> Because of the low percentage of deuteration, the deuterium signal arises from methyl groups having some NOE and, therefore, the deuterium percentage is probably less than the amount calculated from eq 2. <sup>j</sup> Severe decomposition noted, see text. <sup>k</sup>  $\sim 0.03$  M  $Na_2CO_3$ , 10 min, 400 °C. <sup>l</sup>  $\sim 0.016$  M NaOD, 30 min, 400 °C.

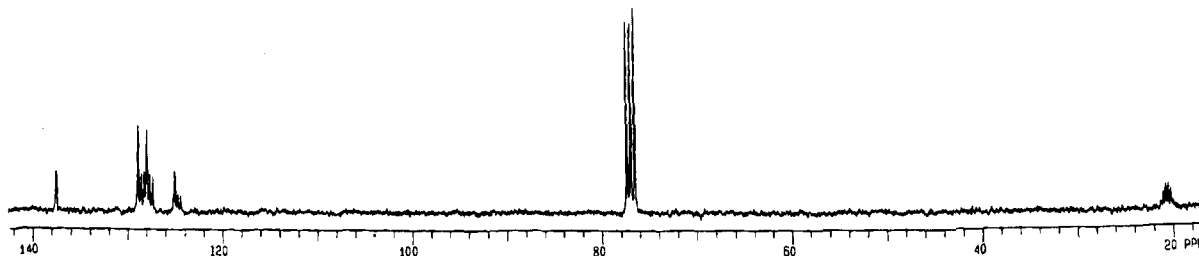
resulting deuteroxide solutions contained some residual <sup>1</sup>H, the amount of <sup>1</sup>H introduced into the reaction mixture was negligible as only a small quantity of base solution relative to the deuterium oxide solvent was used in each reaction. In a few cases, deuteration was observed when  $\sim 0.03$  M  $Na_2CO_3$  was used as the base.

In a typical experiment, the compound being studied was weighed and placed into the reaction tube along with a weighed amount of deuterium oxide or deuterium oxide plus one of the basic solutions. The total amount of solution added to the tube was chosen to yield a solvent density of 0.35 g/mL in the 1.1 mL tube volume. Sample sizes were chosen to be 20% by weight of the deuterium oxide amount. For example, a typical sample consisted of 0.4 g of deuterium oxide, 0.08 g of sample, and 0.06 mL of sodium or potassium deuteroxide solution. The base concentrations reported in Table 1 are the final values expected under supercritical conditions where the sample is homogeneous and occupies the entire tube volume. Each sample was deaerated by bubbling nitrogen gas through it for 5 min. While 5 min of deaeration is probably not sufficient to completely remove all of the oxygen, evidence for oxidation of the solute was found in only one case. Under these conditions, it is estimated from the water-vapor specific volume table that a pressure of approximately 300 bar (4500 psi) is developed at 400 °C.<sup>28</sup> Following sample preparation, the sealed tube reactor was placed into a preheated Leco 571-18 carbon filament furnace. The temperature was measured with a Fluke 52 K/J thermometer equipped with a 80 PK-2A immersion probe. Temperature measurement is believed to be accurate to approximately  $\pm 5$  °C. After heating for the desired time, normally 10 min, the sample tube was removed as quickly as possible and rapidly cooled to room temperature. In all of these experiments, the heat-up time is a small fraction of the total heating

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**Figure 1.**  $^{13}\text{C}$  NMR spectrum of toluene following reaction with 0.016 M NaOD for 30 min at 400 °C. Sample extracted into  $\text{CDCl}_3$  for spectral acquisition.

time and is believed to contribute only slightly to the experimental uncertainty in the deuteration results. Because the same sample heat capacity and heat-up/cool-down times were utilized for each replicate, errors due to the finite heat-up and cool-down rates are believed to be unimportant. Obviously, correction for heat-up/cool-down would be necessary if accurate kinetic information was desired. **Caution:** While this procedure worked well without incident in most cases, occasional tube failure or end cap failure occurred with ejection of material from the furnace. Thus, one must take adequate safety precautions to protect personnel, equipment, and surroundings from this possibility. Tubes could be reused three or four times normally.

