Kinetics of Deuterium Exchange on Resorcinol in D_2O at High Pressure and High Temperature

Shi Bai, Bruce J. Palmer, and Clement R. Yonker*

Environmental and Energy Sciences Division, Pacific Northwest National Laboratory,
Richland, Washington 99352

Received: April 12, 1999; In Final Form: August 23, 1999

The kinetics of deuteration of resorcinol in pure D_2O were studied for the first time using a flow-through capillary tubular reactor with on-line, proton, and deuterium NMR detection at high temperatures and high pressure. The global rate constants for hydrogen/deuterium (H/D) exchange were determined from temperatures of 200−450 °C (723 K) at a pressure of ∼400 bar (the critical temperature and pressure of water are 374.2 °C and 218.3 bar, respectively). The H/D exchange rate in resorcinol (1,3-dihydroxybenzene) under these extreme conditions was determined using proton NMR as a function of the resorcinol residence time in a capillary tubular reactor, which also served as a high-pressure NMR cell. The ^1H and ^2H NMR results indicate that H/D exchange in resorcinol for the ring protons was observed at temperatures as low as 200 °C. The kinetics of H/D exchange in resorcinol and the activation energy was extracted from the experimental ^1H NMR data.

Introduction

In subcritical and supercritical water the hydrothermal oxidation of many organic compounds is enhanced due to the increased reactivity of the substrate with water and the enhanced solubility of nonpolar organic compounds at these high temperatures. The increased reactivity of organic compounds in subcritical water shows potential for the oxidative destruction of toxic and organic wastes.[1,2] Because of the enhanced miscibility of many nonpolar organic compounds with supercritical water, this solvent may prove to be a new reaction medium for organic chemistry.[3,4]

Hydrogen/deuterium (H/D) exchange of some extremely weak organic acids in subcritical and supercritical water has been investigated.[5−7] Yao and Evilia[5] estimated the equilibrium constant for H/D exchange of benzene with OD^- to be 3 orders of magnitude higher at 400 °C than at 25 °C in water. The hydrogen in the ortho position was found to be slightly more acidic than those in the meta or para positions for the substituted benzene compounds of fluorobenzene, 1,2-diphenylhydrazine, and nitrobenzene, when reacted under basic conditions in D_2O at 400 °C.[5] However, Yao and Evilia encountered difficulties when attempting to obtain quantitative chemical kinetic data for these reactions due to the large experimental errors in determining temperature, pressure, and heating time when using a batch reactor. Kuhlmann et al.[6] reported the first-order global rate constant (1.47×10^{-4} s^{-1}) for H/D exchange of the α-methyl protons in pinacolone at 225 °C and 25.4 bar using a batch reactor.

In situ, real time Raman spectroscopy has been used in the kinetic investigations of the oxidation of methane,[8] methanol,[9] and water−gas shift reactions[10] in supercritical water. Fiber-optic[11] and other Raman spectroscopic methods[12] have been applied to examine the rates of chemical reactions in supercritical water. Other techniques, such as fluorescence, UV−vis, and IR, have also been used to characterize reactions in subcritical and supercritical water.[11] Recently, a review of reactions at supercritical water conditions has been published by Savage.[13]

NMR has not been widely used for in situ investigations of reactions in supercritical water; its main use has been to monitor batch reaction products after quenching.[6,14] There is one report of the in situ monitoring by NMR of hydrogen exchange in supercritical water.[15] The use of NMR detection for the in situ study of chemical kinetics generally requires that the NMR data acquisition time for a spectrum be much shorter than the reaction half-life. With flow-through NMR,[16−18] it is possible to investigate chemical reactions provided the equilibrium Boltzmann distribution of nuclei spin states is not violated by rapid flow rates. Applications and technical concerns using flow NMR have been previously discussed.[19−21]

We describe our experimental effort using a novel combination of a high-pressure, high-temperature flow-through capillary tubular reactor with on-line NMR detection for the investigation of reaction kinetics in subcritical and supercritical water. High-temperature, high-pressure ^1H NMR allowed the measurement of peak area, and therefore concentration of reactant as a function of reactor residence time. ^2H NMR was used to monitor the extent of the deuteration reaction under similar conditions. We assume that steady-state concentration conditions are rapidly achieved in the heated portion of the capillary due to the very low thermal impedance of the capillary reactor wall (∼90 μm thick), which should contribute to the rapid heating of the solution. Of course, this is dependent on the flow rate through the capillary, but over the flow range studied, we believe this assumption to be valid. Using this high-temperature, high-pressure, microvolume flowing NMR technique, the kinetics of H/D exchange of resorcinol in subcritical and supercritical water were studied. The global rate constant for H/D exchange was determined by the disappearance of the α-hydrogens in resorcinol (reactant) under these extreme conditions. The kinetic data for the resorcinol H/D exchange reaction in pure D_2O and

---

* Corresponding author. E-mail: clem.yonker@pnl.gov.

