

## Reversible *in Situ* Catalyst Formation

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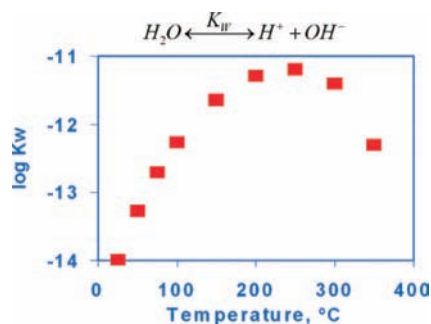
### CONSPECTUS

**A**cid catalysts play a vital role in the industrial synthesis and production of a plethora of organic chemicals. But, their subsequent neutralization and disposal is also a giant source of waste. For example, for a Friedel–Crafts acylation with  $\text{AlCl}_3$ , a kilogram of product yields up to 20 kg of (contaminated) waste salt. Other processes are even worse, and this waste is both an environmental and economic shortcoming. Here we address this issue by showing a series of acid catalysts where the neutralization is “built in” to the system and thus eliminates waste. Clearly these will not replace all organic and mineral acid catalysts, but they can replace many. Further, we show how these self-neutralizing catalysts can often eliminate unwanted byproducts, improve selectivity, or elimination of mass transfer limitations by changing from heterogeneous to homogeneous systems. They readily facilitate separations and promote recycling, to promote both green chemistry and good economics.

First is near-critical water, or liquid water under pressure, where the  $K_w$  for dissociation goes up 3–4 decades between 0 °C and 250 °C, thus facilitating both acid and base catalysis. Moreover, as the exothermic hydrogen bonding diminishes, the dielectric constant goes down to the point at which both salts and organics are soluble in this very hot water. For example, toluene and water are completely miscible at 305 °C. This eliminates mass transfer limitations for the reactions, and postreaction cooling not only lowers the  $K_w$  to neutralize the ions without waste but also results in facile separations from simple liquid–liquid immiscibility.

Further, we show the formation of catalysts with alkylcarbonic acids from alcohols and  $\text{CO}_2$ , analogous to carbonic acid from water and  $\text{CO}_2$ . We show a number of applications for these self-neutralizing catalysts, including the formation of ketals, the formation of diazonium intermediates to couple with electron-rich aromatics to produce dye molecules, and the hydration of  $\beta$ -pinene. Here also these systems often enhance phase behavior to cut mass transfer resistance. In an analogous application we show that peroxide and  $\text{CO}_2$  gives peroxy-carbonic acid, also reversible upon the removal of the  $\text{CO}_2$ , and we show application to epoxidation reactions.

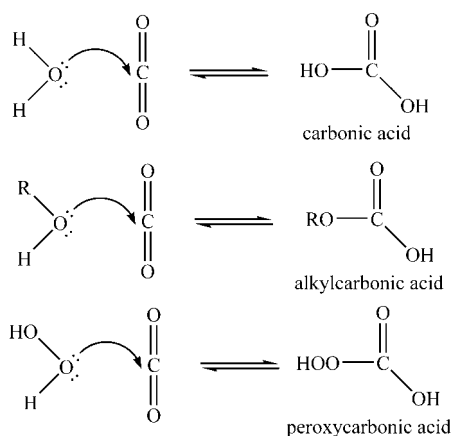
The bottom line is that these catalysts afford profound advantages for both green chemistry and improved economics. The methods outlined here have potential for abundant applications, and we hope that this work will motivate such opportunities.



### Introduction

Acids are the most used catalysts in industry, and they produce more than  $1 \times 10^8$  t/year of products.<sup>1</sup> Common acids include Bronsted acids such as  $\text{HCl}$ ,  $\text{H}_2\text{SO}_4$ , and  $\text{H}_3\text{PO}_4$  and Lewis acids such as  $\text{AlCl}_3$  and  $\text{BF}_3$ . But acid-catalyzed industrial processes often suffer from large amounts of waste, toxicity, corrosion, and difficulty of separation. For example,

in the Friedel–Crafts acylation of methyl benzoate with acetic anhydride, approximately 20 kg of  $\text{AlCl}_3$  are used per kilogram of product produced.<sup>2</sup> The neutralization of the  $\text{AlCl}_3$  after the reaction produces huge quantities of impure salt byproducts, which must be removed and disposed of as they constitute toxic waste. The most popular approach to solving these problems is the use of solid acids.<sup>1</sup>

**SCHEME 1.** Formation of Carbonic Acid, Alkylcarbonic Acid, and Peroxycarbonic Acid

However, solid acids can bind irreversibly with anything in the system that is basic, destroying the catalytic activity. Therefore, there is significant demand for an easily recycled, environmentally benign acid.<sup>3</sup>

We have developed processes that utilize several reversible acid catalysts, generated *in situ* and requiring no downstream neutralization, remediation, or regeneration.<sup>4</sup> The three major catalysts that form the focus of this Account are (1) near-critical water (NCW), (2) alkylcarbonic acids, and (3) peroxydicarbonic acid.

Near-critical water (water heated to 200–300 °C) has exciting potential for sustainable processing because of the advantages for clean reactions and facile separations.<sup>5</sup> Alkylcarbonic acids are self-neutralizing acids that form *in situ* in alcohol–CO<sub>2</sub> systems at mild pressures (10–47 bar) and then revert during depressurization.<sup>6</sup> These species are analogous to carbonic acid (see Scheme 1) formed from CO<sub>2</sub> and water. Peroxydicarbonic acid is another carbonic acid relative; this species is formed from hydrogen peroxide and CO<sub>2</sub> (see Scheme 1). Peroxydicarbonic acid is a prospective reagent for olefin epoxidation reactions, an important class of industrial reactions often plagued by large amounts of waste from organoperoxides, metal catalysts, or bromide salts. These three reagents are each formed *in situ*, and the elimination of each after the reaction is both easy and nonpolluting, placing them at the forefront of sustainable technology.