Following cool down, sample deuteration was measured by  $^{13}\text{C}$  NMR spectroscopy of the aqueous solution for those compounds that were soluble in water. Compounds that were not soluble in water were extracted into  $\text{CDCl}_3$  for spectral examination. All spectra were obtained on a Varian Gemini 300 NMR spectrometer.

## Results

In order to assess the potential for base-catalyzed deuteration the amount of deuterium incorporation into various locations of the test molecules had to be determined. Because of the relatively large experimental error in both temperature and heating time measurement, it was not considered reasonable to perform quantitative kinetic analyses of the various reactions. Therefore, the amount of deuteration was determined semi-quantitatively. Briefly, the percent deuteration at each site was estimated from the relative signal intensity (peak height) of the singlet obtained for a proton decoupled protonated carbon and the 1:1:1 triplet of the deuterated form of that carbon. Because of a small isotope shift, the 1:1:1 triplet was offset by about 0.5 ppm to more shielded in most cases.<sup>29</sup> A typical experimental spectrum is shown in Figure 1. Because of the nuclear Overhauser enhancement and singlet nature of the proton-decoupled signal, the sensitivity to protonated carbons is much greater than that for deuterated carbons. Assuming that the intensities are not effected by relaxation time differences, the percent deuteration is estimated by eq 2

$$\%D = 900I_D / (9I_D + I_H) \quad (2)$$

where  $I_D$  is the peak height of one of the deuterated triplet signals and  $I_H$  is the peak height of the protonated signal corrected for overlap.

Equation 2 provides a rapid and easy approach to estimating the amount of deuteration at each site in a molecule from its  $^{13}\text{C}$  NMR spectrum. The use of peak heights rather than integrated intensities is justified by the fact that no difference in the experimental peak widths is observable. Because of the reduced dipolar relaxation expected upon deuteration, the CD relaxation time should be longer than the CH, suggesting that relaxation effects will favor the proton signal, and therefore, eq 2 is expected to underestimate the deuteration percentage. Despite the approximations and assumptions inherent in eq 2,

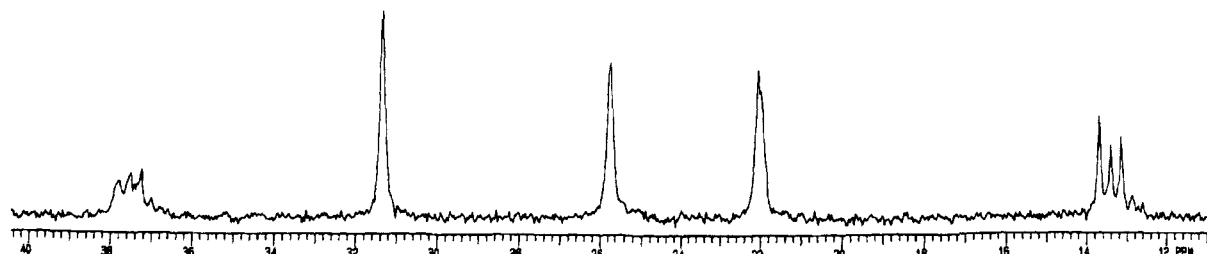
a test spectrum of a synthetic mixture of benzene and benzene- $d_6$  yielded only a 3% (relative) low value for the percentage deuteration when the experimental pulse delay of 20 s was employed. If one considers the number of protons introduced into the reaction medium upon exchange of the sample protons, the maximum possible deuteration in any single experiment (i.e. the equilibrium isotopic purity of the solvent) is approximately 90%, assuming no equilibrium isotope effect. Thus, if the reaction equilibrium and/or rate constants are sufficiently large to produce equilibrium scrambling of the hydrogen isotopes, a %D of approximately 90% is anticipated (this value will vary slightly from experiment-to-experiment depending upon the %H in the sample).

