Reactivity of Organic Anions Promoted by a Quaternary Ammonium Ion Dendrimer

Jeng-Jong Lee and Warren T. Ford*

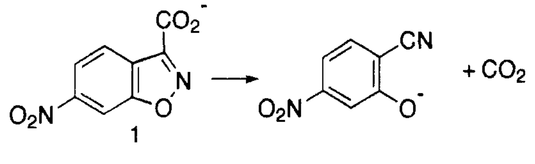
Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078-0447

J. A. Moore and Yufei Li

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590

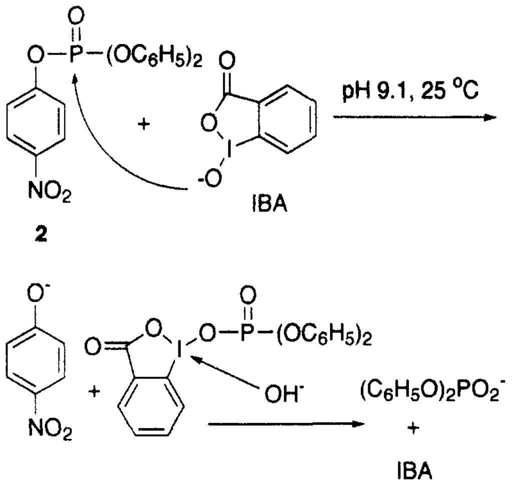
Received April 14, 1994
Revised Manuscript Received June 8, 1994

We report here the first use of a dendrimer for catalysis. The rates of unimolecular decarboxylation of 6-nitrobenzisoxazole-3-carboxylate (1; eq 1) and bimolecular hydrolysis



(1)

of *p*-nitrophenyl diphenyl phosphate (**2**) catalyzed by *o*-iodosobenzoate ion (IBA; eq 2) are accelerated by the



(2)

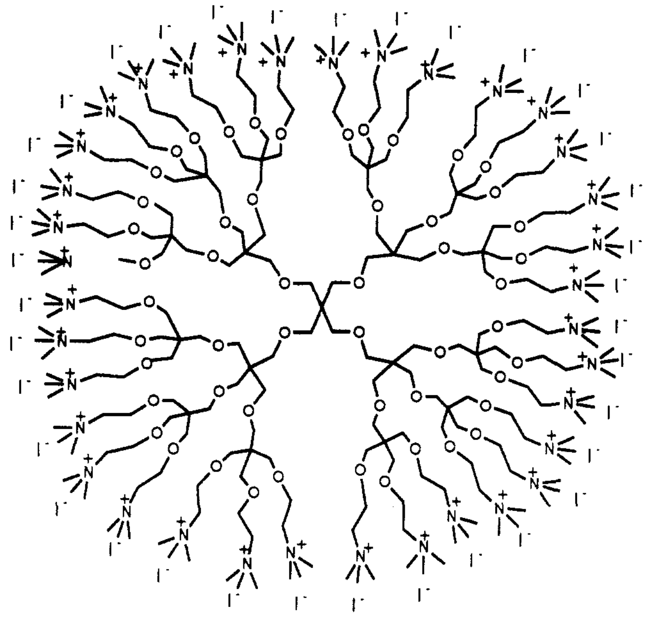
quaternary ammonium ion dendrimer PE-TMA36.

The catalytic effect of PE-TMA36 is analogous to that of other colloidal and polymeric quaternary ammonium ions. Micelles,[1a–i] microemulsions,[1a–d,j] bilayer vesicles,[1a–d,k,l] polyelectrolytes,[2] latexes,[3] and anion-exchange resins[4] often enhance rates of chemical reactions in aqueous mixtures. The rate enhancements may arise from high concentrations of reactants bound to the association colloid or polymer, to greater reactivity of the bound reactant than in water, or to both. For example, the observed rate constants of the unimolecular decarboxylation of 1 range from 220 to 10 500 times greater than in water using hydrophilic poly[(styrylmethyl)trimethylammonium] ion and lipophilic poly[(styrylmethyl)tributylammonium] ion latexes, respectively, and the intraparticle rate constants are 310 and 21 000 times greater at ambient temperature.[3b] Similarly, the bimolecular rate constants of hydrolysis of 2 catalyzed by IBA are 730 to 6300 times greater than in water using the same quaternary ammonium ion latexes.[3c,d]