## Near-Critical Water (NCW)

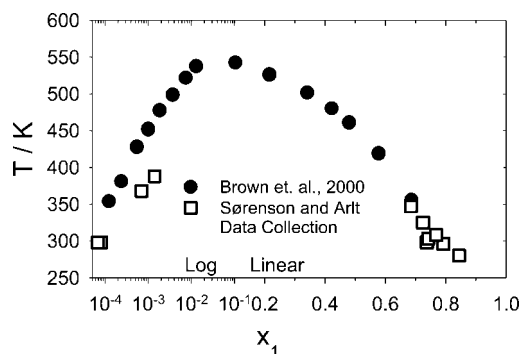
**A. Definition of NCW.** NCW is defined as water that has been heated to 200–300 °C, where its properties have begun to differ significantly from those of ambient water.<sup>5</sup> Generally, we use NCW at its saturation pressure, which varies from about 15 to 90 bar over this range. In this subcritical region, water does not exhibit all of the same destructive properties

as those of supercritical water in oxidation processes (400–500 °C); therefore, it is still useful for chemical transformations. In addition to several studies on the solvent properties of NCW,<sup>7–11</sup> we have performed hydrolyses,<sup>12,13</sup> hydrations,<sup>14</sup> and also carbon–carbon bond-forming reactions such as alkylations,<sup>15,16</sup> acylations,<sup>17</sup> and aldol-type condensations.<sup>18</sup>

**B. Properties of NCW.** Important differences in the physicochemical properties of NCW relative to ambient water are the density, dielectric constant, and autodissociation constant. These changes are due to the reduction of the extensive hydrogen bonding; specifically, water loses approximately 55–60% of its hydrogen-bonding network as the temperature is increased from 25 to 300 °C.<sup>19</sup> For example, on heating water from 25 to 300 °C, the density decreases from 1 g/mL to about 0.75 g/mL,<sup>20</sup> while the dielectric constant decreases from 78 to approximately 20.<sup>21</sup> These resulting properties correspond to a moderately polar solvent, similar to acetone (dielectric constant = 21.4 at 25 °C), and are also tunable with changes in pressure. The reduction in dielectric constant enables a greatly enhanced solubility of relatively nonpolar organic species in NCW,<sup>8,9,22</sup> though at a cost of some reduction in inorganic salt solubility.

Perhaps the most striking feature of NCW is the large increase in the autodissociation constant. The  $K_w$  of water increases by as much as 3 orders of magnitude, from  $10^{-14}$  at 25 °C to nearly  $10^{-11}$  at around 250 °C (at saturation pressure, about 40 bar),<sup>23</sup> where a maximum occurs. The increased autodissociation constant of NCW provides, in principle, a means of performing both acid and base catalysis without adding mineral acids or bases. By simply heating the solution, the autodissociation of water increases, providing an enormous increase in the concentration of hydronium and hydroxide ions, resulting in a catalytic medium for the chemical transformation. Cooling the mixture restores the “normal” ambient ion concentrations of these ionic species, thus constituting a self-neutralizing catalytic medium. This is important for ease of separations (no catalyst to be recovered), elimination of processing steps (no neutralization required), and waste reduction (no salt disposal) and provides a prototype for *in situ* catalyst formation.

One consequence of the decreased polarity and hydrogen bonding in NCW is a corresponding increase in the solubility of relatively nonpolar organics. This solubility increase is vital, because it enables the dissolution of substrates in sufficient quantities for homogeneous reactions to take place. The dramatic reversal of solubility with temperature provides the opportunity in NCW to dissolve simultaneously nonpolar and ionic species at high temperature with subsequent phase sep-

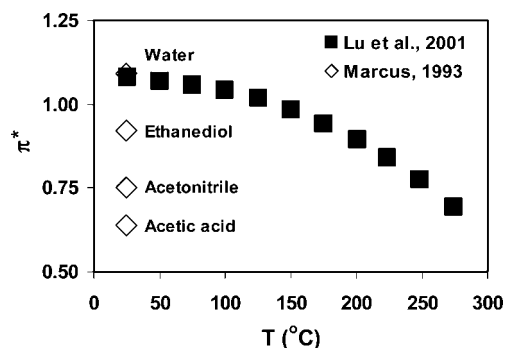


**FIGURE 1.** Liquid-liquid equilibria for 1-octanol(1)-water(2). The data were taken at a variety of pressures.<sup>8,24</sup>

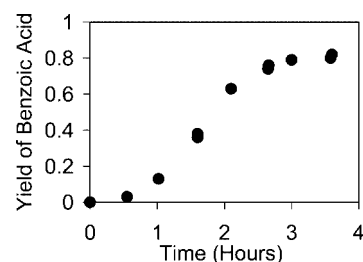
aration of the organic products by simply cooling the postreaction mixture. This enables a simple decantation of products to replace more difficult forms of product recovery.