In the interpretation of the deuteration results listed below, the semiquantitative deuteration percentages are interpreted in the following way: if the measured %D is 80% or greater, the relevant reaction is presumed to reach equilibrium under the experimental conditions and the equilibrium and rate constants for reaction 1 are large; if the measured %D is between 80% and 40%, the reaction is considered to be close to equilibrium and the constants for reaction 1 are intermediate; if the %D is less than 40% (but observable), the reaction occurs but is far from equilibrium and the effects of reaction 1 are small; and if no deuterated carbons are observable in the spectrum, either the equilibrium or rate (or both) constants of reaction 1 are too small to observe under the experimental conditions.

Table 1 summarizes the results for a number of compounds of varying acidity. In all cases studied the deuteration either did not occur when base was absent, occurred to a lesser extent, or occurred at fewer sites. For example, acetophenone deuterates only at the methyl position in  $\text{D}_2\text{O}$ , but the methyl and all ring positions deuterate completely (i.e., reach equilibrium) in 10 min at 400 °C in 0.016 M NaOD solution. This result is consistent with those reported by Kuhlmann et al. in which deuteration of  $\alpha$  and  $\alpha'$  positions of ketone carbonyl groups occurred in  $\text{D}_2\text{O}$  at subcritical temperatures but not of less acidic sites ( $\text{p}K_a > 40$ ) such as the toluene methyl group.<sup>10</sup> In this study, deuteration is observed for many sites with  $\text{p}K_a > 40$ , including toluene which deuterates completely at all position (methyl and ring) in basic solution at 400 °C. Although base-catalyzed deuteration has been observed many times, these results are unusual in that deuteration is observed at a variety of unactivated or poorly activated sites.

The base concentrations listed in Table 1 assume that the base is soluble at the experimental conditions employed and that the sample is homogeneous beyond the critical point. While many common salts are highly insoluble in low-density supercritical water, sodium hydroxide is soluble and dissociated in supercritical water.<sup>1</sup> The fluid density employed in this work is more than 3 times greater than the density where low salt solubilities have been measured and the reaction temperature employed is relatively low leading to expectation that the base remains dissolved under the supercritical conditions.<sup>37</sup> Fur-

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**Figure 2.**  $^{13}\text{C}$  NMR spectrum of hexanoic acid following reaction with 0.16 M KOD for 30 min at 400 °C. Carboxylate resonance not shown.

thermore, we have found that deuteration is eliminated or greatly reduced when base is omitted from the reaction medium. Thus, we believe that the enhanced reactivity is not simply a temperature effect but does involve reaction with dissolved base and that the base concentrations under our experimental conditions are those listed in Table 1. The increase in deuteration with increase in base concentration is consistent with a solution reaction rather than a surface reaction with a precipitate.

### Discussion

Examination of the results shown in Table 1 shows that the deuteration reaction can be interpreted in terms of the simple acid–base reaction given in eq 1. Of course, it is possible that under these conditions the product of the acid–base reaction remains together as a  $\text{RHOD}^-$  group rather than as separated  $\text{R}^-$  and  $\text{HOD}$  entities and our results do not distinguish between these possibilities. Nevertheless, it is clear that the ease of deuteration follows the expected acid strengths of the CH bonds involved and that the deuteration rate increases with increases in the basicity of the solvent. Thus, we see that electron-withdrawing groups generally increase the ease of deuteration and that sites nearest the electron-withdrawing groups on aromatic rings deuterate most easily.