The kinetics of reactions in micelles,[1d–i] microemulsions,[1j] vesicles,[1k,l] polyelectrolytes,[2b–e] and latexes[3b,d] all have been described by fundamentally the same model, in which the overall rate of reaction is the sum of the rates of reaction of the species bound to the polycation and of the unbound species in water (eq 3). The overall rates depend upon the

$$\text{rate} = k_w[S]_w + k_c[S]_b \qquad (3)$$

rate constants k_w and k_c and upon the equilibrium constants for partitioning of the reactants between the two phases. In all cases the local equilibrium concentrations of lipophilic organic anions are much higher in the polymer phase or colloidal pseudophase than in water. The rate constants of reactions in the two phases depend on the reactivity of the anion, which is generally higher in organic media than in water, where the ground state of the nucleophile is stabilized by hydrogen bonding.



PE--TMA iodide(36)

Dendritic polymers made by stepwise divergent or convergent synthesis can have many different functional groups on the surface.[5] We have used the quaternary ammonium iodide PE-TMA36 prepared from the corresponding primary amine by complete alkylation with methyl iodide.[6] For purposes of understanding the catalytic effects, PE-TMA36 is an excellent example of a polycation having a high concentration of ions only on the surface. It is a polymeric micelle. Other known dendritic polyamines have functional groups both inside and on the surface[5a,f,g] and if quaternized would not allow differentiation of the effects of interior from exterior ammonium ions on rates of reaction of bound anions.

The rate constants of decarboxylation of 6-nitrobenzisoxazole-3-carboxylate in water, reported in Table 1, show that the reaction in the presence of dendrimer PE-TMA36 is 10 times faster than with the analogous smaller dendrimer PE-TMA12, 20 times faster than in water alone, and 10 times slower than with the hydrophilic polystyrene latex TMAQ60x1 that contains 60 mol % of (styrylmethyl)trimethylammonium ion repeat units. An experiment (not shown) with the tetrakis(quaternary ammonium iodide) analogous to PE-TMA36 gave a reaction at a rate no different from that in water. Experiments with varied concentrations of the dendrimer, and analysis of the data by an enzyme-like mechanism,[1d] enable dissection of the overall effect of the dendrimer into equilibrium and kinetic effects reported in Table 2 as binding constant K and the ratio of the catalytic rate constant k_c to the rate constant in water k_w.

0024-9297/94/2227-4632$04.50/0 © 1994 American Chemical Society

Table 1. Rate Constants of Decarboxylation of 1 at 25.0 °C

polymer[a]	mg/mL[b]	$10^3[N^+]$ (M)[c]	$10^{-5}k_{obsd}$ (s^{-1})[d]	k_{obsd}/k_w[e]
PE-TMA36	0.477	1.77	5.87	18.9
PE-TMA36	0.762	2.83	6.47	20.9
PE-TMA36	1.14	4.25	6.81	22.0
PE-TMA12	1.12	4.24	0.65	2.1
TMAQ60x1[f]	0.559	1.91	68	220

[a] Concentration of 1 was 7.82×10^{-5} in PE-TMA36 experiments and 13.04×10^{-5} M in the TMAQ60x1 experiment. The kinetic method is described in ref 3b. [b] The amount of polymer used. [c] Concentration of quaternary ammonium units. [d] In 2 mM NaOH. [e] The first-order rate constant in water was $k_w = 3.1 \times 10^{-6}$ s^{-1}. [f] Reference 3b.

Table 2. Binding Constants and Rate Constants of Decarboxylation of 1

	10^3k_c (s^{-1})[a]	k_c/k_w[b]	K (M^{-1})
PE-TMA36[d]	0.0772[c]	25	1700
TMAQ60x1[d]	0.95	310	1300
TMAQ39x1[d]	1.0	340	2600
TMAQ24x1[d]	65	21000	1200
cetyltrimethylammonium bromide[e]	0.387	130	
cetyltributylammonium bromide[f]	8.53	2800	2 to 5000
1-methyl-4-dodecylpyridinium iodide[g]	0.342	160	1160
tri-*n*-octylethylammonium methanesulfonate[h]	27	9000	5000

[a] k_c = intrinsic rate constant in the colloidal pseudophase. [b] The first-order rate constant in water, $k_w = 3.1 \times 10^{-6}$ s^{-1}. [c] The correlation coefficient (*r*) in the Menger–Portnoy analysis was 0.999. [d] Reference 3d. [e] Bunton, C. A.; Minch, M. J.; Hidalgo, J.; Sepulveda, L. *J. Am. Chem. Soc.* **1973**, *95*, 3262. [f] Germani, R.; Ponti, P. P.; Romeo, T.; Savelli, G.; Spreti, N.; Cerichelli, G.; Luchetti, L.; Mancini, G.; Bunton, C. A. *J. Phys. Org. Chem.* **1989**, *2*, 533. [g] Engberts, J. B. F. N.; Rupert, L. A. M. *J. Org. Chem.* **1982**, *47*, 5015. [h] Biresaw, G.; Bunton, C. A. *J. Phys. Chem.* **1986**, *90*, 5854.