10.1021/jp991192r CCC: $19.00

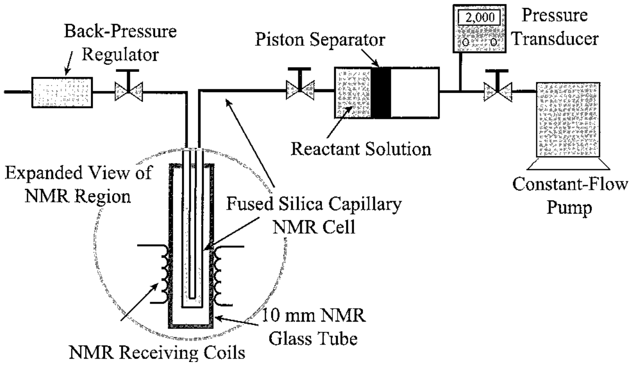

Figure 1. Schematic diagram of the apparatus used for the high-pressure, high-temperature flow-through capillary tubular reactor with on-line NMR detection.

the difference in the reactivity between the α- and β-hydrogens in resorcinol are discussed.

Experimental Section

Sample Preparation. Resorcinol (Aldrich Chemical Co., Inc., 99+%) was used without further purification. To deoxygenate the solution, D_2O (Cambridge Isotope Laboratories) was boiled for 5 min under dry nitrogen and a 20% (w/w) (~2.2 M) resorcinol−D_2O solution was prepared and purged using dry nitrogen for 10 min.

Flow-Through NMR. A schematic of the experimental system is shown in Figure 1. This system includes a high-pressure syringe pump (ISCO 260D), a tubular piston separator (HIP), a fused-silica capillary NMR cell (180 μm i.d. by 360 μm o.d., Polymicro Technologies, Inc), and back-pressure regulators (Upchurch Scientific). In practice, the resorcinol−D_2O solution was loaded into one side of the piston separator and the other side was filled with water and connected to the syringe pump. The fused silica capillary was bent in a U shape and placed in a 10 mm glass NMR tube so that the bent end did not extend below the bottom edge of the NMR sensitive region along the *z*-axis. One end of the capillary tube was connected to the solution outlet of the piston separator, and the other end of the capillary was connected to the back-pressure regulators. When the high-pressure syringe pump was operated in a constant volumetric flow rate mode, the sample pressure was controlled by the back-pressure regulators. Five back-pressure regulators (~80 bar each) were used in series so that the sample pressure was maintained between 380 and 400 bar depending on the flow rate.

The residence time (t_R) of the resorcinol in the heated region of the capillary can be determined as

$$t_R = V^{cap}(\rho'/M_R) \tag{1}$$

where ρ' is the density in the heated region, V^{cap} is the volume of the capillary within the NMR detection region, and M_R is the mass flow rate of the solution in the heated reactor. The difficulty is accurately determining the mass flow rate of the solution. Since, the mass flow rate is constant throughout all temperature regions of the capillary, one can write a similar equation for residence time at room temperature. Equating the two mass flow rates, allows one to express the residence time of resorcinol in the heated region in terms of the volumetric flow rate at room temperature as

$$t_R = (\rho'/\rho)(V^{cap}/f_r) \tag{1'}$$

Here ρ is the solution density at room temperature and f_r is the volumetric flow rate of the high-pressure pump at room temperature. A step profile is assumed for the temperature gradient in the reactor region. Using the inner diameter (180 ± 6 μm) of the capillary and twice the length of the NMR receiving coil (3.90 cm), the volume of the NMR detection region was estimated to be $\sim 9.8 \times 10^{-4}$ mL (0.98 μL). The density at high temperature was approximated using the density of pure D_2O at the experimental temperature and pressure.[22]

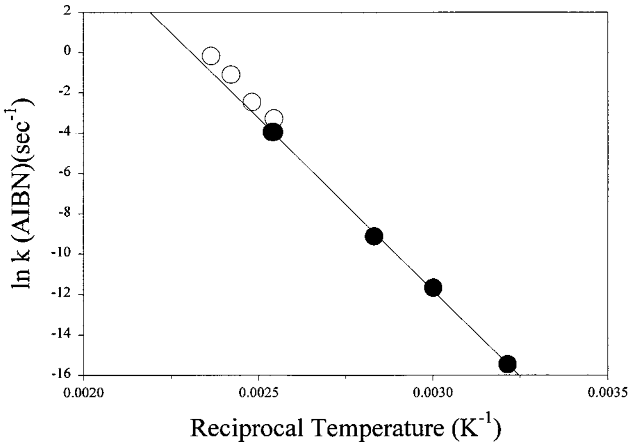

Figure 2. Plot of the natural logarithm of the rates for the thermal decomposition of AIBN from ref 24 (●) versus reciprocal temperature compared to the experimental rate constants (○) determined by the flow-through NMR technique.