The functionality of the organic substrate is still a major factor in its solubility in NCW. We measured upper critical solution temperatures (UCSTs) for several functionalized organics, for example, acetophenone (228 °C), 1-octanol (278 °C), and anisole (291 °C),<sup>8</sup> which are lower than those for benzene (305 °C), toluene (310 °C), and *n*-hexane (355 °C).<sup>22</sup> The solubility of *n*-hexane increases by 5 orders of magnitude from ambient water to NCW, demonstrating the enormous potential NCW has for effecting simple separations based on thermal solubility swings. The structural effect due to substituent position on solubility are much less significant, because the UCST for 1-hexanol (221 °C) and 2-hexanol (230 °C) are quite similar.<sup>9</sup> An example solubility curve for 1-octanol and water as a function of temperature is provided in Figure 1.<sup>8,24</sup> The solubility of 1-octanol in water increases rapidly upon heating from  $x = 7.5 \times 10^{-5}$  at 25 °C to  $x = 0.013$  at 265 °C and full miscibility at 278 °C. This rapid increase in mutual solubility at moderate temperatures, compared with a flat solubility profile near the UCST, is typical for nonpolar organics with water and provides an excellent opportunity for highly efficient phase separations.

The Kamlet-Taft method is a powerful technique for assessing the local environment surrounding a probe molecule in solution. The three parameters that are central to the method are  $\pi^*$  (dipolarity/polarizability),  $\alpha$  (hydrogen bond acidity), and  $\beta$  (hydrogen bond basicity). We reported the Kamlet-Taft parameters for water from 25 to 275 °C.<sup>10</sup> The  $\pi^*$  values and density of saturated liquid water are shown in Figure 2;<sup>10,25</sup>  $\pi^*$  continuously decreases as the temperature increases, from a value of 1.08 at 25 °C to 0.69 at 275 °C. Thus, NCW at 275 °C has a dipolarity/polarizability comparable to that of ambient acetic acid. Despite the loss in polarity, NCW retains considerable hydrogen bond acidity, with  $\alpha$

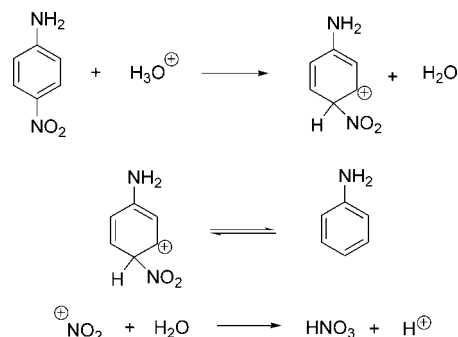


**FIGURE 2.** Dipolarity/polarizability ( $\pi^*$ ) of saturated liquid water as a function of temperature.<sup>10,25</sup>



**FIGURE 3.** Fractional conversion of *n*-propyl benzoate vs time at 250 °C.<sup>12</sup>

**SCHEME 2.** Acid-Catalyzed Mechanism for the Hydrolysis of 4-Nitroaniline in Near-Critical Water<sup>11</sup>



values decreasing from 1.16 at 25 °C to 0.84 at 275 °C, values comparable to that of ambient ethanol. In contrast to  $\pi^*$  and  $\alpha$ ,  $\beta$  changes only slightly from 25 to 275 °C.

**C. Reactions in NCW.** We utilized the Kamlet-Taft parameters to correlate the rates of decomposition in NCW of two of the dyes used in solvatochromic studies, 4-nitroaniline and *N,N*-dimethyl-4-nitroaniline, which produce aniline and *N,N*-dimethylaniline, respectively.<sup>11</sup> Rates associated with these reactions were studied at 200–275 °C. Since the mechanism of reaction involves acid catalysis and since nitric acid is produced in both reactions (Scheme 2), the reaction kinetics follow an autocatalytic pathway. A linear solvation energy relationship (LSER) for the kinetic results revealed no dependence on the  $\beta$  (hydrogen bond basicity) parameter for this acid-catalyzed decomposition but yielded a good correlation

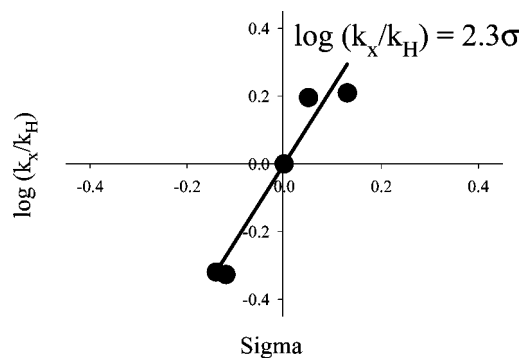
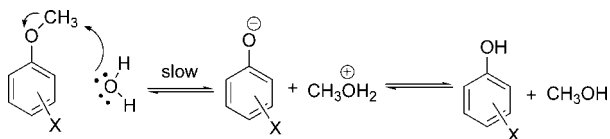


FIGURE 4. Hammett plot for anisole hydrolysis.<sup>13</sup>

**SCHEME 3.** Mechanism for the Hydrolysis of Anisole<sup>13</sup>



with  $\alpha$  and  $\pi^*$ , demonstrating the correlation of kinetic rate constants in NCW with solvatochromic properties.

For the hydrolysis of a series of benzoate esters in near-critical water, the conversion versus time yielded S-shaped curves (Figure 3), suggesting an autocatalytic mechanism.<sup>12</sup> The data were consistent with the  $A_{AC2}$  mechanism for acid-catalyzed hydrolysis of esters, where the protonation of the carbonyl oxygen of the ester functionality is part of the rate-controlling step. We further measured the rates of hydrolysis of isobutyl benzoate at 260–300 °C and calculated an activation energy of  $24 \pm 3$  kcal/mol, similar to that for the acid-catalyzed hydrolysis of substituted benzoic acid esters in ambient water.<sup>13</sup> The rate of hydrolysis decreased as the length or branching of the alkyl alcohol chain increased, and the rate of hydrolysis of substituted isobutyl benzoates was independent of ring substituents. As a consequence, Hammett analysis yielded a negligible  $\rho$ -value, characteristic of the acid-catalyzed ester hydrolyses in ambient aqueous systems. In contrast, the literature indicates that the base-catalyzed mechanism gives a  $\rho$ -value of 2.4. Therefore, we concluded that the increased  $K_w$  of NCW, resulting in greater concentrations of hydronium ion, is the dominant effect controlling the rate of hydrolysis of benzoate esters.

