Acid/base-catalyzed ester hydrolysis in near-critical water

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Hydrolyses of substituted benzoic acid esters in near-critical water (250–300 ºC) show autocatalytic kinetic behavior and surprisingly give the same rate constant regardless of substituent, suggesting that an acid-catalyzed mechanism predominates under our reaction conditions.

Liquid water in the near-critical region (250–300 °C) is a unique, environmentally benign solvent which affords opportunities for pollution minimization in a wide variety of commercially important chemical processes.[1–3] As the temperature is raised, the hydrogen bonding in water diminishes.[4,5] Both the relative permittivity and the density decrease,[6] giving near-critical water properties similar to those of typical polar organic solvents. While near-critical water can still solubilize salts, it can also dissolve organic compounds.[7]

In addition, the ionization constant of water increases by three orders of magnitude in going from ambient to near-critical conditions,[8] making it a strong source of both hydronium and hydroxide ions. These ions can act as catalysts in acid- or base-catalyzed conversions, respectively.[1,9] Because the protons and hydroxide ions derived from the auto-ionization of hot water do not require neutralization, formation of unwanted salt by-products can be reduced or eliminated in many processes. Further, the ease of separation of products from water by cooling to ambient conditions makes it an economically viable replacement for less environmentally benign solvents.

Because near-critical water is such a promising solvent for a wide variety of processes, we sought a more thorough understanding of chemical reactions and mechanisms in this medium. We chose to study the hydrolysis of several simple benzoic acid esters as a model system (Scheme 1) to elucidate mechanistic pathways followed in near-critical water. It has previously been shown that the main products formed from the hydrolyses of di-*n*-butyl phthalate[10] and ethyl acetate[11] in near-critical water are the corresponding acids and alcohols. The formation of thermolysis products, such as alkenes and carbon oxides, is considerably slower in near-critical water than when performed neat.

Several 3.0 ml titanium reactors were loaded with benzoate ester and an excess of water (Aldrich, HPLC grade), where the excess of water makes the back reaction negligible. Reactors were placed in a heating block at 250 °C, and pairs of reactors were removed and quenched at various reaction times. Reactor contents were diluted in acetone and analyzed using GC-FID and GC-MS.

Data measuring conversion *vs.* time yielded S-shaped curves (Fig. 1), suggesting an autocatalytic mechanism. Because benzoic acid is one of the products, autocatalysis suggests the
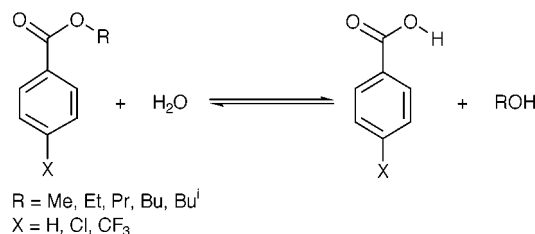
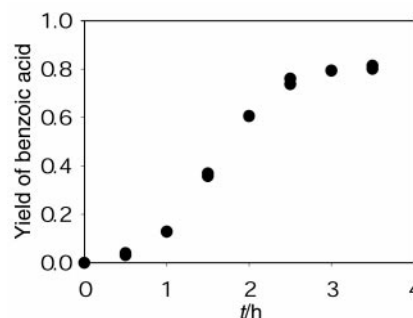**Fig. 1** Fractional conversion of *n*-propyl benzoate *vs.* time.

reaction is acid-catalyzed. The $A_{AC}2$ mechanism for acid-catalyzed hydrolysis of esters yields a rate equation of the form shown in eqn. (1),

$$\frac{dx}{dt} = k[\text{ester}][H_2O][H^+] \qquad (1)$$

where $k = k_2 K_1$;[12] k_2 is the rate constant for the addition of water to the protonated ester, and K_1 is the equilibrium constant for the protonation of the ester (Scheme 2). The second step is rate-determining, and its product equilibrates rapidly to benzoic acid and the alcohol. The concentration of protons is determined from the dissociation constant of water and that of benzoic acid at 250 °C. The dissociation constant of benzoic acid under our conditions is 3.7×10^{-6} M,[13,14] and the Hammett reaction constant ρ for this dissociation increases by only 2% from 25 to 250 °C.[15] We calculated values for the dissociation constants of *p*-chlorobenzoic acid and *p*-trifluoromethylbenzoic acid at 250 °C and integrated numerically to ascertain k for each reaction. Table 1 reports these rate constants as products of k_2 and K_1*, where K_1* is the equilibrium constant for protonation of the nonsubstituted ester. For the acidity of the substituted benzoic acids, we assumed that the effect of substituents on the equilibrium constant for acid dissociation is the same as that for protonation of the ester.

