4.1-3.6 (m, 24 H, CH_2O), ^{13}C NMR δ 153.6 (Ar C-2, C-6), 146.8 (Ar C-4), 124.4 (Ar C-3, C-5), 70.6-68.5 ($ArCH_2$, CH_2O). No satisfactory elemental analysis could be obtained due to loss of H_2O. Anal. Calcd for $C_{19}H_{36}NO_{13}Cl$: C, 43.72; H, 6.95; N, 2.68. Found: C, 43.51; H, 6.40; N, 2.27.

X-ray Diffraction. X-ray measurements were performed on a single-crystal diffractometer (Philips PW1100) using the ω-2θ scanning mode. The most important data-collection parameters are presented in Table IV. Measured intensities were corrected for the decrease in intensity during data collection, using the intensities of three standard reflections measured every hour.

The structures were solved by direct methods[49] and refined by full-matrix least-squares analysis,[50] using reflections having an intensity larger than some threshold value ($\sigma(I)$ for uncomplexed 2,6-pyrido-18-crown-6 (**1**, n = 1) and for its complex with perchloric acid and water (**5**) and $3\sigma(I)$ for the other three water complexes (**6**-**8**), $\sigma(I)$ being the estimated standard deviation from counting statistics). All hydrogen atoms in the complexes could unambigiously be located from difference-Fourier maps.

Parameters refined were the overall scale factors, isotropic secondary extinction parameters, positional parameters of all atoms, anisotropic thermal parameters for non-hydrogen atoms, and isotropic thermal parameters for hydrogens. The weight for each reflection was taken to be $w = \{\sigma(F_o) + 0.01|F_o|\}^{-2}$, where $\sigma(F_o)$ is the estimated standard deviation of the observed structure factor (F_o) derived from counting statistics. Scattering factors for non-hydrogen atoms were taken from "International Tables for X-ray Crystallography";[51] for H, the scattering factors of Stewart et al.[52] were used. No absorption corrections were applied.

For the crystalline 2,6-pyrido-21-crown-7·H_2O·$HClO_4$ (1:1:1) complex, a second modification exists at lower temperature (transition temperature 216 ± 2 K). The structure of this complex at 193 K was also solved by using X-ray diffraction.[53] The low-temperature modification has a doubled unit cell (with two independent moieties of the compound in the asymmetric unit). The two perchlorate anions in the asymmetric unit have a markedly different orientation. The two independent crown ether-water entities are related by approximate translation symmetry and hardly differ in structure. They also have the same conformation as the higher-temperature modification **7** discussed above.

Acknowledgment. This investigation was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

Registry No. 1 (n = 0), 99747-84-9; **1** (n = 1), 64726-19-8; **1** (n = 2), 99747-85-0; **1** (n = 3), 99747-86-1; **1** (n = 4), 99747-87-2; **1** (n = 5), 99764-92-8; **1** (n = 6), 99747-88-3; **2**, 64726-18-7; **3**, 99747-89-4; **5**, 95731-92-3; **6**, 99747-91-8; **7**, 99747-92-9; **8**, 99747-93-0; 2,6-bis(bromomethyl)pyridine, 7703-74-4.

Supplementary Material Available: Lists of anisotropic thermal parameters for heavy atoms and isotropic thermal parameters for hydrogens and positional parameters for all atoms as well as complete lists of bond lengths, bond angles, and torsional angles (46 pages). Ordering information is given on any current masthead page.

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(50) Busing, W. R.; Martin, K. O.; Levy, H. A. "ORFLS"; Oak Ridge National Laboratory: Oak Ridge, TN, 1962; Report ORNL-TM-305.
(51) "International Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, 1974; Vol. IV, 72-98.
(52) Stewart, R. F.; Davidson, E. R.; Simpson, W. T. *J. Chem. Phys.* **1965**, *42*, 3175-3187.
(53) Relevant data-collection parameters of the lower-temperature modification of the crystalline 2,6-pyrido-21-crown-7·H_2O·$HClO_4$ (1:1:1) complex are as follows: lattice type: triclinic; space group $P\bar{1}$; T = 193 K. Cell dimensions: a = 15.073 (4) Å, b = 14.729 (3) Å, c = 11.593 (3) Å, α = 114.41 (1)°, β = 74.07(2)°, γ = 111.61 (2)°; V = 2156.12 Å^3; Z = 4; D_c = 1.420 × 10^3 kg m^{-3}; Mo Kα radiation; μ = 0.11 × 10^3 m^{-1}. S-range: 0.10-0.48 Å^{-1}; 7575 reflections measured, of which 3378 with $I > 3\sigma(I)$ were used in the refinement; 780 final variables. Final R and R_w: 3.3 and 3.5%, respectively.

Efficient Catalytic Cleavage of Reactive Phosphates by an *o*-Iodosobenzoate Functionalized Surfactant

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Contribution from the Department of Chemistry, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903. *Received August 5, 1985*

Abstract: 5-(*N*-(*n*-Hexadecyl)-*N*,*N*-dimethyl-*N*-(β-ethyloxy)ammonium)-2-iodosobenzoate, **1c**, cleaved *p*-nitrophenyl diphenyl phosphate (PNPDPP), *p*-nitrophenyl diethyl phosphate (PNPDEP), and *p*-nitrophenyl isobutyl methylphosphonate (PNPIMP) in aqueous cetyltrimethylammonium chloride (CTACl) at pH 8 and 25 °C. With 4 × 10^{-5} M **1c** in 2 × 10^{-4} M CTACl, second-order cleavage rate constants (L/(M-s)) were PNPDPP, 28 500, PNPDEP, 0.865, and PNPIMP, 215. These represented kinetic advantages of 14 700, 43 600 and 846, respectively, over nonfunctional CTACl-catalyzed cleavages of the substrates. In the presence of excess PNPDPP at pH 8, catalyst **1c**/CTACl "turned over" with $k \sim 0.17$ s^{-1} for the hydrolysis of the putative **1c**-diphenyl phosphate intermediate.