We have reported the rates of hydrolysis of a series of substituted anisoles,<sup>13</sup> where we found a Hammett  $\rho$ -value of 2.3 (Figure 4), consistent with a simple  $S_N2$  displacement by water on the methyl group of the substituted anisole (Scheme 3). The rates of hydrolysis of the anisoles were substantially faster than those of the more sterically hindered phenetoles, also consistent with the postulated  $S_N2$  mechanism.

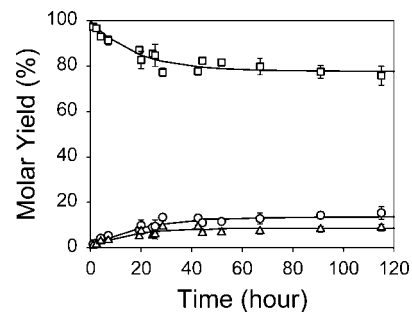
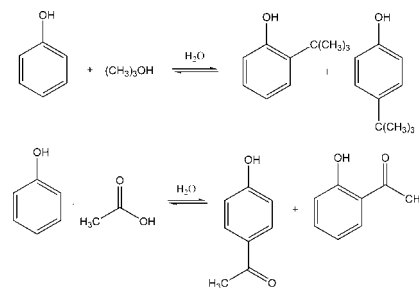


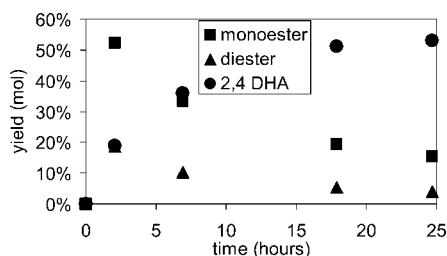
FIGURE 5. Mole fraction product yields as a function of time for the reaction of phenol with *tert*-butyl alcohol in water at 250 °C and 172 bar: phenol ( $\square$ ); 2-*tert*-butylphenol ( $\circ$ ); 4-*tert*-butylphenol ( $\triangle$ ).<sup>16</sup>

**SCHEME 4.** Alkylation and Acetylation of Phenol in Near-Critical Water<sup>17</sup>



In the hydration of  $\beta$ -pinene in NCW at 200–250 °C,<sup>14</sup> the product distribution obtained was identical to that generated under ambient aqueous acid-catalyzed conditions; as a consequence, we postulated that the reaction in NCW proceeded *via* carbonium ion intermediates. The reaction of  $\beta$ -pinene in water at 200 °C was relatively fast with 90% conversion in 20 min. However, the yield of the target terpeneols was small (10%) with the formation of hydrocarbons dominating the products under these conditions. Reactions performed at 250 °C showed even greater hydrocarbon formation. These poor selectivities are in contrast to those obtained for this reaction using alkylcarboxylic acids, discussed below.

We studied the Friedel–Crafts alkylation of phenol with *tert*-butanol in NCW to produce 2-*tert*-butylphenol and 4-*tert*-butylphenol (Scheme 4), with product yields shown in Figure 5.<sup>15,16</sup> The kinetics were described using a simple reaction network involving two reversible first-order reactions, with the reversibility confirmed by back-reaction of the product in NCW. The selectivity of the reaction could be tuned with temperature; the equilibrium concentration of the 2-isomer decreased while that of the 4-isomer increased with increasing temperature. Other alkylation reactions involved reacting *p*-cresol with *tert*-butanol to form 2-*tert*-butyl-4-methylphenol and the reactions of phenol with isopropyl alcohol and *n*-propyl alcohol; although these proved less-active alkylating



**FIGURE 6.** Reaction of resorcinol and acetic acid to 2,4-dihydroxyacetophenone (2,4-DHA, ●), resorcinol monoacetate (■), and resorcinol diacetate (▲) at 290 °C.<sup>17</sup>

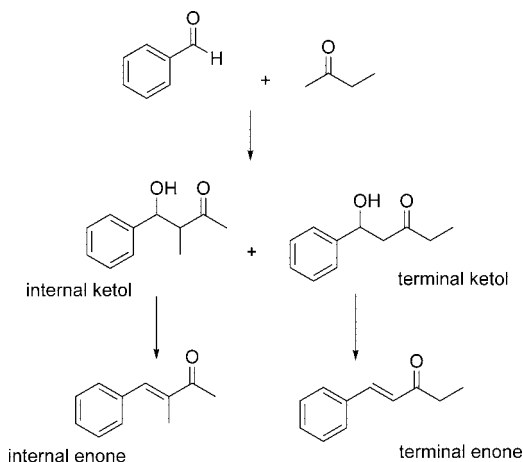
agents compared with *tert*-butanol, the major product from each of the isomeric propanols was 2-isopropylphenol, consistent with a carbocation-like intermediate, followed by a rearrangement. In all cases, we reported rate constants and activation energies at 250–300 °C.<sup>15</sup>

Like classical Friedel–Crafts alkylations, the corresponding classical acylation reactions require the presence of Lewis or Brønsted acids. Unlike the alkylation process, acylations usually require more than stoichiometric quantities of the acid. In addition, the electrophilic reaction partner is usually an expensive and hydrolytically unstable acid chloride, usually dissolved in a chlorinated solvent. Neutralization of the final reaction mixture results in large quantities of contaminated salt waste.<sup>26</sup> We successfully acetylated phenol (Scheme 4) and resorcinol using acetic acid in near-critical water and in neat acetic acid at 250–300 °C.<sup>17</sup> As with the alkylation reactions, the acetylations are reversible at high temperatures in the presence of water but with less favorable equilibrium yields of acylation product. In aqueous acetic acid at 290 °C, phenol was primarily converted to 2-hydroxyacetophenone, 4-hydroxyacetophenone, and phenyl acetate in approximately equal amounts, with a combined equilibrium yield of less than 1%. Under the same conditions, resorcinol was converted to primarily 2,4-dihydroxyacetophenone with an equilibrium yield of 4%. Acetylations are generally irreversible with traditional Friedel–Crafts catalysts. Thus, the low yields represent a significant obstacle to adoption of the NCW process.