Rates of hydrolysis of isobutyl benzoate were also measured at 260 and 300 °C. Utilizing dissociation constants of benzoic acid at these temperatures,[13,15] the activation energy was

R = Me, Et, Pr, Bu, Bu^i
X = H, Cl, CF₃
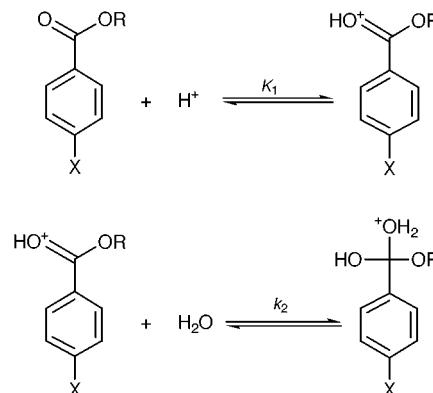
Scheme 1

Scheme 2

Table 1 Rate constants at 250 ºC for the hydrolysis of benzoate esters, where K_1* is the equilibrium constant for the protonation of nonsubstituted ester

R	X	$k_2 K_1$*/l^2 mol^{-2} h^{-1}
Me	H	26.9 ± 2.5
Et	H	25.7 ± 0.9
Pr	H	10.4 ± 0.5
Bu	H	17.1 ± 0.6
Bu^i	H	6.7 ± 0.3
Bu^i	Cl	7.4 ± 0.6
Bu^i	CF$_3$	7.0 ± 0.5

calculated to be 101 ± 13 kJ mol^{-1}, indicating that mass transfer limitations were negligible. Similar activation energies were obtained for the acid-catalyzed hydrolysis of substituted benzoic acid esters in low temperature aqueous solvents with a stoichiometric addition of acid.[16]

As expected, longer alkyl chains on the esters yield slower hydrolyses, and the branched butyl benzoate hydrolyzes more slowly than the linear butyl benzoate. As the carbonyl carbon becomes more sterically hindered, nucleophilic attack by water becomes more difficult, resulting in a slower hydrolysis.

Hydrolyses of substituted isobutyl benzoates provide further evidence that an acid-catalyzed mechanism predominates under near-critical conditions. It is clear from Table 1 that substituents have very little effect on rates of hydrolysis of benzoic acid esters under these conditions. Because of competing effects in the first two steps of the A$_{AC}$2 mechanism (Scheme 2), substituents exhibit a negligible effect on the rate constants. This negligible substituent effect is a well-documented characteristic of ester hydrolysis *via* an acid-catalyzed mechanism in aqueous solvents at lower temperature.[17] Hammett plots of acid-catalyzed ester hydrolyses have $\rho = 0$, compared to $\rho = 2.4$ for base-catalyzed hydrolyses of esters.[17] In addition to the reactions reported in Table 1, the hydrolysis of isobutyl *p*-hydroxybenzoate was also attempted, but the hydroxy group is strongly electron donating ($\sigma = -0.38$), and the ester decarboxylated.

In summary, benzoate esters can be cleaved to benzoic acid and the corresponding alcohol in near-critical water without the addition of any acid or base catalyst. Preliminary investigations indicate that the pathway for acid-catalyzed hydrolysis accord-ing to an A$_{AC}$2 mechanism is dominant. First, the S-shaped conversion *vs.* time curve is consistent with autocatalysis. The acidity of near-critical water seems sufficient to initiate hydrolysis of the benzoate and formation of the autocatalytic species benzoic acid. Also, the addition of electron-withdrawing substituents does not affect reaction rate, as predicted by the proposed acid-catalyzed mechanism and demonstrated for many acid-catalyzed hydrolyses in the literature. Thus, despite the fact that near-critical water is quite different from water under ambient conditions, hydrolyses in it follow the mechanistic pathway commonly observed at lower temperatures.

Notes and references

1 A. R. Katritzky, S. M. Allin and M. Siskin, *Acc. Chem. Res.*, 1996, **29**, 399.
2 J. An, L. Bagnell, T. Cablewski, C.R. Strauss and R.W. Trainor, *J. Org. Chem.*, 1997, **62**, 2505.
3 L. J. Seacock, Jr., D. C. Elliot, E. G. Baker and R. S. Butner, *Ind. Eng. Chem. Res.*, 1993, **32**, 1535.
4 Y. Guissani and B. Guillot, *J. Chem. Phys.*, 1993, **98**, 8221.
5 E. T. Ryan, T. Xiang, K. P. Johnston and M. A. Fox, *J. Phys. Chem. A*, 1997, **101**, 1827.
6 R. W. Shaw, T. B. Brill, A. A. Clifford, C. A. Eckert and E. U. Franck, *Chem. Eng. News*, 1991, **69**, 26.
7 B. Kuhlmann, E. M. Arnett and M. Siskin, *J. Org. Chem.*, 1994, **59**, 3098.
8 W. L. Marshall and E. U. Franck, *J. Phys. Chem. Ref. Data*, 1981, **10**, 295.
9 K. Chandler, F. Deng, A. K. Dillow, C. L. Liotta and C. A. Eckert, *Ind. Eng. Chem. Res.*, 1997, **36**, 5175.
10 J. M. L. Penninger, *Fuel*, 1988, **67**, 490.
11 P. Krammer, S. Mittelstädt and H. Vogel, *Chem. Eng. Technol.*, 1999, **22**, 126.
12 T. H. Lowry and K. S. Richardson, *Mechanism and Theory in Organic Chemistry*, Harper and Row, New York, NY, 1987, pp. 717–723.
13 A. J. Read, *J. Solution Chem.*, 1981, **10**, 437.
14 R. M. Kettler, D. J. Wesolowski and D. A. Palmer, *J. Solution Chem.*, 1995, **24**, 385.
15 E. L. Shock, *Am. J. Sci.*, 1995, **295**, 496.
16 E. W. Timm and C. N. Hinshelwood, *J. Chem. Soc.*, 1938, 862.
17 H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.

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