A standard reaction was chosen for initial investigation with the capillary flow-through reactor using the well-characterized thermal decomposition of 2,2′-azobis(isobutyronitrile) (AIBN), a radical initiator. The thermal decomposition of this molecule was investigated in the same manner as outlined in the Experimental Section for resorcinol. The temperature range investigated was 120−150 °C at ~190 bar, in this case using perdeuterated benzene as the solvent. The first-order rate constants were determined at four different temperatures and from an Arrhenius plot of the data, an *A* factor of 1.57×10^{18} s^{-1} ($\ln A = 41.9 \pm 3.2$) and an activation energy (E_a) of 35.3 ± 2.6 kcal/mol were obtained. The values reported in the literature using standard techniques for AIBN are $A = 1.58 \times 10^{15}$ s^{-1} and $E_a = 30.8$ kcal/mol.[23,24] At 120 °C the rate constant for thermal decomposition of AIBN is 0.0193 s^{-1}.[24] The value determined using the flow-through NMR technique is 0.0375 ± 0.0118 s^{-1}. Figure 2 is a plot of the natural logarithm of the experimental rates for AIBN compared with the literature values versus reciprocal temperature.[24] The two sets of data are comparable. The derivations of the concentration profile in the NMR reactor cell will be discussed in the next section.

The accuracy of the solute residence time in the heated region also depends on the volumetric flow rate of the pump. A system calibration was performed at room temperature and a pressure of 400 bar by collecting and weighing the water eluted from the capillary at specific flow rates over a set time interval. We found a 1:1 relationship between the pump volumetric flow rate and the measured volumetric flow rate over the range of interest.

NMR Measurements. The NMR data for the AIBN thermal degradation experiments was obtained on a Varian VXR 300 NMR spectrometer, while the resorcinol−D_2O H/D exchange experiments were performed on a Chemagnetics CMX-300 wide-bore spectrometer operating at 299.3 and 46.13 MHz for proton and deuterium detection, respectively. A high-temperature, high-resolution, specially built broad band 10 mm NMR probe (Doty Scientific, Inc.) was used for the D_2O experiments.

The resolution was 8−10 Hz for proton and 4−8 Hz for deuterium in the resorcinol−D_2O solution in the capillary cell at room temperature, which generally improved at higher temperatures due to a decrease in viscosity of the resorcinol−D_2O solution. The *z*-axis temperature profile for the high-temperature probe was determined. The temperature at various positions in the NMR sensing region was measured using a calibrated thermocouple along the *z*-axis at 325 °C. A temperature deviation of ±5 °C was noted in this calibration. The relative reproducibility in the temperature setting of the probe is estimated to be about ±2 °C for low (<250 °C) and ±5 °C for high (>250 °C) temperatures, respectively. The calculated Reynolds number for the conditions investigated in the capillary was <200, indicating laminar flow. On the basis of laminar, parabolic flow, the average heat-transfer coefficient can be determined by assuming a uniform wall temperature at the capillary surface. The bulk solution temperature can then be determined at some distance, *x*, down the capillary reactor. The temperature of the bulk solution was determined to be equal to the wall temperature at the capillary surface at 10% or less of the total reactor length for all conditions studied. The only exception was determined to be at the highest flow rate and the highest temperature where the value was 14%.

In a typical experiment, the resorcinol−D_2O solution is flowing through the capillary high-pressure NMR cell[25,26] at constant temperature and pressure. Concurrent with solution flow, a NMR experiment is co-adding transients until a satisfactory spectrum with an adequate signal-to-noise ratio is obtained. Since the heated region of the capillary is an integral part of the NMR capillary cell, a steady-state concentration of the product and reactant is established during the experiment. Generally, 64 and 128 transients were accumulated for proton and deuterium measurements, respectively. The sample temperature was changed with each flow rate at a constant pressure and the ^1H peak area was determined. The parameters for ^1H NMR were an acquisition time of 0.25 s, spectral line broadening of 1 Hz, and a flip angle of 45° and for ^2H NMR, an acquisition time 0.7 s, spectral line broadening of 1 Hz, and a flip angle of 36°, respectively.