An efficient method of cleavage of reactive phosphates is needed for the decontamination of areas affected by these toxic compounds.[1] The problem has been under attack for more than a decade, with micellar and other aggregated reagents a focus of attention.[2] Particularly in the pioneering work of Bunton and his associates, many functional groups have been surveyed for their reactivity toward phosphates, including hydroxide and phenoxide,[3] peroxide and hydroperoxide,[4] fluoride ion,[5] imidazole and benz-

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(2) Reviews of the earlier literature appear in: (a) Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecuclar Systems"; Academic Press: New York, 1975; pp 150-161. (b) Moss, R. A.; Ihara, Y. *J. Org. Chem.* **1983**, *48*, 588.
(3) (a) Bunton, C. A.; Robinson, L.; Stam, M. *J. Am. Chem. Soc.* **1970**, *92*, 7393. (b) Bunton, C. A.; Ionescu, L. G. *Ibid.* **1973**, *95*, 2912. (c) Bunton, C. A.; Gan, L-H.; Savelli, G. *J. Phys. Chem.* **1983**, *87*, 5491. (d) Biresaw, G., Bunton, C. A.; Quan, C.; Yang, Z.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 7178. (e) Bunton, C. A.; Cerichelli, G.; Ihara, Y.; Sepulveda, L. *Ibid.* **1979**, *101*, 2429. (f) Bunton, C. A.; Sepulveda, L. *Isr. J. Chem.* **1979**, *18*, 298.
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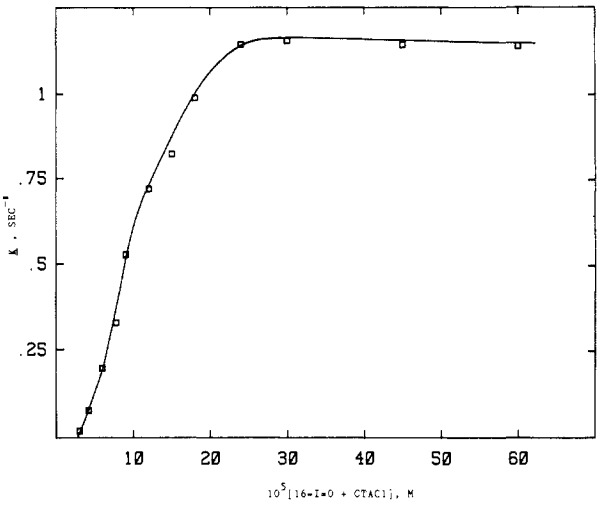
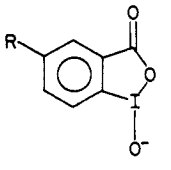


Figure 1. Pseudo-first-order rate constants (k_ψ, s^{-1}) for the cleavage of PNPDPP by 1:5 **1c** (16-I=O)/CTACl as a function of [total surfactant] at pH 8.0. See text for reaction conditions and Table I for k_ψ^{max}.

imidazole,[6] and hydroxamates and oximates.[7] Lately, vesicular[2b,5b],[8] and microemulsified[9] reagents have been studied. Most recently, Menger described an aldehyde–hydrate functionalized surfactant that cleaved *p*-nitrophenyl diphenyl phosphate (PNPDPP) at pH 9 with $k_\psi = 2.0 \times 10^{-2}$ s^{-1} (a catalytic advantage of 1800) and with catalytic turnover.[10]

However, from the viewpoint of the efficient cleavage of reactive phosphates, many of the foregoing reagents exhibit one or more of these disadvantages: the cleavage reaction is too slow, high reagent concentrations or high pH (≥10) are required, or reagent turnover (catalysis) is absent. In the latter case, the reagent must be used in stoichiometric quantities because it forms a phosphorous derivative that is stable under the reaction conditions.

We have found that the *o*-iodosobenzoate moiety, in its preferred 1-hydroxy-1,2-benziodoxolin-3-one (or 1-hydroxy-1,2-benziodoxol-3(1*H*)-one) valence tautomeric form, is a superior catalyst for phosphate cleavage.[11,12] In pH 8 aqueous cetyltrimethylammonium chloride (CTACl) micellar solution, the parent iodosobenzoate **1a**[11] is about as efficient as Menger's catalyst,



1

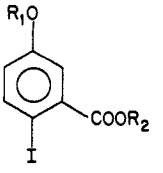
(a) R=H; (b) R=*n*-$C_8H_{17}O$; (c) R=*n*-$C_{16}H_{33}N^+Me_2CH_2CH_2O$

whereas the *p*-octyloxy derivative **1b** is ~100 times more reactive, cleaving PNPDPP with $k_\psi = 1.04$ s^{-1} (corresponding to a bimolecular rate constant of 14400 L/(M-s)).[12] These reactions occur with catalyst turnover.[11,12]

Now we report the synthesis and catalytic properties of the first iodosobenzoate functionalized surfactant, **1c**, which we believe to be the most versatile reagent yet developed for the efficient destruction of a variety of phosphorylating compounds.

Results

Synthesis. Surfactant **1c** was prepared in five steps and 24% overall yield from 2-iodo-5-hydroxybenzoic acid, **2a**.[12] Esterification of **2a** (EtOH/HCl) gave 78% of the ethyl ester **2b** which, in its sodium phenoxide salt form, was alkylated with dibromoethane, affording bromoethyl ether **2c** (54%). The latter was

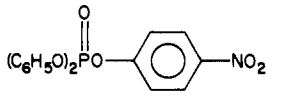


2a, R_1=R_2=H
2b, R_1=H; R_2=C_2H_5
2c, R_1=CH_2CH_2Br; R_2=C_2H_5
2d, R_1=*n*-$C_{16}H_{33}N^+Me_2CH_2CH_2$; R_2=C_2H_5 (Br^- salt)
2e, R_1=*n*-$C_{16}H_{33}N^+Me_2CH_2CH_2$; R_2=H (Br^- salt)

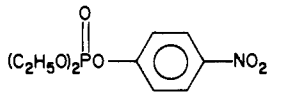
reacted with *N,N*-dimethyl-*n*-hexadecylamine to yield 75% of the quaternary ammonium salt **2d**, from which the free iodo acid **2e** was obtained in 95% yield by saponification with NaOH/MeOH. Finally, iodo acid **2e** was oxidized (79%) to the desired iodosobenzoate surfactant, **1c**, by the standard chlorination/hydrolysis procedure.[13]

The iodoso surfactant, **1c**, was isolated as the I–OH quaternary ammonium chloride salt; it showed 98 ± 4% I=O activity by $KI/Na_2S_2O_3$ iodometric titration.[13] The limited solubility of **1c** in both organic and aqueous solvents made difficult the control of the oxidation step and purification of the product. As a result, each repetition gave iodoso surfactant of somewhat different titrimetric and kinetic activity. This is discussed in greater detail below.