To address the equilibrium limitation, the acetylations were performed in neat acetic acid. At 290 °C, phenol acetylation proceeded with a combined equilibrium yield of 8%. Under the same conditions, resorcinol was successfully converted with an equilibrium yield of more than 50% in less than 12 h (Figure 6). Thus, the use of “near-critical” acetic acid may be an option where NCW fails for Friedel–Crafts acylations.

A variety of condensation reactions have been explored in NCW to elucidate the behavior of this medium. We examined the Claisen–Schmidt condensation between benzaldehyde and butanone to form  $\alpha,\beta$ -unsaturated ketones.<sup>18</sup> Due to the

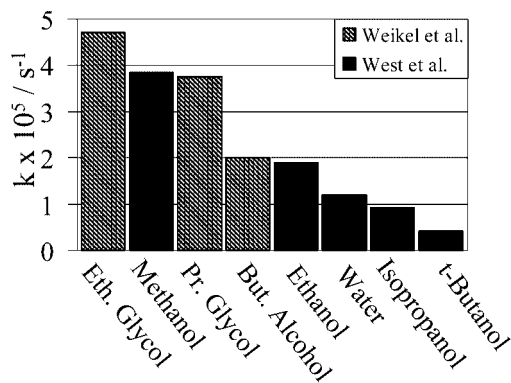
**SCHEME 5.** Claisen–Schmidt Reaction of Benzaldehyde with 2-Butanone Showing the Two Possible Condensation Products, 4-Phenyl-3-methyl-3-buten-2-one (Internal Enone) and 1-Phenyl-1-penten-3-one (Terminal Enone), as Well as Their Precursor Intermediate Ketols<sup>18</sup>



asymmetry of the butanone with respect to the carbonyl group, two products are formed (Scheme 5). Classically, the terminal enone condensation product is the primary product under acidic conditions, while the internal enone is the primary product under basic conditions.<sup>27</sup> Our results in NCW over a temperature range of 250–300 °C demonstrated that both the terminal (4-phenyl-3-methyl-3-buten-2-one) and internal (1-phenyl-1-penten-3-one) enones were formed, along with byproduct. However, the formation of 1-phenyl-1-penten-3-one was dominant at all temperatures, with selectivity increasing with temperature. These results were closer to those obtained under classical basic conditions at ambient temperature. The same study also explored the self-condensation reaction of butyraldehyde, yielding a wide variety of products, with a maximum yield of the 2-ethyl-2-hexenal of 40% before the formation of byproducts became dominant at longer residence times.

## Alkylcarbonic Acids

**A. Probing the Strength of Alkylcarbonic Acids.** The reversible reaction of carbon dioxide with water to form carbonic acid (Scheme 1) is well-known; analogously, CO<sub>2</sub> reversibly reacts with alcohols to form alkylcarbonic acids. This provides *in situ* acid formation of catalysts that can be neutralized readily by the removal of carbon dioxide. The use of CO<sub>2</sub> with organic solvents to form gas-expanded liquids has been the subject of much of our recent research.<sup>28–33</sup> We verified the presence of alkylcarbonic acids in CO<sub>2</sub>-expanded alcohols using diazodiphenylmethane (DDM) as a reactive probe to trap the carbonic acid species.<sup>28</sup> Product analysis confirmed that DDM was reacting with an alkylcarbonic acid spe-



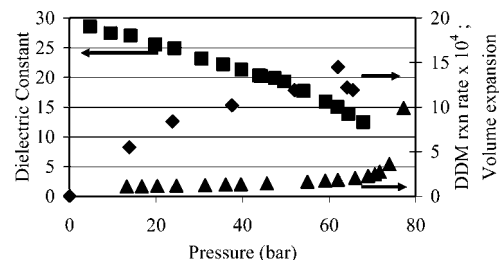
**FIGURE 7.** Comparison of the effect of various alcohols, diols, and water on the pseudo-first-order reaction rate constant ( $k$ ,  $s^{-1}$ ) of DDM (with corresponding carbonic acid) in 60 mol % acetone/20 mol % ROH/20 mol %  $CO_2$  at 40 °C.<sup>28,29</sup>

cies and not just the protic alcohol. The rates of reaction of a series of alcohols with DDM indicate that the relative reaction rates follow the order  $1^\circ > 2^\circ > 3^\circ$ .

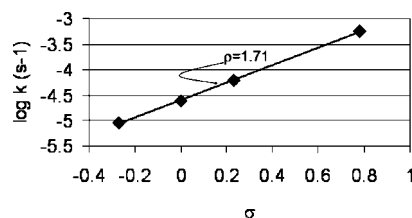
To characterize further these types of acids, the relative reaction rates of DDM were measured in both methanol and ethanol with 20 mol %  $CO_2$ , with the rate in methanol found to be roughly 2.8 times that in ethanol. This suggests that the expanded methanol solution is more acidic than the expanded ethanol. However, the rates are influenced by both the actual strength of the acids ( $pK_a$ ) and the prior equilibria to form the alkylcarbonic acids (concentration). The addition of  $CO_2$  to the system will affect both of these equilibria, as increasing the amount of  $CO_2$  will drive the formation of the alkylcarbonic acid but simultaneously decrease the polarity of the solvent mixture and thereby decrease acid dissociation.