Table 3. Rate Constants of Hydrolysis of *p*-Nitrophenyl Diphenyl Phosphate Catalyzed by IBA with Dendrimers and a Latex[a]

	mg/mL[b]	$10^3[N^+]$ (M)[c]	10^4[IBA] (M)	10^4k_{obsd} (s^{-1})
PE-TMA36	0.770	2.86	3.85	4.13
PE-TMA36	0.770	2.86	3.10	3.85
PE-TMA36	0.770	2.86	2.33	3.14
PE-TMA36	0.770	2.86	1.56	2.85
PE-TMA36	0.385	1.43	1.56	2.56
PE-TMA12	0.788	2.99	3.10	2.47
TMAQ60x1	0.20	0.682	3.85	1425[d]
buffer only			3.10	2.28

[a] 5.0×10^{-2} M TAPS buffer, pH 9.10, 1.95×10^{-5} M 2. The kinetic method is described in refs 3c,d. [b] Amount of dendrimer. [c] Concentration of quaternary ammonium ions. [d] Calculated from $k_{obsd} = k_{IBA}[IBA]$ and $k_{IBA} = 370$ M^{-1} s^{-1} in Table 3 of ref 3d.

The decarboxylation of 1 is the most sensitive to solvent of any known organic reaction, being 10^8 times faster in hexamethylphosphoramide than in water.[7] It has been studied in numerous other polymeric and colloidal media, and selected examples of micelles are compared with the dendrimer and latex results in Table 2. The results show differences of equilibrium binding constants of less than a factor of 5 among these colloids, including dendrimer PE-TMA36, whereas the relative rate constants vary over a factor of 840, being fastest in the lipophilic poly(styrylmethyl)tributylammonium ion latex TMAQ24x1 and slowest with the dendrimer PE-TMA36. The major environmental effect controlling the rate of decarboxylation of 1 is stabilization of the ground-state carboxylate ion by hydrogen bonding.[7c] The relatively slow rate constant with the reactive anion bound to PE-TMA36 shows the dendrimer surface to be more hydrated than the interiors of any of the quaternary ammonium ion latexes and more hydrated than the surfaces of any of the quaternary ammonium ion micelles.

The hydrolysis of *p*-nitrophenyl diphenyl phosphate (2) catalyzed by IBA is markedly accelerated by micelles,[8] microemulsions,[8d,9] and polycations.[3c,d,10] Rate constants in pH 9.1 buffer solutions containing PE-TMA36 are reported in Table 3. A plot of k_{obsd} vs IBA concentration gave second-order rate constant $k_{IBA} = 0.60$ M^{-1} s^{-1}, compared with $k_{IBA} = 0.51$ M^{-1} s^{-1} in TAPS [3-[[tris(hydroxymethyl)methyl]amino]propanesulfonic acid] buffer solution alone. The rate enhancement by PE-TMA36 is small but significant. Under similar conditions the hydrophilic latex TMAQ60x1 gave $k_{IBA} = 370$ M^{-1} s^{-1} and a much faster pseudo-first-order rate constant, as reported in Table 3. Two equilibrium constants, for binding of IBA and for binding of 2 to the polycation, and the intraparticle second-order rate constant of reaction of the bound species determine the overall second-order rate constant k_{IBA} of this reaction. The binding of IBA is an anion-exchange equilibrium, which can be expressed in terms of a selectivity coefficient