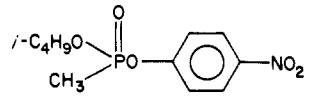
Substrates. Three substrates were investigated: *p*-nitrophenyl diphenyl phosphate (**3**, PNPDPP), *p*-nitrophenyl diethyl phosphate (**4**, "Paraoxon", PNPDEP), and *p*-nitrophenyl isobutyl methylphosphonate (**5**, PNPIMP). PNPDEP was commercially available (Aldrich), whereas PNPDPP[14] and PNPIMP[15] were prepared by literature methods.



3 (PNPDPP)



4 (PNPDEP)



5 (PNPIMP)

Kinetic Studies. The pK_a of **1c** is ~6.5 under our micellar reaction conditions (see below), so that the surfactant is nearly fully ionized to its $N^+/I{-}O^-$ zwitterionic form at pH 8. This may be largely responsible for its very low solubility in basic aqueous solution. Indeed, it was necessary to comicellize **1c** with CTACl to enhance its solubility. The two surfactants were therefore cosonicated in aqueous Tris buffer. (Tris buffer provided greater solubility for **1c**/CTACl than the previously employed[11,12] phosphate buffer.) Preliminary experiments indicated that a 1:5

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(7) (a) Sloan, K. B.; Bodor, N.; Higuchi, T.; Little, R.; Wu, M.-S. *J. Chem. Res. Synop.* **1977**, 290. (b) Bunton, C. A.; Ihara, Y. *J. Org. Chem.* **1977**, *42*, 2865. (c) Bunton, C. A.; Nelson, S. E.; Quan C. *Ibid.* **1982**, *47*, 1157. (d) Rutkovskii, G. V.; Begunov, A. V.; Kuznetsov, S. G. *J. Org. Chem. USSR (Engl. Transl.)* **1983**, *19*, 788. (e) Rutkovskii, G. V.; Begunov, A. V.; Ignat'ev, Yu. A. *Ibid.* **1983**, *19*, 793.

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(9) Bunton, C. A.; de Buzzaccarini, F.; Hamed, F. H. *J. Org. Chem.* **1983**, *48*, 2457.

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(13) Cf., ref 12 and: Lucas, H. J.; Kennedy, E. R. In "Organic Syntheses; Horning, E. C.; Ed.; Wiley: New York, 1955; Collect. Vol. 3, pp 482–484.

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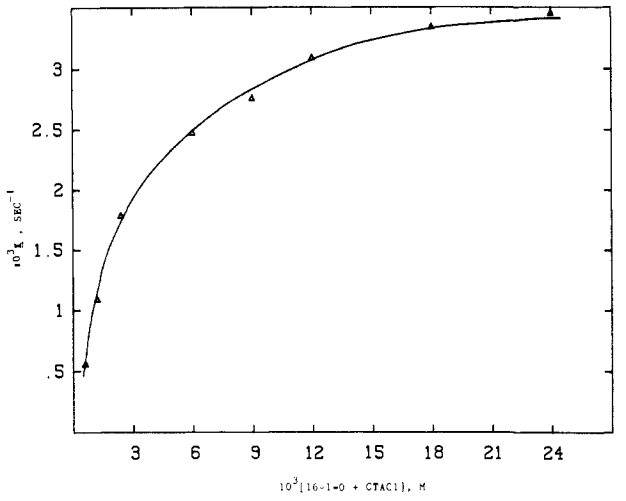


Figure 2. Pseudo-first-order rate constants (k_ψ, s^{-1}) for the cleavage of PNPDEP by 1:5 **1c** (16-I═O)/CTACl as a function of [total surfactant] at pH 8.0. See text for reaction conditions and Table I for k_ψ^{max}.

Table I. Cleavage Reactions Catalyzed by Surfactant **1c**/CTACl[a]

substrate	k_ψ^{max}, s^{-1}	[**1c**], M[b]	k_2, L/(M-s)[c]	k_0, s^{-1} [d]	k_ψ^{max}/k_0
PNPDPP	1.14	4.0×10^{-5}	28 500	7.77×10^{-5}	14 700
PNPDEP	0.003 46	4.0×10^{-3}	0.865	7.94×10^{-8}[e]	43 600[f]
PNPIMP	0.215	1.0×10^{-3}	215	2.54×10^{-4}	846

[a] Kinetic data are taken from Tables I–III of the supplementary data. Conditions are described in the text. k_ψ^{max} is measured at the beginning of the plateau region for PNPDPP and PNPIMP; cf. Figures 1 and 3. Reproducibilities are <±3%. [b] Concentration of **1c** at which k_ψ^{max} was observed; [CTACl] = 5[**1c**]. [c] Second-order rate constant, taken as k_ψ^{max}/[**1c**]. [d] Rate constant for substrate cleavage with iodo surfactant **2e** (and CTACl) instead of iodoso surfactant **1c**; other conditions as for k_ψ^{max}. [e] Value is extrapolated to pH 8 from five runs over the pH range 12.97–9.5; see text. [f] Comparison of k_ψ^{max} and k_0 is made at [**1c**] or [**2e**] = 1.0×10^{-3} M, [CTACl] = 5.0×10^{-3} M.

molar ratio of **1c**/CTACl gave optimal cleavage rates with PNPDPP, and this comicellar composition was used for all phosphate cleavage reactions. We observed that a 1×10^{-5} M **1c**/5×10^{-5} M CTACl solution in Tris buffer (pH 8) cleaved 1×10^{-5} M PNPDPP with experimentally identical rate constants at 30 min, 8 h, 12 h, and 24 h after preparation. Therefore, dilute catalyst solutions are stable for at least 24 h at 25 °C in the dark. Nevertheless, freshly prepared solutions were routinely used for our studies.

The catalytic properties of **1c** were assessed by determining full rate constant vs. [total surfactant] profiles for the cleavages of PNPDPP, PNPDEP, and PNPIMP. These were all done under identical conditions: 0.01 M pH 8.0 aqueous Tris buffer, μ = 0.01 (KCl), 0.2 vol % CH_3CN, 25.0 ± 0.10 °C, [substrate] = 1.0×10^{-5} M. A 1:5 molar ratio of **1c**/CTACl was maintained in all experiments.

Tables I–III of the supplementary material present rate constants for the cleavages of the three substrates by **1c**/CTACl as functions of **1c** and total surfactant concentrations. These data are graphically represented in Figures 1–3; the associated values of k_ψ^{max} as well as the concentrations of **1c** needed to obtain k_ψ^{max} are collected in Table I. Note that k_ψ^{max} is taken as the measured rate constant at the beginning of the plateau region in the rate constant–[surfactant] profiles; cf., Figures 1 and 3. In the case of PNPDEP (Figure 2), it is not clear that k_ψ^{max} has been reached at the highest surfactant concentration we could use; the largest measured k_ψ is therefore taken as k_ψ^{max}.