To compare the rates of the DDM reaction with alkylcarbonic acids to the rate with carbonic acid, we used acetone as a diluent to maintain a single liquid phase with constant  $CO_2$  concentration.<sup>28</sup> Kinetics were run at 40 °C using a solution containing 60 mol % acetone, 20 mol %  $CO_2$ , and 20 mol % R-OH, where R = alkyl or hydrogen (Figure 7). The rates of the reactions run in alcohols follow a logical progression with the fastest rate in methanol and the slowest in *tert*-butanol. This relationship is consistent with steric and electronic factors affecting the equilibrium and dissociation of the alkylcarbonic acids. The corresponding rate using water (carbonic acid) was found to be slower than that with either methanol or ethanol.

We used DDM again as a reactive probe molecule to find more information about alkylcarbonic acids and to understand further how to employ them in reactions.<sup>29</sup> Additionally, we investigated the dielectric constant of gas-expanded liquids in the vapor-liquid equilibrium region. It is important in the case of acid catalysis to know the dielectric constant because it gives some indication of the solvent's ability to support pro-



**FIGURE 8.** Pseudo-first-order rate constant ( $k$ ,  $s^{-1}$ ) for the reaction of DDM with methylcarbonic acid ( $\blacklozenge$ ), dielectric constant of MeOH/ $CO_2$  ( $\blacksquare$ ), and volume expansion of MeOH/ $CO_2$  ( $\blacktriangle$ ) at 40 °C versus pressure.<sup>29</sup>

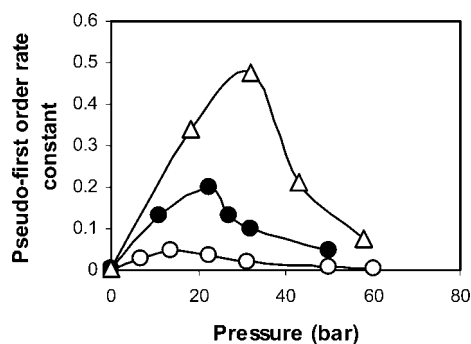


**FIGURE 9.** Hammett plot for pseudo-first-order reaction rates ( $k$ ,  $s^{-1}$ ) for the reaction of substituted benzyl alkylcarbonic acids and DDM in acetone at 40 °C.<sup>29</sup>

ton-transfer reactions. The alcohols investigated in this study included methanol, ethylene glycol, propylene glycol, benzyl alcohol, 4-nitrobenzyl alcohol, 4-chlorobenzyl alcohol, and 4-methoxybenzyl alcohol. The fastest rate was for ethylene glycol, while methanol and propylene glycol lead to similar rates (see Figure 7). The increased rate with ethylene glycol relative to ethanol was attributed to the adjacent alcohol group stabilizing the alkylcarbonic acid through intramolecular hydrogen bonding.

Experiments were performed without the acetone diluent, using instead pure methanol, to investigate  $CO_2$  effects on the rates of the DDM reaction (Figure 8). The presence of a maximum (at 60 bar of  $CO_2$ ) is consistent with our hypothesis that the DDM rate is affected by both the concentration of the carbonic acid (which increases with  $CO_2$  pressure) and the rate of proton transfer to the DDM (which decreases with  $CO_2$  pressure as the dielectric constant of the mixture decreases.) This second effect was confirmed through dielectric constant measurements (Figure 8). The use of a series of substituted benzyl alcohols enabled us to study electronic effects using a Hammett correlation (Figure 9). An excellent linear fit yielded a  $\rho$  of 1.71, indicating that the reaction is very sensitive to electronic effects.

**B. Applications of Alkylcarbonic Acid.** To show applications, we used  $CO_2$ -expanded methanol and  $CO_2$ -expanded ethylene glycol to catalyze the formation of ketals from cyclohexanone.<sup>30</sup> Acetals and ketals are commonly used to protect aldehyde and ketone functionalities in basic media. Acetal



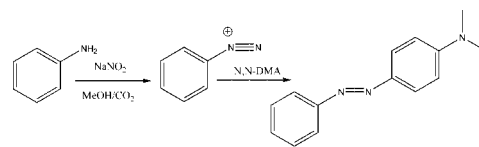
**FIGURE 10.** The pseudo-first-order rate constants of cyclohexanone acetal formation in CO<sub>2</sub>-expanded methanol at various CO<sub>2</sub> pressures and 25 °C (○), 40 °C (●), and 50 °C (△).<sup>30</sup>

groups are normally formed by reacting the carbonyl-containing substrate with an excess of protecting alcohol in the presence of a strong acid catalyst. In our work, we employed the alkylcarbonic acids of methanol and ethylene glycol, two of the most common protection agents, to form the dimethyl ketal and cyclic ethylene ketal of cyclohexanone. Initial rates under pseudo-first-order conditions for the ketal formation reaction between methanol and cyclohexanone in methanol and CO<sub>2</sub>-expanded methanol at 25–50 °C are shown in Figure 10, where the catalytic effect of CO<sub>2</sub> addition is clear. Also, when CO<sub>2</sub> was replaced by ethane, the rate of ketal formation was similar to the (very slow) rate in pure alcohol (with no added CO<sub>2</sub>). This result negates the possibility that simple pressure or viscosity reduction<sup>34</sup> was responsible for the increased rate in CO<sub>2</sub>-expanded methanol.