Although the reaction conditions employed in this study are very vigorous, in most cases the post heating spectra did not show any indication of any products other than the starting material and its deuterated analogs. Four exceptions to this general observation were cyclohexanol, nitrobenzene, 4-bromophenyl phenyl ether, and benzoic acid. In the case of cyclohexanol, product peaks were observed that indicated the formation of cyclohexanone, presumably formed by oxidation *via* residual oxygen in the solvent and cyclohexene, assumed to form *via* high-temperature dehydration. Similarly dehydrations of cyclohexanol and other alcohols in superheated water have been previously reported.<sup>5,10</sup> The deuterations reported in Table 1 for nitrobenzene are the results from one of many separate experiments. In all these experiments, except the one reported in the table, extensive decomposition, accompanied by gas evolution, in addition to deuteration, occurred. The products of the decomposition were not identified but are presumed to be the result of oxidation by the nitro group and the evolved gas to be one of the nitrogen oxides. Despite several attempts and care in the preparation of samples and duplication of experimental conditions, the successful deuteration without decomposition experiment has not been duplicated to date. It is believed that the inability to repeat these experimental results reflects the fact that the deuteration and oxidation reactions proceed at nearly identical rates and that minor differences in conditions can result in one reaction predominating over the other. Nevertheless, these results do show that it is possible to successfully deuterate even highly energetic nitroaromatics if the proper reaction conditions are employed. Decomposition products were also observed in the 4-bromophenyl phenyl ether

spectrum after one heating experiment, but not another. These decomposition products were not characterized but are assumed to involve loss of bromide. Benzoic acid underwent decarboxylation, and neither it nor other aromatic carboxylic acids were studied further in this work. Decarboxylation of naphthanoic acid formed by the hydrolysis of methyl 1-naphthoate in hot water has been previously reported.<sup>30</sup> Despite our best efforts, the experimental method has sufficient variability from run-to-run that experiments requiring close control of temperature and reaction time are not possible. A flow reactor, currently under construction, should alleviate this problem and allow for meaningful quantitative analysis of these reaction equilibria and kinetics.

Most of the deuteration reactions listed in Table 1 resulted in attainment of equilibrium isotopic distribution in relatively short times despite the fact that some of the compounds studied are extremely weak acids. Among the compounds reported in Table 1, 2-methylpentane is expected to be the weakest acid with a  $\text{p}K_a$  on the order of 50, similar to that of ethane.<sup>26</sup> Although stronger base (0.16 M KOD) and a much longer heating time (150 min) compared to compounds with  $\text{p}K_a$ 's < 45 was required to achieve measurable deuteration of this compound, these results indicate that hydrogens with  $\text{p}K_a$ 's on the order of 50 can be exchanged in reasonable times under supercritical conditions. It is interesting to note that only the methyl groups deuterated under the conditions employed, demonstrating that the methyl CH bonds, while exceedingly weak acids are stronger acids than the other carbon hydrogen bonds in this alkane (and presumably, others as well). This is consistent with the greater stability of a carbanion centered on methyl and is consistent with the view that the reaction ease is governed by the acid strength of the reactant.<sup>31</sup>

The greater acidity of terminal methyls on long chain alkyl groups was observed also in the reactivity of the straight chain carboxylic acids: valeric, hexanoic, and palmitic acids. In each of these compounds, the carbon  $\alpha$  to the carboxylate deuterated quickly under typical conditions (0.016 M NaOD, 10 min, 400 °C) as expected from the strong electron-withdrawing power of the carboxylate group. However, when heated in 0.16 M KOD for 30 min at 400 °C, in each case the terminal methyl group, and only the terminal methyl group, also deuterated. Because in these cases mono-, di-, and trideuteriomethyl carbons were formed in comparable amounts and partially deuterated groups would be expected to have at least partial Overhauser enhancements, the error involved in estimating the percent deuteration from eq 2 was deemed too large to allow for even semiquantitative estimation. Therefore, no attempt was made to quantify the percent deuteration. The spectrum shown in Figure 2 demonstrates that substantial deuteration has occurred, however. This was not a problem for the data in Table 1 because those deuterations either involved CH groups where

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(31) Bates, R. B.; Ogle, C. A. *Carbanion Chemistry*; Springer-Verlag: New York, 1983; pp 17–25.

only monodeuteration was possible or resulted in almost complete trideuteration of the methyl. Thus, the >80% deuteration of the toluene methyl means >80% production of CD<sub>3</sub>.