In flow NMR, the observed spin−lattice relaxation rate can be considered a summation of the static relaxation rate ($1/T_1$) and a contribution from the sample flow,[19,20,27]

$$(1/T_1)_{\mathrm{obs}} = (1/T_1) + 1/t_{\mathrm{R}} \tag{2}$$

where t_R is the residence time. The proton T_1 for water in our resorcinol−D_2O solution ranges from 4.1 to 8.3 s over 25−350 °C. The proton T_1 for resorcinol is shorter than water in the resorcinol−D_2O solution. According to eq 2, the observed T_1 over the experimental volumetric flow range is smaller than the static values reported above. A ^1H NMR pulse repetition time of $3T_1$(static) was used throughout the measurements in order to facilitate quantitative analysis and compare results for different flow rates and temperatures. The reproducibility of the proton peak area integral for resorcinol is ∼10%.

Results and Discussion

Resorcinol Proton NMR. The proton spectra as a function of temperature are shown in Figure 3, at a constant volumetric flow rate of 0.010 mL/min. The chemical shifts were referenced externally with respect to tetramethylsilane (TMS). Of the two peaks between 6 and 8 ppm, the lower field peak is the *β*-hydrogen and the higher field peaks are the α- and α′-hydrogens, respectively. The peak at ∼4 ppm represents protons from residual water and HDO, which results from the exchange between the D_2O solvent and the hydroxyl protons on resorcinol. A second source of HDO results from the H/D exchange reaction of the ring protons on resorcinol. Note that the relative peak area of the α-hydrogens decreases and the peak area of hydrogen in HDO increases as the reaction temperature increases due to exchange with D_2O. Another observation in Figure 3 is that the chemical shift of the water peak moves to a higher field strength. This chemical shift change is composed of two contributions, a change in the solution's magnetic susceptibility with density and a weakening of the hydrogen bond network in water at higher temperatures.[28] This observation has been seen for both water and methanol[29,30] at supercritical conditions. The opposite behavior is noted for both the α- and *β*-protons in resorcinol. The variation in chemical shift of the resorcinol ring protons is related to a change in solution density (change in magnetic susceptibility) with temperature.

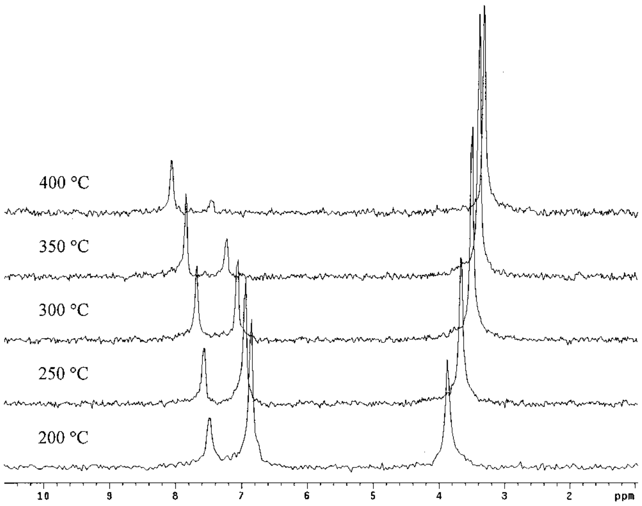

Figure 3. Temperature-stacked ^1H NMR spectra at a constant volumetric flow rate of 0.010 mL/min. The disappearance of the α and the α′-proton in resorcinol can be seen.

The reaction of substituted benzene in basic solutions of D_2O has been discussed by Yao and Evilia.[5] The H/D exchange mechanism for resorcinol in pure D_2O is facilitated by the presence of electron-withdrawing groups on the aromatic ring. This activated aromatic ring is deuterated through an electrophilic substitution mechanism, which increases the ease of deuteration under these experimental conditions and eliminates the need of either an acid or base to catalyze the reaction.[5,31] Resorcinol is an ortho/para director in electrophilic substitution reactions.[32] Therefore, H/D substitution would be facilitated for the α- and α′-hydrogens and not for the meta hydrogen (*β*-hydrogen). The experimental results presented in Figure 3 demonstrate the positional selectivity of the H/D electrophilic substitution reaction under these extreme conditions. The *β*-hydrogen can serve as an internal molecular standard relating the stability of resorcinol to hydrothermal oxidation or hydrolysis reactions under these conditions. Benzene, toluene, and fluorobenzene[5] (400 °C, 300 bar), and *o*-, *m*-, and *p*-cresol[33] (460 °C, 254 bar), were found to be relatively stable to hydrolysis in supercritical water under the conditions listed for residence times of 30 s to 10 min. In fact, hydrolysis of resorcinol at 460 °C and 254 bar was reported to produce a maximum of 10% conversion, for residence times of 1−7 s at 0.01 M solution concentration.[33] Our ^1H NMR results demonstrated the relative stability of the *β*-proton to any side reactions during our experimental investigations.