Also included in Table I are the second-order rate constants for the cleavages by **1c** ($k_2 = k_\psi^{max}$/[**1c**]), and k_0, the rate constants for substrate cleavage in the *absence* of the iodoso catalyst. In the latter situation, iodo surfactant **2e** was substituted for **1c**, so that k_0 represents *nonfunctional* micellar catalysis by 1:5 **2e**/CTACl at pH 8.[16] Accordingly, the last column of Table I, k_ψ^{max}/k_0, gives the kinetic advantage of iodosobenzoate-functionalized relative to nonfunctional micelle-catalyzed cleavage of the substrates.

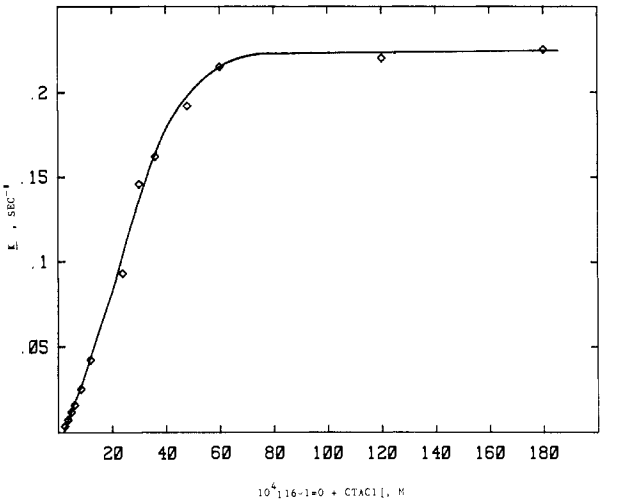


Figure 3. Pseudo-first-order rate contants (k_ψ, s^{-1}) for the cleavage of PNPIMP by 1:5 **1c** (16-I═O)/CTACl as a function of [total surfactant] at pH 8.0. See text for reaction conditions and Table I for k_ψ^{max}.

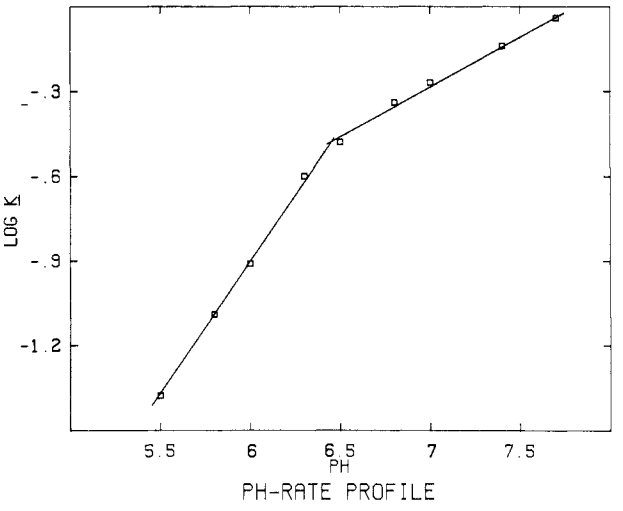


Figure 4. pH-rate profile for the cleavage of PNPDPP by 4.0×10^{-5} M **1c** in 2.0×10^{-4} M CTACl; log k_ψ (s^{-1}) vs. pH. The discontinuity at pH 6.45 is taken as the systematic pK_a of **1c**. See text for reaction conditions.

The data in Table I and Figures 1–3 were obtained with our most active sample of surfactant **1c**. Two other preparations of this material from **2e** gave compounds with iodometric iodoso titers of ~93 ± 4% and reactivities toward PNPDPP which were ~52% and ~26% that of the most active sample (as judged by the ratio k_ψ/k_ψ^{max} for the two samples of surfactant).

pK_a Determination. A pH-rate-constant profile was determined for reactions of 1.0×10^{-5} M PNPDPP with 4.0×10^{-5} M **1c** in 2.0×10^{-4} M aqueous CTACl in 0.01 Tris (pH 8.0–7.4), Bis–Tris (pH 7.0–6.0), or acetate (pH 5.8–5.5) buffers. In all cases, μ = 0.01 (KCl). A plot of log k_ψ vs. pH (Figure 4) gave a sharp break at pH 6.45, which we take as the systematic pK_a of the I–OH function of **1c** under our (micellar) reaction conditions. Similarly determined pK_a values of **1a** and **1b** are ~7.2,[11,12] so that the covalently attached quaternary ammonium ion of **1c** appears to be responsible for an additional pK_a depression of ~0.8 units. At

(16) The values of k_0 for PNPDPP and PNPIMP were measured directly at pH 8. PNPDEP, however, cleaved so slowly in aqueous **2e**/CTACl at pH 8 that the direct determination of k_0 was impractical. Accordingly, k_0 was determined at pH 12.97, 12.53, 11.23, 10.3, and 9.5. A good linear relation was obtained between log k and pH: log k = 1.06(pH) − 15.54 (correlation coefficient = 0.998). From this expression, we extrapolate k_0 at pH 8 as 7.94 × 10^{-8} s^{-1}.

Table II. Cleavage of Excess PNPDPP by **1c**/CTACl[a]

run	10^5[**1c**], M	10^4[PNPDPP], M	10^5[$PNPO^-$], M[b]	10^6A, M-s^{-1}[c]	k_{turn}, s^{-1}[d]
1	4.00	1.00	4.18	6.90	0.17
2	4.00	1.50	4.16	6.85	0.17
3	4.00	2.00	3.92	6.85	0.17
4	2.00	1.00	1.88	3.22	0.16
5	3.00	1.00	3.00	5.28	0.18
6	4.00	1.00	4.25	6.87	0.17

[a] Conditions: 0.01 M pH 8.0 aqueous Tris buffer, μ = 0.01 (KCl), 3.3 vol % CH_3CN, 25.0 ± 0.1 °C. The [CTACl] was 5 times the [**1c**] in all experiments. [b] The initially observed "burst" of $PNPO^-$; see also Figure 5. [c] A is the slope of the linear portion of [$PNPO^-$] vs. time; cf., Figure 5. [d] The "turnover" rate constant is obtained from A/[**1c**].[17]

pH 8, micellar **1c** will be ~97% in the I–O^- form. Under our reaction conditions, therefore, **1c** will be present as a N^+/O^- zwitterion, although the comicelle as a whole will be net positively charged due to the excess of CTACl.