$$K_{IBA/X} = [IBA]_b[X]_f/[IBA]_f[X]_b \tag{4}$$

where X = I^- for the dendrimer, X = Cl^- for the latex, and subscripts b and f refer to bound and free anions. In latex TMAQ60x1 $K_{IBA/Cl} = 2.4$ and $K_{TAPS/Cl} = 0.58$.[3d] If we approximate (a) $K_{I/Cl} = 10$ for the dendrimer, as in a typical anion-exchange resin,[11] and (b) the dendrimer has the same selectivity coefficients as latex TMAQ60x1, the fraction of the IBA bound to the dendrimer is 0.15 and to the latex is 0.33 under the conditions of the experiments of Table 3 where [IBA] = 3.85×10^{-4} M. Thus a factor of 0.33/0.15 = 2.2 faster rate in the latex than in the dendrimer is due to a higher concentration of bound IBA.[12] The intraparticle second-order rate constant for hydrolysis of 2 catalyzed by IBA in the hydrophilic latex TMAQ60x1 is the same as k_{IBA} in water[3d] and will be about the same at the surface of dendrimer PE-TMA36. Therefore, since neither a much lower amount of IBA bound to the dendrimer nor a lower rate constant for reaction of IBA with 2 at the dendrimer surface can account for the much lower k_{IBA} in the 0.77 mg mL^{-1} dendrimer PE-TMA36 solution than in a 0.20 mg mL^{-1} dispersion of latex TMAQ60x1, the rate difference is due mainly to a much lower equilibrium constant for binding of hydrophobic phosphate ester 2 to the dendrimer than to the latex.

The surface of the dendrimer PE-TMA36 is more hydrophilic than the cores of latexes, the random coils of poly[(styrylmethyl)trimethylammonium chloride], and the cationic micelles investigated previously as media for reactions of anions 1 and IBA. The local concentration of quaternary ammonium ions at the dendrimer surface is very high. In contrast, long-chain quaternary ammonium polyelectrolytes than can assume random-coil conformations have much lower local concentrations of ionic groups. The high density of quaternary ammonium ions limits binding of high concentrations of lipophilic organic compounds and allows strong hydrogen bonding of water to reactive anions. We expect that dendrimers having much more lipophilic quaternary ammonium ions on the surface, or even in the interior, would show larger rate enhancements for decarboxylation of 1 and IBA-catalyzed hydrolysis of 2.

Acknowledgment. This research was supported by the U.S. Army Research Office. We thank the U.S. Army

Edgewood Research Development and Engineering Center for the sample of *p*-nitrophenyl diphenyl phosphate. The dendrimers were prepared during a project sponsored by the National Science Foundation (Grant BCS9112481).

References and Notes

(1) (a) Fendler, J. H.; Fendler, E. J. *Catalysis in Micellar and Macromolecular Systems*; Academic Press: New York, 1975. (b) Fendler, J. H. *Membrane Mimetic Chemistry*; John Wiley and Sons: New York, 1982. (c) Grätzel, M.; Kalyanasundaram, K. *Kinetics and Catalysis in Microheterogeneous Systems*; Marcel Dekker, Inc.: New York, 1991. (d) Menger, F. M.; Portnoy, C. E. *J. Am. Chem. Soc.* **1967**, *89*, 4698. (e) Cordes, E. H.; Dunlap, R. B. *Acc. Chem. Res.* **1969**, *2*, 329. (f) Quina, F. H.; Chaimovich, H. J. *J. Phys. Chem.* **1979**, *83*, 1844. (g) Romsted, L. S. In *Surfactants in Solution*; Mittal, K. L., Lindman, B., Eds.; Plenum: New York, 1984; pp 1015–1068. (h) Bunton, C. A.; Savelli, G. *Adv. Phys. Org. Chem.* **1986**, *22*, 213. (i) Bunton, C. A.; Nome, F.; Quina, F. H.; Romsted, L. S. *Acc. Chem. Res.* **1991**, *24*, 357. (j) Mackay, R. A.; Hermansky, C. *J. Phys. Chem.* **1987**, *85*, 739. (k) Fendler, J. H.; Hinze, W. L. *J. Am. Chem. Soc.* **1981**, *103*, 5439. (l) Cuccovia, I. M.; Quina, F. H.; Chaimovich, H. *Tetrahedron* **1982**, *38*, 917.

(2) (a) Overberger, C. G.; Salamone, J. C. *Acc. Chem. Res.* **1969**, *2*, 217. (b) Morawetz, H. *Acc. Chem. Res.* **1970**, *3*, 354. (c) Fernandez-Prini, R.; Turyn, D. *J. Chem. Soc., Faraday Trans. 1* **1973**, *69*, 1326. (d) Ise, N.; Okubo, R.; Kunugi, S. *Acc. Chem. Res.* **1982**, *15*, 171. (e) Couvercelle, J.-P.; Huguet, J.; Vert, M. *Macromolecules* **1993**, *26*, 5015.