Kinetics of the H/D Exchange Reaction. The peak areas of the α- and α′-protons were determined as a function of residence time at constant temperature for a series of different temperatures. Harris[34] has discussed the influence of isotope effects and concluded that H/D exchange will always be approximately first order. This is also supported from the results of Kuhlmann et al.[6] From the NMR investigation of the qualitative behavior of both the α- and β-protons in resorcinol, it appears that a possible reaction scheme is

$$\begin{tikzcd} \mathrm{R{-}H} \arrow[r, "k_h"] \arrow[d, "k_T"] & \mathrm{R{-}D} \arrow[d, "k_T"] \\ \mathrm{X} & \mathrm{X} \end{tikzcd} \tag{3}$$

where R−H is resorcinol, R−D is deuterated resorcinol, k_h is the rate of H/D substitution determined from α-proton disappearance, k_T is the hydrolysis rate, and X represents a potential hydrolysis product. The hydrolysis rate can be determined from the rate of disappearance of the β-proton and is assumed constant and independent of the reactant (R−H or R−D). The rate expressions for H/D exchange are

$$dC_H/dt = -k_hC_H - k_TC_H \tag{4}$$

$$dC_D/dt = k_hC_H - k_TC_D \tag{4′}$$

where C_H is the concentration of the resorcinol, C_D is the concentration of the deuterated resorcinol, and t is time.

For the sake of simplicity, we assume an ideal plug-flow tubular reactor under the experimental conditions investigated. Therefore, the local rate equation in the capillary tubular reactor under flowing conditions is

$$dC_H/dt = -k_hC_H - k_TC_H - u\,dC_H/dl = 0 \tag{5}$$

where u is the solution linear velocity and l is the length along the tubular reactor. The steady-state solution for this equation is

$$C_H = C_H{}'e^{-(k_h+k_T)l/u} \tag{6}$$

where the concentration at the reactor inlet ($l' = 0$) is $C_H{}'$ ($C_H{}'$ is the initial concentration of resorcinol).

NMR measures the number of protons in the capillary cell, which is assumed to be equal to the length of the heated region of the capillary. Thus,

$$\mathrm{C_H} = 1/L\int C_H\,dl \tag{7}$$

where L is the length of the tubular reactor. The average concentration of the protonated resorcinol, $\mathrm{C_H}$, can be determined by substituting the concentration profile for C_H (eq 6) into eq 7 and then integrating over the NMR detection length. The average concentration of the protonated resorcinol measured by ^{1}H NMR, $\mathrm{C_H}$, expressed in terms of the reaction rate constant and residence time, t_R, is

$$\mathrm{C_H} = [C_H{}'/(k_h + k_T)t_R](1 - e^{-(k_h+k_T)t_R}) \tag{8}$$

$C_H{}'$ is approximated by the peak area of the α-protons of resorcinol at 25 °C. As $t_R \rightarrow \infty$, $\mathbf{C_H} \rightarrow 0$ and one would anticipate that the H/D substitution reaction goes to completion and the average protonated resorcinol concentration in the reactor is negligible. As $t_R \rightarrow 0$, $\mathbf{C_H} \rightarrow C_H{}'$, the H/D substitution reaction does not occur and the resorcinol concentration will equal the starting resorcinol concentration, $C_H{}'$.

TABLE 1: Global First-Order Rate Constants of H/D Exchange in Resorcinol Determined Using High-Pressure/High-Temperature ^{1}H NMR

T (°C)	$k_h{}^a$ (s^{-1})
200	0.018(±0.006)
250	0.11(±0.04)
300	0.40(±0.15)
350	0.92(±0.34)
400	2.6(±0.8)
450	2.8(±1.1)

[a] Global first-order rate constants determined from the α-proton disappearance in resorcinol using eq 8. The nonlinear least squares fit for k_h was constrained by $0.0 < k_T < 0.046$. The values in parentheses represent the error in the determined rate constants.