Figure 10 shows maxima in the rate constants at each temperature, a result consistent with that reported previously,<sup>29</sup> probably due to the tradeoff between methylcarbonic acid formation and the rate of the proton transfer step when CO<sub>2</sub> concentration is increased. The shifting of the maximum from about 20 bar at 25 °C to 35 bar at 50 °C strengthens this argument, because more pressure would be required to maintain a similar CO<sub>2</sub> concentration in the liquid phase at higher temperatures. Equation-of-state modeling<sup>30</sup> revealed that the mole fractions of CO<sub>2</sub> at the various maxima are similar, though not identical. The catalytic effects observed in the CO<sub>2</sub>/ethylene glycol system demonstrate that the alkylcarbonic acid species can exist even at low CO<sub>2</sub> concentrations (approximately 2% at 40 bar).<sup>35</sup>

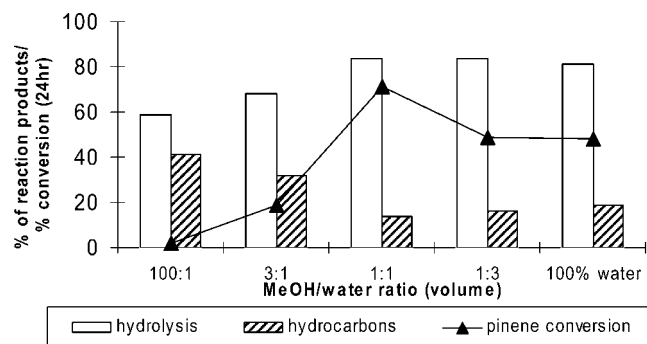
We examined a variety of reactions using methylcarbonic acid as an acid catalyst for the formation of the diazonium intermediates.<sup>31</sup> These diazonium species were then coupled with electron-rich aromatics to produce dye molecules. Methyl yellow, an industrial dye, was synthesized in a single pot reaction from aniline, sodium nitrite, *N,N*-dimethyl aniline, and CO<sub>2</sub> in methanol as shown in Scheme 6. The most success-

**SCHEME 6.** Synthesis and Mechanism for Formation of Methyl Yellow from Aniline<sup>31</sup>



ful coupling reaction conditions were at 5 °C with excess nitrite salt and a high CO<sub>2</sub> loading. The reaction was run for 24 h and produced an average yield of 72% methyl yellow and 97% conversion of aniline. The major byproduct was benzene formed from the elimination of molecular nitrogen from the diazonium intermediate followed by hydrogen abstraction from the solvent. Higher CO<sub>2</sub> loading gave improved yields up to 47 bar; apparently, under these conditions, the CO<sub>2</sub> concentration did not sufficiently lower the dielectric constant of the solvent to hinder proton transfer and the formation of the diazonium intermediate. Other products were synthesized using this method, including *N,N*-diethyl-4-[(4-nitrophenyl)azo]aniline (DENAB) and iodobenzene (Sandmeyer reaction).

In addition to the results in NCW mentioned above, we used a mixture of methanol and water with CO<sub>2</sub> to catalyze the hydration of  $\beta$ -pinene.<sup>14</sup> In contrast to the results in near-critical water, the major products produced were those from the addition of water to form alcohols. The major difference in this work compared with other alkylcarbonic acid studies is the presence of water in the gas-expanded alcohol. Water will also contribute to *in situ* acid creation through the formation of carbonic acid. Previous work done on CO<sub>2</sub>/water systems has shown that a pH as low as 2.8 can be attained.<sup>36</sup> However in CO<sub>2</sub>/water/methanol systems, a minimum in pH of 4.22 occurred at 5.6 mol % CO<sub>2</sub>,<sup>37</sup> due to the competition between increased acid concentration and decreased dielectric constant as CO<sub>2</sub> composition is increased. With CO<sub>2</sub>/methanol/water (1:1 methanol/water) at 75 °C, a  $\beta$ -pinene conversion of 71% was achieved, but without methanol essentially no reaction took place. Since the reaction requires the presence of water but methylcarbonic acid ( $pK_a$  of 5.61) is a stronger acid than carbonic acid ( $pK_a$  of 6.37), there should be an optimal water loading. Figure 11 demonstrates that both the reaction rate and product distribution were optimal for the 1:1 volume ratio of methanol/water. The conversion drops off quickly at higher methanol ratios, perhaps due to the lowering of dielectric constant. The conversion also drops off with increasing water content.



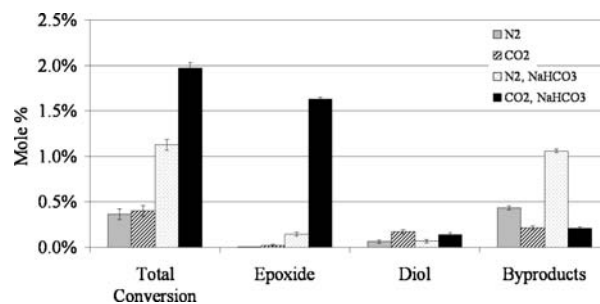
**FIGURE 11.**  $\beta$ -Pinene conversion and product distribution variations with different methanol/water ratios (75 °C, 24 h, 0.127 M  $\beta$ -pinene).<sup>14</sup>