(3) (a) Ford, W. T.; Badley, R. D.; Chandran, R. S.; Hari Babu, S.; Hassanein, M.; Srinivasan, S.; Turk, H.; Yu, H.; Zhu, W. *ACS Symp. Ser.* **1992**, *492*, 422 and references therein. (b) Lee, J.-J.; Ford, W. T. *J. Org. Chem.* **1993**, *58*, 4070. (c) Ford, W. T.; Yu, H. *Langmuir* **1993**, *9*, 1999. (d) Lee, J.-J.; Ford, W. T. *J. Am. Chem. Soc.* **1994**, *116*, 3753.

(4) (a) Ford, W. T.; Tomoi, M. *Adv. Polym. Sci.* **1984**, *55*, 49. (b) Tomoi, M.; Ford, W. T. In *Syntheses and Separations Using Functional Polymers*; Sherrington, D. C., Hodge, P., Eds.; Wiley: Chichester, U.K., 1988; pp 181–207. (c) Helfferich, F. *Ion Exchange*; McGraw-Hill: New York, 1962; pp 519–550.

(5) (a) Tomalia, D. A.; Naylor, A. M.; Goddard, W. A., III *Angew Chem., Int. Ed. Engl.* **1990**, *29*, 138. (b) Newkome, G. R.; Gupta, V. K.; Baker, G. R.; Yao, Z.-Q. *J. Org. Chem.* **1985**, *50*, 2003. (c) Mekelburger, H.-B.; Jaworek, W.; Vögtle, F. *Angew Chem., Int. Ed. Engl.* **1992**, *31*, 1571. (d) Fréchet, J. M. J. *Science* **1994**, *263*, 1710. (e) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638. (f) de Brabander-van den Berg, E. M. M.; Meijer, E. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1308. (g) Wörner, C.; Mülhaupt, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1306.

(6) The dendrimers were synthesized by an improved procedure based on the work of Hall: (a) Padias, A. B.; Hall, H. K., Jr.; Tomalia, D. A.; McConnell, J. R. *J. Org. Chem.* **1987**, *52*, 5305. (b) Hall, H. K., Jr.; Polis, D. W. *Polym. Bull.* **1987**, *17*, 409. The detailed procedure is described in: Moore, J. A.; Li, Y.; Cramer, S.; Jayaraman, G. *React. Polym.*, submitted for publication.

(7) (a) Kemp, D. S.; Paul, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 7305. (b) Kemp, D. S.; Cox, D. D.; Paul, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 7312. (c) Grate, J. W.; McGill, R. A.; Hilvert, D. *J. Am. Chem. Soc.* **1993**, *115*, 8577.

(8) (a) Moss, R. A.; Alwis, K. W.; Bizzigotti, G. O. *J. Am. Chem. Soc.* **1983**, *105*, 681. (b) Moss, R. A.; Alwis, K. W.; Shin, J.-S. *J. Am. Chem. Soc.* **1984**, *106*, 2651. (c) Moss, R. A.; Alwis, K. W.; Bizzigotti, G. O. *J. Am. Chem. Soc.* **1986**, *108*, 788. (d) Hammond, P. S.; Forster, J. S.; Lieske, C. N.; Durst, H. D. *J. Am. Chem. Soc.* **1989**, *111*, 7860. (e) Moss, R. A. Presented at the U.S. Army Edgewood Research, Development, and Engineering Center Scientific Conference, Nov 1993, and personal communication.

(9) (a) Mackay, R. A.; Longo, F. R.; Knier, B. L.; Durst, H. D. *J. Phys. Chem.* **1987**, *91*, 861. (b) Burnside, B. A.; Knier, B. L.; Mackay, R. A.; Durst, H. D.; Longo, F. R. *J. Phys. Chem.* **1988**, *92*, 4505.

(10) (a) Moss, R. A.; Chung, Y.-C.; Durst, H. D.; Hovanec, J. W. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1350. (b) Moss, R. A.; Chung, Y.-C. *J. Org. Chem.* **1990**, *55*, 2064. (c) Moss, R. A.; Chung, Y.-C. *Langmuir* **1990**, *6*, 1614. (d) Ford, W. T.; Yu, H. *Langmuir* **1991**, *7*, 615.

(11) Helfferich, F. *Ion Exchange*; McGraw-Hill: New York, 1962; p 175.

(12) We assumed no dissociation of counterions, which is a good approximation for the latex but not for the dendrimer. If the fraction of counterions dissociated from the dendrimer is 0.5, the fraction of IBA bound would be 0.075 rather than 0.15. This does not alter our conclusion that the lesser binding of **2** is the main factor responsible for the lower activity of the dendrimer.