Turnover Experiments. The "turnover" capacity of **1c** was carefully studied with substrate PNPDPP using the kinetic methods described by Bender et al.[17] According to this scheme, **1c** should be very rapidly phosphorylated by excess substrate PNPDPP, releasing a "burst" of *p*-nitrophenoxide ($PNPO^-$) stoichiometrically equivalent to the amount of **1c**. Thereafter, the cleavage of PNPDPP and the accompanying release of $PNPO^-$ should be linear with time and occur at a rate governed by the rate of hydrolytic dephosphorylation of **1c**–diphenyl phosphate. Moreover, the slope, A, of the linear portion will be equal to the dephosphorylation or "turnover" rate constant, multiplied by [**1c**].[17]

An appropriate series of experiments was carried out to test the applicability of this scheme to the **1c**/CTACl–PNPDPP reaction. In this study, we employed a sample of **1c** with ~52% of the activity of the material used in the cleavage studies summarized in Table I. That is, k_ψ = 0.59 ± 0.02 s^{-1} for the cleavage of PNPDPP, under conditions identical with those of Table I, where our most reactive **1c** exhibited k_ψ = 1.14 s^{-1}.

The data collected in Table II summarize the burst kinetics spectroscopically followed at 400 nm for the cleavage of excess PNPDPP by **1c**/CTACl at pH 8. In runs 1–3, the concentration of catalyst **1c** is held constant at 4 × 10^{-5} M with [CTACl] = 2 × 10^{-4} M, the conditions maintained in the studies of Table I. The concentration of substrate PNPDPP is increased from 1.0 to 2.0 × 10^{-4} M, so that the substrate/catalyst ratio is raised from 2.5:1 to 5:1. In accord with expectations,[17] each run affords a rapid "burst" of $PNPO^-$, experimentally equal in concentration to [**1c**], followed by a linearly time-dependent release of $PNPO^-$. As demanded by the kinetic treatment,[17] the $PNPO^-$ burst and the slope A are independent of increasing [substrate] at constant [catalyst]. From slope A, we derive[17] k_{turn} ~ 0.17 s^{-1}. The turnover rate constant for dephosphorylation of **1c**–diphenyl phosphate is thus about a third of k_ψ (0.59 s^{-1}) for the initial cleavage of PNPDPP; i.e., the dephosphorylation step is rate-limiting in the presence of excess substrate under the conditions of Table II.

In runs 4–6, [substrate] is held constant, [**1c**] is varied, and the ratio of substrate/surfactant again moves between 5:1 and 2.5:1. Runs 4–6 are shown graphically in Figure 5. Once again following expectations,[17] the $PNPO^-$ bursts are equal to the initial [**1c**], but now slope A linearly increases with increasing [**1c**]. The turnover rate constant, equal to A/[**1c**], remains ~0.17 s^{-1}.

Additional experiments revealed that k_{turn} could be enhanced to 0.32 s^{-1} at pH 8 by increasing the ratio of CTACl/**1c** from 5:1 (Table II) to 20:1 ([**1c**] = 4 × 10^{-5} M, [CTACl] = 8 × 10^{-4} M). In this case, k_ψ for the initial **1c**–PNPDPP cleavage decreased from 0.59 to 0.25 s^{-1}. Here, the first step has become rate-limiting. Alternatively, maintaining **1c** and CTACl concentrations at the levels of Table I (4 × 10^{-5} and 2 × 10^{-4} M, respectively), k_{turn} could be enhanced by raising the pH: 0.17 s^{-1} at pH 8, 0.48 s^{-1} at pH 9, and 0.56 s^{-1} at pH 10. k_ψ for the initial PNPDPP cleavage remained constant at ~0.60 s^{-1} in this series of experiments.

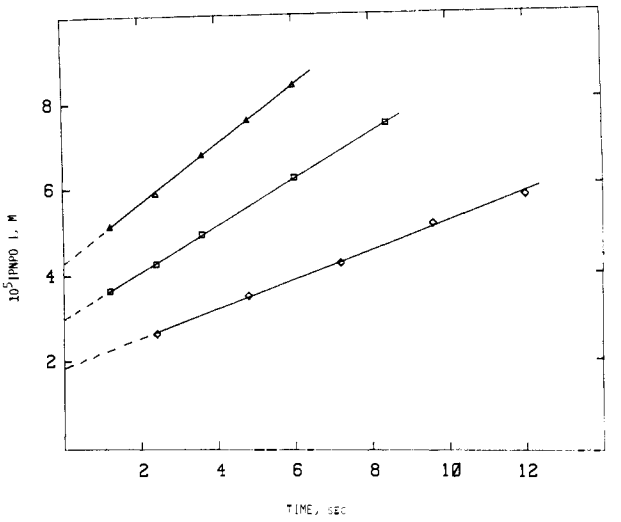


Figure 5. Burst kinetics for the cleavage of excess PNPDPP by 1c/CTACl. These are run 4–6 of Table II; see the table for conditions. Plotted is [$PNPO^-$] vs. time (s) for the cleavage of 1.0 × 10^{-4} M PNPDPP by 2.0 × 10^{-4} M PNPDPP by 2.0 × 10^{-5} (◇), 3.0 × 10^{-5} (□), and 4.0 × 10^{-5} M (△) **1c**. The values of [$PNPO^-$] at zero time are extrapolated from the data points.

Finally, a preliminary study of substrate PNPIMP with **1c**/CTACl afforded turnover results that were generally parallel to those found with PNPDPP. At pH 8, **1c**/CTACl cleaved excess PNPIMP with k_{turn} equal to ~50% of k_ψ for the initial step.

Discussion

Previously, we demonstrated that *o*-iodosobenzoates **1a** and **1b** were powerful O-nucleophiles in their preferred heterocyclic, valence tautomeric 1-oxido-1,2-benziodoxolin-3-one forms. In CTACl micellar solution, they cleaved active esters and phosphates rapidly and with efficient turnover of O-acylated or O-phosphorylated intermediates.[11,12] The new reagent, **1c**, maintains these advantages, and because of the flexibility of its synthesis and its applicability to cleavages of the persistent phosphate PNPDEP and the phosphonate PNPIMP, **1c** must be considered the premier example of this remarkable class of iodooxide reagents.