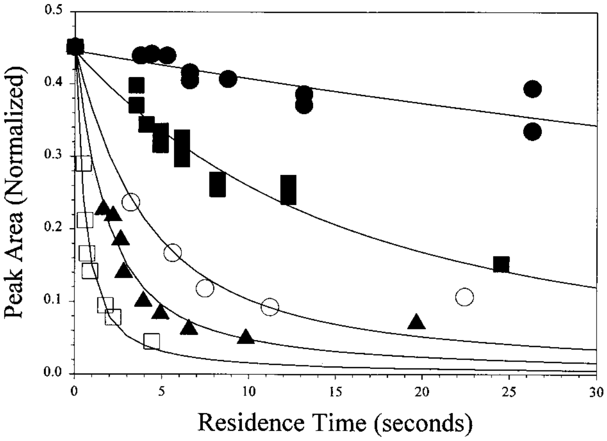

Figure 4. Plot of the normalized peak area of the proton concentration measured by ^{1}H NMR versus residence time for the different temperatures of (●) 200 °C, (■) 250 °C, (○) 300 °C, (▲) 350 °C, and (□) 450 °C. The solid lines are the nonlinear least squares fit to the data using eq 8. The rate constants determined from the fit to the data are listed in Table 1.

One can determine the first-order global rate constant for H/D substitution by solving for k_h, at the different temperatures using the experimental $\mathrm{C_H}$ values and the various volumetric solution flow rates. The importance of hydrolysis was determined using eq 8 with k_h set to zero using the peak area of the β-proton for all the temperatures investigated. The average value for k_T determined in this manner was ~0.046 ± 0.011 s^{-1}, because it was so small its variation with temperature was outside our limits of determination. Therefore, the hydrolysis rate is not anticipated to be significant over this temperature range as compared to the H/D exchange rate. The first-order global rate constants for H/D substitution determined by α-proton disappearance are listed in Table 1. These values were determined by allowing k_T to vary between 0.0 and 0.046 s^{-1} during the nonlinear least-squares fit to eq 8 of the experimental data. A plot of $\mathrm{C_H}$ versus residence time for several temperatures ranging between 200 and 450 °C is shown in Figure 4. The solid lines are the fit to the experimental ^{1}H NMR data using eq 8 and the parameters listed in Table 1. From the temperature dependence of the first-order global rate constants, the activation energy may be estimated from an Arrhenius plot, which is shown in Figure 5. The activation energy for H/D substitution obtained from the ^{1}H NMR data of resorcinol for α-proton disappearance is 14.1 ± 1.8 kcal/mol.

Deuterium NMR. As the reaction temperature increases to 200 °C, the deuterium NMR spectrum showed a new peak with a chemical shift of 7.2 ppm. The chemical shift difference between this peak and that of D_2O at 200 °C is 3.0 ppm, which is the same as the chemical shift difference between the

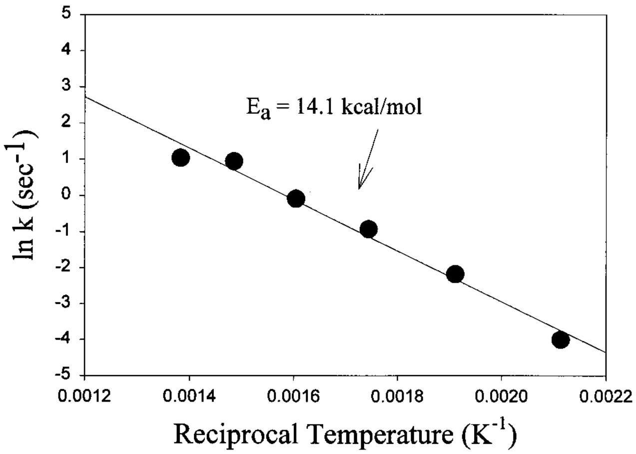

Figure 5. Arrhenius plot of ln *k* versus reciprocal temperature for proton disappearance in resorcinol.

α-hydrogens and water in the ^{1}H NMR measurement at the same temperature. Therefore, this resonance was assigned to resorcinol deuterated at the α-position. This observation demonstrated that H/D exchange did indeed occur for the resorcinol−D_2O solution at 200 °C for long reactor residence times. Deuterium NMR proved useful in following the reaction and confirming that H/D substitution had occurred at the different temperatures in the flow-through reactor.

Conclusions

An advantage of the flowing capillary NMR technique is the combination of the capillary tubular reactor with the high-pressure, high-temperature NMR cell. The microvolume and low thermal impedance of the capillary tubing contribute to the rapid temperature equilibration in the flow-through reactor region in the NMR probe. There are criteria to consider in using a flow-through NMR probe to study reaction kinetics. One important criteria includes the reaction half-life, which must fall within the ability to control solute residence time through volumetric flow rates. Realistically, this limits the reaction half-lives in the flowing system to between ~0.1 and 60 s. Faster reactions require higher volumetric flow rates (shorter residence time) and would be impossible to quantitatively measure if the T_1 value (relaxation time) of the molecule is too large, due to the Boltzmann distribution of the nuclei not being established in the magnet prior to chemical reaction in the flow-through reactor region. Slower reactions are difficult to quantitate due to the lower limit set by the pump volumetric flow rate control.