## Peroxycarbonic Acids

Olefin epoxidations are industrially important catalytic reactions<sup>38</sup> performed using oxygen or a peroxide; generally either requires a metallic catalyst and high temperatures. These catalytic systems provide excellent selectivities and yields, even with minimal catalyst loadings, but limited catalyst stability and metal contamination produce additional processing challenges. Aqueous solutions of hydrogen peroxide are cheap and readily available, with the innocuous decomposition products water and oxygen providing a significant environmental advantage over organic peroxides. Unfortunately, the use of hydrogen peroxide for epoxidations is hindered by the need for activation by metallic catalysts or conversion to a more reactive peroxy acid. Peroxy acids obviate the need for metallic catalysts<sup>39</sup> but must be formed *in situ* because of their instability. In addition, carboxylic acids must be present in stoichiometric quantities and must be recovered for reuse or disposal, providing an economic and environmental disincentive for peroxide utilization. In order to ameliorate these drawbacks of conventional epoxidations, we developed a process using the simplest possible activated hydrogen peroxide species, peroxycarbonic acid.<sup>40</sup>

The reaction of  $\text{CO}_2$  with hydrogen peroxide to generate peroxycarbonic acid is analogous to the formation of carbonic or alkylcarbonic acids (Scheme 1). We epoxidized cyclohexene and 3-cyclohexen-1-carboxylate sodium salt using peroxycarbonic acid as the oxidant in a  $\text{CO}_2$ /water biphasic solvent to yield epoxides and diols. Also, we explored the effects of sodium bicarbonate, hydrogen peroxide stabilizers, and cosolvents. In addition to the environmentally benign and density-tunable properties of supercritical  $\text{CO}_2$ , we take advantage of the nonflammable nature of  $\text{CO}_2$  and the elimination of several explosion hazards.

Results at 40 °C and 120 bar  $\text{CO}_2$  are presented as Figure 12. Only small amounts of epoxide are formed using  $\text{CO}_2$  and



**FIGURE 12.** Conversions for cyclohexene epoxidations after 20 h at 40 °C and 120 bar with and without  $\text{NaHCO}_3$  in  $\text{N}_2$  and  $\text{CO}_2$ .<sup>40</sup>

$\text{H}_2\text{O}_2$  alone, although a significant enhancement is revealed when  $\text{NaHCO}_3$  is added as a promoter. Control experiments, in which  $\text{CO}_2$  was replaced with  $\text{N}_2$ , enabled us to attribute the bulk of oxidation activity to peroxycarbonic acid. Addition of  $\text{NaHCO}_3$  improved epoxide yield, from 0.02 mol % (without  $\text{NaHCO}_3$ ) to 1.6 mol % (with 1 wt %  $\text{NaHCO}_3$ ) in  $\text{CO}_2$ . Unfortunately, further increasing the  $\text{NaHCO}_3$  concentration did not increase product yield. This was attributed to  $\text{NaHCO}_3$  accelerating the decomposition of hydrogen peroxide, which proved a major factor in limiting the ultimate yield.

Besides hydrogen peroxide decomposition, mass transport limitations provided the largest hindrance to product yield. The solubility of peroxycarbonic acid is negligible in the non-polar  $\text{CO}_2$ /olefin phase; therefore, we conjectured that epoxidation occurred at the interface between phases or in the aqueous phase. The transport of  $\text{CO}_2$  to the aqueous phase was found to be rapid; however the transfer of cyclohexene into the aqueous phase is not, as evidenced by increased yields at higher stirring speeds. Without a cosolvent, cyclohexene solubility in the aqueous phase is very small,  $\sim 10^{-5}$  mol/mol of solvent. Hydrophilic cosolvents such as acetonitrile and dimethylformamide increased the yield to 17%, emphasizing the importance of bringing the reactive species into contact with each other in the same phase.

Epoxidations of the water-soluble olefin 3-cyclohexen-1-carboxylate sodium salt (3-CCSS) can occur homogeneously because of the very rapid transport of  $\text{CO}_2$  into the aqueous phase. The epoxidation of 3-CCSS at 40 °C and 120 bar  $\text{CO}_2$  resulted in  $\sim 100$  mol % conversion, with an epoxide yield of 89 mol % and a diol yield of 11 mol %. This dramatic improvement in epoxide yield with 3-CCSS strongly supports the hypothesis that epoxidation occurs within the aqueous phase.

Further environmental gains could be derived from this process via the *in situ* generation of  $\text{H}_2\text{O}_2$  from  $\text{H}_2$  and  $\text{O}_2$  in the  $\text{CO}_2$ /water biphasic system prior to the formation of peroxycarbonic acid, as described by Beckman for oxidation reac-



tions in these systems.<sup>41</sup> Such an approach would greatly reduce the waste inherent to H<sub>2</sub>O<sub>2</sub> production and may help overcome limitations deriving from H<sub>2</sub>O<sub>2</sub> instability.

## Conclusions

Mineral and Lewis acids constitute the largest set of industrial catalysts in use today. The large volume of toxic waste generated from the neutralization of the acids represents a significant challenge to the implementation of the principles of green chemistry for acid technologies. We have demonstrated that the use of *in situ* generated acids that require no neutralization can eliminate the waste resulting from acid neutralization in a variety of processes. In addition to solid acid catalysts, the use of near-critical water, alkylcarbonic acids, and peroxy-carbonic acids has significant potential. In addition to the environmental benefits from waste reduction, the use of these tunable solvents presents economic processing advantages (higher selectivities, simplified separations) fostering the implementation of sustainable technologies.

Future adaptation of these techniques to an even broader range of chemical reactions is possible, as the vast array of acid-catalyzed processes provides endless opportunities for new applications. Further, as environmental concerns become more pressing and as waste disposal becomes more costly, ever greater benefits will be derived from more benign methods.

## BIOGRAPHICAL INFORMATION

**Jason P. Hallett** was recently a Research Engineer in the Eckert–Liotta Research Group at Georgia Institute of Technology, where he received a Ph.D. in Chemical Engineering. He is currently a Marshall-Sherfield Fellow at Imperial College where he studies solvent effects on reactions in ionic liquids.

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## FOOTNOTES

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