Some kinetic comparisons are in order. Micellar **1b**/CTACl was shown to be superior to phenoxide-, benzimidazole-, imidazole-, or oximate-based micellar reagents for the cleavage of PNPDPP.[12] Comparison of the data for **1c**/PNPDPP (Table I) with analogous reports for **1b**[12] indicates that **1c** is better. Thus, k_2, the second-order rate constants for cleavage, and k_χ^{max}/k_0, the kinetic advantages relative to nonfunctional micellar CTACl, are 28 500 L/(M-s) and 14 700, respectively, for **1c**/CTACl, but only 14 400 L/(M-s) and 1800 for **1b**/CTACl.[18]

In a kinetic comparison to the recently introduced hydrated aldehyde surfactant **6**,[10] **1c** also proves superior. At pH 9, 8 × 10^{-3} M **6** cleaves PNPDPP with k_ψ^{max} = 2.0 × 10^{-2} s^{-1} (k_2 = 2.5 L/(M-s)) and a kinetic advantage of 210, relative to nonfunctional micellar dodecyltrimethylammonium bromide. With 4.0 × 10^{-5}

$$n\text{-}C_{12}H_{25}N^+Me_2CH_2CH(OH)_2$$
6

M **1c** in 2.0 × 10^{-4} M CTACl at pH 8.0, cleavage of the identical substrate proceeds with k_ψ^{max} = 1.14 s^{-1}, k_2 = 28 500 L/(M-s), and a kinetic advantage of 14 700. On the basis of the k_2 comparisons, under optimal conditions, **1c**/CTACl is ~11 000 times more reactive toward PNPDPP and at a lower pH.[19]

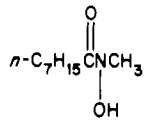
(17) Bender, M. L.; Kézdy, F. J.; Wedler, F. C. *J. Chem. Educ.* **1967**, *44*, 84.

(18) These comparisons are at pH 8.0. However, the data were obtained in different buffers: 0.01 M Tris, μ = 0.01 (KCl) for **1c**, and 0.02 M phosphate, μ = 0.08 (NaCl) for **1b**.

(19) Both **6** and **1c**/CTACl exhibit turnover in the presence of excess substrate; cf., ref 10 and this discussion.

PNPDEP (**4**) is a much less reactive substrate than PNPDPP. Comparison of k_0 values (Table I) shows that PNPDEP is ~980 times less reactive in nonfunctional micellar-catalyzed hydrolysis at pH 8. As anticipated, the **1c**/CTACl *catalyzed* cleavage of PNPDEP is also slower (by ~330 times) than the analogous scission of PNPDPP. Nevertheless, the k_ψ^{max}/k_0 entry in Table I indicates that **1c**/CTACl provides a kinetic advantage of more than 40 000 in the cleavage of PNPDEP. Put more dramatically, the half-life of PNPDEP in 2.0×10^{-2} M micellar CTACl at pH 8 is ~100 days. When 4.0×10^{-3} M **1c** is added to this solution, the half-life is reduced to ~3.3 min.

Sloan et al. have studied the hydroxamate-catalyzed cleavage of PNPDEP in 10^{-2} M CTABr at pH 9.3 and 37 °C.[7a] Under these conditions, 4.0×10^{-3} M **7** reacted with PNPDEP with $k_\psi = 0.0022$ s^{-1}, almost the same value as the pseudo-first-order rate

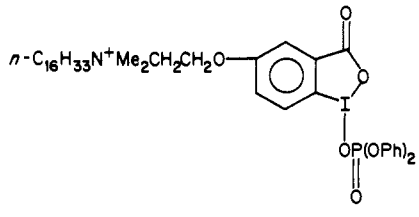


7

constant we obtained with comparable concentrations of **1c** and CTACl (Table I). However, reagent **7** requires both higher temperature and pH to match the kinetic performance of **1c**.

Table I demonstrates that PNPIMP is a substrate of intermediate reactivity compared to PNPDPP and PNPDEP. The reduced value of k_ψ^{max}/k_0 may be a property of phosphonate as compared to phosphate substrates. Rutkovskii et al. have studied the reactivity of para-substituted benzaldoximates toward PNPIMP in $2\text{–}6 \times 10^{-3}$ M micellar CTABr at pH 9 and 30 °C.[7d,e] Under these conditions, (*E*)-*p*-nitrobenzaldoximate exhibits reactivity comparable to that of **1c**/CTACl at pH 8 and 25 °C. However, in contrast to **1c**, the oximate reagent does not turn over.[7d,e]

The ability of **1c** to turn over in the presence of excess substrate (Table II) is an important feature of its behavior toward phosphate (and phosphonate) substrates. No doubt, as suggested by Menger in the case of **6**,[10] hydroxide ions approximated to the cationic micelles accelerate the cleavage of the phosphorylated intermediate, e.g., **8** in the case of **1c** + PNPDPP. As demonstrated in

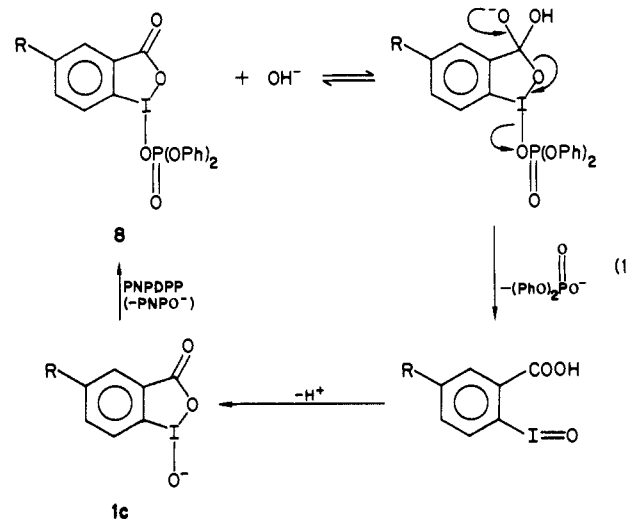


8

the Results section, depending on the ratio of **1c**/CTACl and the pH, either the formation of **8** from **1c** and PNPDPP or the destruction of **8** by micelle bound hydroxide can be the rate-limiting step in the overall hydrolytic, catalyzed destruction of PNPDPP.

It is not yet clear, however, why **8**, and analogous acylated species,[11,12] should be so responsive to base-catalyzed hydrolysis. In the specific case of **8**, we can imagine several mechanisms: (a) attack of OH^- directly at the phosphorus atom; (b) valence tautomerism of **8** to a ring-opened $-CO_2^-/-I^+OP(O)(OPh)_2$ form, followed by OH^- attack on I^+ and loss of diphenyl phosphate (after proton loss, this would leave an *o*-iodosobenzoate which would recyclize to the benziodoxolin-3-one form, **1c**); (c) the cyclical mechanism depicted in eq 1, where OH^- initially attacks the carbonyl group of **8**, with consequences similar to those under (b). We cannot now differentiate between these mechanisms, but we are planning appropriate oxygen labeling experiments.