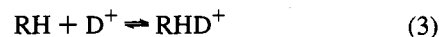
We have also observed an unusual deuteration pattern in the compound dibutylamine. When dibutylamine was reacted in 0.016 M NaOD for 20 min at 400 °C, deuteration was noted at carbons 1 and 3. Reaction for 42 min resulted in some deuteration of the terminal methyls as well. These results suggest an alternation in pK<sub>a</sub> value along the alkyl chain and that the terminal methyl is not the most acidic carbon in this case. We do not have an adequate explanation for this observation at the current time but do note that theoretical calculations have predicted an alternation of electrostatic charge along some alkyl chains, although calculations of electrostatic potentials suggest that no reactivity differences occur as a result of this charge alternation.<sup>32-34</sup> Additional studies aimed at testing the generality of the unusual alternation of deuteration site are currently in progress. In these studies, the deuteration patterns of compounds reported to have large charge alternations are being measured.<sup>32,33</sup>

The results reported in this paper have all been consistent with reaction *via* eq 1 with the ease of deuteration correlating with the acid strength of the CH bond. Other studies still in progress indicate that highly activated aromatic compounds, such as phenol and aniline, deuterate by a mechanism better described as electrophilic substitution.<sup>35,36</sup> These data will be reported when completed in a future communication.

While we cannot unequivocally exclude possible involvement of the metal tube in the mechanisms of these reactions, we believe that any wall involvement is minor. This belief is based upon the observation that no significant difference in deuteration properties are observed when tubes are reused despite the fact that obvious surface changes have occurred from the heating process. Furthermore, in none of the basic studies were any metal ions found in the resulting solution phase after reaction. Finally, we note that difficult to deuterate groups deuterate more easily in the more concentrated base solutions, consistent with a mechanism in which reaction with the dissolved base is involved.

One might reasonably expect that reactivity with D<sup>+</sup>, as in eq 3, would also be enhanced by the small ion product of supercritical water because the equilibrium constant for reaction

3 is equal to K<sub>b</sub>/K<sub>w</sub> where K<sub>b</sub> is the base ionization constant for the weak base RH. In one experiment to test the application



of this complementary reactivity, benzene was found to deuterate in acid solution. However, because of the extremely high temperature and acidic conditions, rapid reaction with the stainless steel tubes used in this work was observed; therefore, no additional experiments were performed. Future studies will examine the applicability of reaction 3 in glass-, quartz-, or sapphire-lined reaction containers that can be expected to survive the acidic reaction conditions better.

## Conclusions

Supercritical water can be an effective reaction medium for acid-base reactions. The great pressure sensitivity of solvent properties, especially the self-ionization constant, near and beyond the critical temperature indicates that it may be possible to adjust the magnitude of the reaction equilibrium constant by adjustment of the reaction pressure, and hence, additional reaction selectivity may be possible. The potential utility of the experimental conditions outlined in this paper for the production of deuterated materials is substantial. While the currently available experimental technique is not sufficiently controllable to selectively deuterate sites of only slightly different acidity, the potential for the selective deuteration according to individual site pK<sub>a</sub>'s is feasible with suitable control of reaction conditions and time. Reactivity in superheated water according to acidities within a molecule has been suggested by Kuhlmann et al.<sup>10</sup> Acids with room temperature pK<sub>a</sub> values as low as 50 can be deuterated in reasonable heating times with sufficiently concentrated basic media. Similar selectivity and equilibrium constants are anticipated for the complementary reaction of D<sup>+</sup> with organic bases. Conceivably, organic bases having pK<sub>b</sub>'s as low as 50 may be reacted in experimentally practical times.

In addition to the practical application to compound deuteration, these exchange reactions can provide important information on the relative acidities of extremely weak acids and the relative ordering of acidities within a molecule. Such information is fundamentally important to understanding many facets of chemical reactivity. In addition to serving as a means to measure relative acid strengths of extremely weak acids, application of reaction 3 in a suitably inert vessel can be anticipated to yield comparable information on the relative basicity of extremely weak bases as well.

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