Considering the large temperature range amenable to NMR studies, coupled with investigating a molecule having a fast T_1 (or combined with a relaxation agent), this technique could prove useful in characterizing first-order kinetics under extreme conditions of temperature and pressure, which are difficult to address by other techniques. The temperature range investigated for the AIBN thermal decomposition in perdeuterated benzene was 120−150 °C and for the H/D exchange reaction of resorcinol in D_2O was 200−450 °C. A potential advantage in a flowing, steady-state concentration experiment is that a large number of spectra can be obtained to enhance the S/N ratio. Solution usage does not limit the experimental time because of the microliter volume of the capillary.

The investigation of the first-order kinetics of the thermal decomposition of AIBN in perdeuterated benzene proved useful in validating the technique for use under pressure and temperature. At 120 °C the rate constant for thermal decomposition of AIBN is 0.0193 s^{-1}.[24] The value determined using the flow-through NMR technique is 0.0375 ± 0.0118 s^{-1}. The reaction half-lives determined using the flow-through NMR method for AIBN over the temperature range 120−150 °C are shown in Figure 2. Over this temperature range the thermal decomposition of AIBN in the capillary reactor appears well behaved and follows the reported literature data.

For resorcinol the H/D exchange reaction occurred at lower temperatures than previously reported for substituted benzene compounds (fluorobenzene, 1,2-diphenylhydrazine, nitrobenzene),[5] but over similar temperatures as reported for 4-ethylphenol by Hoffmann and Conradi.[15] On the basis of ^{2}H NMR, it was apparent that H/D exchange had occurred at 200 °C for long residence times. Kuhlmann et al.[6] reported a rate of deuteration of the α-methyl protons in pinacolone in pure D_2O at 225 °C and 25.4 bar (370 psi) as 8.8×10^{-3} min^{-1} (1.47×10^{-4} s^{-1}) with an activation energy of ~20.0 kcal/mol over a temperature range of 200−250 °C. This rate is more than 2 orders of magnitude smaller than our reaction rate at 250 °C for the α-protons on resorcinol. The larger activation energy of H/D exchange in pinacolone as compared to our measured E_a for resorcinol does support a slower rate constant for pinacolone.

An advantage in using NMR is the detection of specific nuclei of interest and the elimination of spectral interference due to differences in chemical shifts. Of course for NMR, this will be limited on the basis of sensitivity issues. Other nuclei of potential interest, such as ^{19}F, ^{31}P, or ^{13}C, could be investigated under extreme conditions of pressure and temperature. The molecular structure information (α- and β-protons) obtained during these studies proved important in determining the contribution of the hydrolysis reaction during H/D substitution. Global rate constants for higher order reactions could ultimately be determined in a similar manner using this technique.

There have been numerous investigations of hydrogen bond structure and molecular dynamics of subcritical and supercritical water by high-temperature, high-pressure NMR.[35] This investigation demonstrates the use of a microvolume, flow-through tubular reactor with on-line NMR detection to study reaction kinetics under the extreme conditions of subcritical and supercritical water. Considering the assumptions made in this study, the probable error in the rate constants is in the range of 20−50%. These are acceptable in light of the extreme conditions under which they were determined and in light of being obtained in real time using on-line NMR detection. Further efforts are in progress to reduce the error in these measurements and in studying other systems in supercritical water.

Acknowledgment. Work at the Pacific Northwest National Laboratory (PNNL) was supported by the Office of Science, Office of Basic Energy Sciences, Chemical Sciences Division of the U.S. Department of Energy, under Contract DE-AC076RLO 1830. Helpful suggestions from John L. Fulton and Harold R. Udseth were greatly appreciated.

References and Notes

(1) Yang, H. H.; Eckert, C. A. *Ind. Eng. Chem. Res.* **1988**, *27*, 2009.

(2) Webley, P. A.; Tester, J. W.; Holgate, H. R. *Ind. Eng. Chem. Res.* **1991**, *30*, 1745.

(3) Shaw, R. W.; Brill, T. B.; Clifford, A. A.; Eckert, C. A.; Frank, E. U. *Chem. Eng. News* **1991**, Dec. 23, 26.

(4) Siskin, M.; Katrizky, A. R. *Science* **1991**, *254*, 231.

(5) Yao, J.; Evilia, R. F. *J. Am. Chem. Soc.* **1994**, *116*, 11229.