Attempts to directly prepare **8** (R = H) have proved futile. Thus, reactions of **1a** (in the protonated I–OH form) with diphenyl chlorophosphate (CH_3CN, reflux, 48 h) gave the anhydride of *o*-iodosobenzoic acid, mp 201 °C dec. This reaction also failed to give **8** when conducted in either pyridine or DMF. Similarly, attempted phosphorylations with either PNPDPP or $(PhO)_2P(O)OP(O)(OPh)_2$ in CH_3CN or DMF, with or without added pyridine, failed to give the desired **8**; starting **1a** or tarry material was the usual result. The Li salt of **1a** was prepared from *o*-iodobenzoic acid and LiOH, followed by lyophilization. Attempted conversion of this salt to **8** using diphenyl chlorophosphate, PNPDPP, or the diphenyl phosphoric anhydride, under a variety of reaction conditions, proved futile. Although we were unable to prepare **8** and examine its kinetic behavior under the reaction conditions, we point out that the observed burst kinetics in the PNPDPP experiments (Table II and Figure 5) *demand* the presence of an intermediate. Structure **8** is clearly the most reasonable formulation of this species; the analogous *O*-acetyl compound has been prepared from **1a** and acetic anhydride.[12]



1c (1)

Lastly, we should point out that the synthesis of **1c** is more general than the sequence previously used to prepare the octyloxy catalyst, **1b**. In particular, the synthesis of **1c** passes through intermediate **2c**. This bromoethyl ether can be used as an alkylating agent to covalently couple the 5-oxo-2-iodosobenzoate moiety to any nucleophilic center, opening the way to the development of many new kinds of iodosobenzoate derivatives. For example, we are currently preparing iodosobenzoate-functionalized polymers and silica surfaces.

In summary, iodosobenzoate surfactant **1c** has proven to be a most efficient and versatile catalyst for the micellar cleavage of both reactive and persistent toxic phosphates. The reactivity of the iodosobenzoates is not limited to *p*-nitrophenyl phosphates. Catalysts **1a**/CTACl and **1b**/CTACl have shown very substantial cleavage reactivity, with turnover, toward diisopropyl fluorophosphate,[20] and catalyst **1c** will soon be tested against this substrate. We are continuing our studies of these and related reagents.

Experimental Section

General Methods. Melting points and boiling points are uncorrected. NMR spectra were measured with Varian T-60 or FT-80 spectrometers, and chemical shifts are reported relative to internal Me_4Si. Microanalyses were performed by Robertson Laboratory, Florham Park, NJ.

Materials. PNPDEP was obtained from Aldrich Chemical Co. and used as received. PNPDPP was prepared and purified by literature methods.[14] PNPIMP was prepared by de Roos' method[15] and purified by distillation at 165–167 °C/0.3 mmHg. It showed δ_{CDCl_3} 8.4–7.4 (A_2B_2, 4 H, aryl), 3.97 (m, 2 H, CH_2), 1.72 (d, $J_{P\text{–}CH_3}$ = 18 Hz, 3 H, CH_3P), 2.23–1.60 (m, 1 H, $CHMe_2$), 0.97 (d, J = 7 Hz, CH-Me_2).

Anal. Calcd for $C_{11}H_{16}NO_5P$: C, 48.35; H, 5.91; P, 11.34. Found: C, 48.16; H, 6.28; P, 11.11.

CTACl was obtained from Eastman and recrystallized 2 times from 90% EtOH/water and dried under vacuum.

5-(*N*-(*n*-Hexadecyl)-*N*,*N*-dimethyl-*N*-(β-ethyloxy)ammonium)-2-iodosylbenzoic Acid, Chloride (1c). 5-Hydroxy-2-iodobenzoic acid (**2a**)[12] (40 g, 152 mmol) was treated with 200 mL of absolute ethanol saturated with gaseous HCl. The mixture was refluxed for 4 h, allowed to cool,

(20) Durst, H. D., private communication, U.S. Army Chemical Research and Development Center, Edgewood, MD.

and poured over 100 g of crushed ice. The mixture was extracted with 3 × 100 mL of ether. The combined ethereal extract was washed with H_2O (50 mL), 10% aqueous $NaHCO_3$ solution (2 × 50 mL), water (50 mL), and aqueous $Na_2S_2O_3$ solution (50 mL). The ethereal solution was dried ($MgSO_4$), filtered, and stripped of solvent to afford a crude solid. Recrystallization from benzene/hexane afforded 34.5 g of ethyl ester **2b** (118 mmol, 78% yield): mp, 81-82 °C; NMR δ_{CDCl_3} 7.80 (d, J = 8 Hz, 1 H, aryl), 7.33 (d, J = 3 Hz, 1 H, aryl), 6.73 (dd, J = 3, 8 Hz, 1 H, aryl), 4.40 (q, J = 7 Hz, 2 H, OCH_2), 1.37 (t, J = 7 Hz, 3 H, CH_3).

To a solution of sodium ethoxide, prepared by dissolving 1.73 g (75.2 mmol) of sodium in 100 mL of ethanol, was slowly added 20.0 g (68.5 mmol) of ethyl ester **2b**. This solution was added over 4 h to a stirred, refluxing solution containing 38.6 g (205 mmol) of 1,2-dibromoethane in 100 mL of ethanol. Stirring and refluxing were continued for an additional 4 h. The reaction mixture was cooled and filtered (to remove NaBr) and then stripped of ethanol and excess dibromoethane. The crude product (**2c**) was taken up in 250 mL of benzene, washed with cold 10% aqueous NaOH solution (2 × 50 mL), and dried over $MgSO_4$. Solvent was stripped, and the residue was chromatographed (SiO_2, 1:5 EtOAc/hexane) to afford 14.8 g (37.1 mmol, 54%) of pure bromoethyl ether **2c**: NMR δ_{CDCl_3}, 7.90 (d, J = 8 Hz, 1 H, aryl), 7.40 (d, J = 3 Hz, 1 H, aryl), 6.80 (dd, J = 3, 8 Hz, 1 H, aryl), 4.63-4.23 (q + t, 7 H, CH_2O + CH_2O), 3.67 (t, J = 6 Hz, 3 H, CH_2Br), 1.43 (t, J = 7 Hz, CH_3).

Anal. Calcd for $C_{11}H_{12}BrIO_3$: C, 33.09; H, 3.03; Br, 20.03. Found: C, 33.08; H, 3.07; Br, 20.12.

Bromo ether **2c**, 12.0 g (30.1 mmol) and 9.4 g (34.9 mmol) of *N*-(*n*-hexadecyl)-*N*,*N*-dimethylamine (Ethyl Corp.) were refluxed in 150 mL of ethanol for 3 days. Ethanol was removed under reduced pressure, and the residue was stirred in 200 mL of dry ether for 2 h. Filtration (sintered glass) afforded a white solid that was washed with 100 mL of dry ether and recrystallized from EtOAc, yielding 15.2 g (22.7 mmol, 75%) of quaternary salt **2d**: mp 101-102 °C; NMR $\delta_{Me_2SO\text{-}d_6}$ 7.90 (d, J = 8 Hz, 1 H, aryl), 7.29 (d, J = 3 Hz, 1 H, aryl), 6.93 (dd, J = 3, 8 Hz, 1 H aryl), 4.54-4.21 (m + q, 4 H, CH_2O + CO_2CH_2), 3.80 (m, 2 H, $N^+CH_2CH_2O$), 3.45-3.20 (m + br s at 3.32, 8 H, $CH_2N^+Me_2$), 1.33 (t, J = 7 Hz, 3 H, $CO_2CH_2CH_3$), 1.24 (br s, 28 H $(CH_2)_{14}$), 0.85 ("t", 3 H, term. CH_3).

Anal. Calcd for $C_{29}H_{51}BrINO_3$: C, 52.10; H, 7.69; I, 18.98. Found: C, 52.13; H, 7.75; I, 19.12.

Quaternary salt-ethyl ester **2d** was saponified by refluxing 10.0 g (15.0 mmol) in 60 mL of methanol and 10 mL of 2 N aqueous NaOH. The reaction mixture was cooled and acidified with dilute HCl. Ethanol and water were removed under reduced pressure, the residue was taken up in 50 mL of dry ethanol, and NaCl was removed by filtration. Ethanol was stripped to give a sticky yellow solid, which was recrystallized from EtOH/EtOAc, affording 9.1 g (14.2 mmol, 95%) of white quaternary salt/iodo acid **2e** as the bromide salt, mp 103-105 °C. The NMR spectrum of **2e** is very similar to that of **2d** (see above), but the former lacks the signals of the ethyl ester group.

Anal. Calcd for $C_{27}H_{47}BrINO_3$: C, 50.63; H, 7.40; I, 19.81. Found: C, 50.57; H, 7.57; I, 19.72.

Oxidation of **2e** to iodosobenzoate surfactant **1c** was carried out in accord with the chlorination/hydrolysis procedure described in ref 12 and 13. In this way, 5.0 (7.8 mmol) of **2e** was oxidized to 3.8 g (6.2 mmol, 79%) of slightly yellow crystalline **1c**, isolated as the *chloride* salt, mp 125-128 °C. This material showed 98 ± 4% of iodosyl activity by $KI/Na_2S_2O_3$ iodometric titration.[13]

Anal. Calcd for $C_{27}H_{47}ClINO_4$: C, 52.98; H, 7.74; Cl, 5.79. Found: C, 53.25; H, 7.68; Cl, 5.53.

Kinetic Studies. Solutions of **1c**/CTACl were prepared by sonication (Braun Sonic Model 1510 sonicator, small immersion probe, 80 W, 10 min, 50-55 °C) in 0.01 M pH 8.0 Tris buffer, μ = 0.01 (KCl). All kinetic runs employed freshly prepared catalyst solutions.

Slower reactions were followed on a Gilford Model 250 spectrophotometer coupled to a Gilford Model 6051 recorder. Faster reactions were followed on a Durrum Model D-130 stopped-flow spectrophotometer coupled either to a Tektronix Model 5103N/D15 storage oscilloscope or, via a custom-built interface, to a Commodore Model 8032 computer. Constant-temperature circulating baths maintained reaction temperatures at 25 ± 0.1 °C. All buffers were prepared from Steam-Distilled water (distilled, U.S.P., Electrified Water Co., East Orange, NJ). Rate constants were obtained from computer-generated correlations of log $(A_\infty - A_t)$ with time for the appearance of *p*-nitrophenoxide ion at 400 nm. Conditions for all the kinetic runs are described in the Results section. Rate constants are tabulated in Tables I-III of the supplementary material and presented graphically in Figures 1-3. Micellar reactions were followed to >90% completion and showed good first-order kinetics (r > 0.999). Reproducibilities of the rate constants were <±3%. Values of k_ψ^{max} appear in Table I. Turnover experiments are summarized in Table II.

Acknowledgments. We thank S. Chatterjee for technical assistance. We are grateful to the US Army Research Office and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support.

Registry No. **1c** chloride, 99665-69-7; **2a**, 57772-57-3; **2b**, 99665-70-0; **2c**, 99665-71-1; **2d**, 99665-72-2; **2e**, 99665-73-3; **3**, 10359-36-1; **4**, 311-45-5; **5**, 7364-83-2; 1,2-dibromoethane, 106-93-4; *N*-(*n*-hexadecyl)-*N*,*N*,-dimethylamine, 112-69-6.

Supplementary Material Available: Tables I-III containing (respectively) rate constants for cleavages of PNPDPP, PNPDEP, and PNPIMP by **1c**/CTACl (3 pages). Ordering information is given on any current masthead page.

Reactions of Coordinated Molecules. 42. Diels-Alder Reactions Utilizing (Ferra-β-diketonato)BF_2 Complexes Containing Alkenyl Substituents as Activated Dienophiles

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Abstract: Three (ferra-β-diketonato)BF_2 complexes having alkenyl substituents attached to the ferra-chelate ring react as activated dienophiles in Diels-Alder cycloaddition reactions. Ten Diels-Alder adducts are prepared and characterized. The dienes used include isoprene, 2,3-dimethyl-1,3-butadiene, *trans*-2-methyl-1,3-pentadiene, and cyclopentadiene. The X-ray structures of one reactant complex having a methacryl substituent and its cycloaddition adducts with isoprene and *trans*-2-methyl-1,3-pentadiene are reported. These Diels-Alder reactions proceed in good to high yield with a regioselectivity consistent with the analogous reactions of methyl methacrylate and crotonic acid. Furthermore, due to the highly asymmetric Fe center within the methacrylate dienophile, diene cycloaddition occurs with unusually high stereoselectivity when diastereomeric adducts are formed.

The preparation and characterization of (ferra-β-diketonato)boron difluoride complexes,[2,3] **1**, and related compounds[4,5] led to the discovery of an unusual interligand C-C bond formation reaction upon deprotonation of a ferra-chelate ring substituent

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