(6) (a) Kuhlman, B.; Arnett, M.; Siskin, M. *J. Org. Chem.* **1994**, *59*, 3098. (b) Kuhlman, B.; Arnett, M.; Siskin, M. *J. Org. Chem.* **1994**, *59*, 5377.

(7) (a) Werstiuk, N. H.; Timmins, G. *Can. J. Chem.* **1989**, *67*, 1744. (b) Werstiuk, N. H.; Timmins, G. *Can. J. Chem.* **1985**, *63*, 530.

(8) Rice, S. F.; Steeper, R. R.; Aiken, J. D. *J. Phys. Chem. A* **1996**, *100*, 184.

(9) Rice, S. F.; Hunter, T. B.; Ryden, A. C.; Hannush, R. G. *Ind. Eng. Chem. Res.* **1996**, *35*, 2161.

(10) Rice, S. F.; Steeper, R. R.; Aiken, J. D. *J. Phys. Chem. A* **1998**, *102*, 2673.

(11) Bell, W. C.; Booksh, K.; Myrick, M. L. *Anal. Chem.* **1998**, *70*, 332.

(12) Masten, D. A.; Foy, B. R.; Harradine, D. M.; Dyer, R. B. *J. Phys. Chem.* **1993**, *97*, 8557.

(13) Savage, P. E. *Chem. Rev.* **1999**, *99*, 602.

(14) Grimaldi, J.; Baldo, J.; McMurray, C.; Sykes, B. D. *J. Am. Chem. Soc.* **1972**, *94*, 7641.

(15) Hoffmann, M. M.; Conradi, M. S. *J. Supercrit. Fluids* **1998**, *14*, 31.

(16) Singer, J. R. *Science* **1959**, *130*, 1652.

(17) Fyfe, C. A.; Cocivera, M.; Damji, S. W. H. *Acc. Chem. Res.* **1978**, *11*, 277.

(18) (a) Laude, D. A.; Lee, R. W−K.; Wilkins, C. L. *Anal. Chem.* **1985**, *57*, 1281. (b) Laude, D. A.; Lee, R. W−K.; Wilkins, C. L. *Anal. Chem.* **1985**, *57*, 1286.

(19) Haw, J. F.; Glass, T. E.; Dorn, H. C. *J. Magn. Reson.* **1982**, *49*, 22.

(20) Fyfe, C. A.; Cocivera, M.; Damji, S. W. H.; Hostetter, T. A.; Sproat, D. A.; O'Brien, J. *J. Magn. Reson.* **1976**, *23*, 377.

(21) Günther, U. L.; Sudmeier, J. L.; Albert, K.; Bachovchin, W. W. *J. Magn. Reson., Ser A* **1995**, *117*, 73.

(22) Vargaftik, N. B.; Vinogradov, Y. K.; Yargin, V. S. Handbook of Physical Properties of Liquids and Gases; Pure Substances and Mixtures, 3rd Ed.; Begell House, New York, 1996.

(23) Kochi, J. K. Free Radicals, Volume I, John Wiley & Sons: New York, 1973, Chapter 3.

(24) Walling, C. Free Radicals in Solution, John Wiley & Sons: New York, 1957, Chapter 10.

(25) Yonker, C. R.; Zemanian, T. S.; Wallen, S. L.; Linehan, J. C.; Franz, J. A. *J. Magn. Reson., Ser A* **1995**, *113*, 102.

(26) Linehan, J. C.; Wallen, S. L.; Yonker, C. R.; Bitterwolf, T. E.; Bays, J. T. *J. Am. Chem. Soc.* **1997**, *119*, 10170.

(27) Albert, K. *J. Chromatogr A* **1997**, *785*, 65.

(28) Hoffmann, M. M.; Conradi, M. S. *J. Am. Chem. Soc.* **1997**, *119*, 3811.

(29) Hoffmann, M. M.; Conradi, M. S. *J. Phys. Chem. B* **1998**, *102*, 263.

(30) Bai, S.; Yonker, C. R. *J. Phys. Chem. A* **1998**, *102*, 8641.

(31) Maksić, Z. B.; Kovačević, B.; Kovaček, D. *J. Phys. Chem. A* **1997**, *101*, 7446.

(32) Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 3rd ed.; Allyn and Bacon, Inc.: Boston, 1973; p 340.

(33) Martino, C. J.; Savage, P. E. *Ind. Eng. Chem. Res.* **1997**, *36*, 1385.

(34) Harris, G. M. *Trans. Faraday Soc.* **1951**, *47*, 716.

(35) Jonas, J., Ed. *High-Pressure NMR*; Springer-Verlag: Berlin, 1991; Chapters 2−4.