from N-methylation of **2** as obtained below.

B. N-Methylation of 2 to 9. To a solution of **2** (1.65 g, 10 mmol) in THF (50 mL) was added iodomethane (3.55 g, 25 mmol), powdered KOH (1.40 g), and tetrabutylammonium bromide (0.64 g, 2 mmol).[15] The mixture was stirred overnight at room temperature, concentrated, and distilled [Kugelrohr at 60 °C (0.3 mm)] to give 1.69 g (94%) of pale yellow **9**: ^{1}H NMR ($CDCl_3$) δ 1.06–1.28 (m, 1 H), 1.19 (d, 3 H, J = 6 Hz), 1.38–1.57 (m, 1 H), 1.65 (s, 3 H), 1.73–1.86 (m, 1 H), 1.92–2.06 (m, 1 H), 2.21–2.35 (m, 2 H), 2.72 (q, 1 H, J = 9 Hz), 3.01 (s, 3 H), 5.66 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.8 (q), 21.0 (q), 31.4 (t), 33.0 (t), 33.9 (q), 40.0 (d), 42.4 (d), 51.1 (d), 115.5 (s), 123.2 (d), 170.6 (s).

Catalytic Hydrogenation of 2 to Dihydronepetalactam (10a,b). A sample of **2** (1.00 g) was hydrogenated in the presence of 10% Pd/C (0.10 g) in acetic acid. The product was distilled [Kugelrohr at 120 °C (0.2 mm)] to give 1.00 g of a 1:5 mixture of **10a** and **10b** as shown by GC analysis. The hydrogenation was repeated by using PtO_2 in ethanol and $Pd/BaSO_4$ in ethanol to give the same results. The major isomer **10b** showed the following: ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3 H, J = 7 Hz), 1.08–1.24 (m, 1 H), 1.19 (d, 3 H, J = 7 Hz), 1.28–1.44 (m, 1 H), 1.61–1.74 (m, 1 H), 1.79–1.92 (m, 1 H), 2.00–2.18 (m, 2 H), 2.25 (dd, 1 H, J = 10, 7 Hz), 2.30–2.43 (m, 1 H), 3.07 (dd, 2 H, J = 8, 3 Hz), 7.79 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.0 (q), 21.1 (q), 25.3 (t), 30.4 (d), 34.2 (t), 40.9 (d), 41.9 (d), 43.9 (t), 51.3 (d), 176.7 (s). Signals due to **10a** were as follows: ^{13}C NMR ($CDCl_3$) δ 17.2 (q), 33.1 (d), 39.0 (d), 44.6 (d), 47.4 (t), 50.2 (d).

Synthesis of *N*-Methyl-3,4-dihydronepetalactam (11a,b). A. Hydrogenation of 9 to 11a,b. A sample of **9** (1.00 g), prepared by methylation of **2**, was dissolved in ethanol and treated with H_2 in the presence of 10% Pd/C (0.10 g) catalyst. The product, 0.90 g of colorless oil, gave the following NMR data, which closely matched that of **11a,b** prepared through methylation of **10a,b**. Major isomer **11b**: ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 3 H, J = 7 Hz), 1.05–1.24 (m, 1 H), 1.17 (d, 3 H, J = 7 Hz), 1.26–1.41 (m, 1 H), 1.58–1.72 (m, 1 H), 1.75–1.88 (m, 1 H), 1.98–2.09 (m, 1 H), 2.11–2.40 (m, 3 H), 2.92 (s, 3 H), 2.99 (dd, 1 H, J = 12, 5 Hz), 3.20 (t, 1 H, J = 12 Hz); ^{13}C NMR ($CDCl_3$) δ 15.5 (q), 20.7 (q), 24.5 (t), 29.4 (d), 33.4 (t), 34.4 (q), 40.3 (d), 41.6 (d), 51.1 (d), 51.2 (t), 172.3 (s). Minor isomer **11a**: ^{13}C NMR ($CDCl_3$) δ 16.4 (q), 20.4, 29.2, 32.2 (d), 34.0, 38.4 (d), 44.4 (d), 50.3 (d), 55.0 (t), 172.0 (s).

B. N-Methylation of 10a,b to 11a,b. To a solution of **10a,b** (1.67 g, 10 mmol) in THF (50 mL) were added iodomethane (3.55 g, 25 mmol), powdered KOH (1.40 g), and tetrabutylammonium bromide (0.60 g, 2 mmol). The mixture was stirred at room temperature for 12 h, concentrated, and distilled [Kugelrohr at 60 °C (0.3 mm)] to give 1.67 g of **11a,b**. This mixture showed essentially the same NMR spectra as obtained in the previous section.

Deoxygenation of 11a,b to 12a,b. A sample of **11a,b** (1.00 g) dissolved in dry THF (1.0 mL) was brought to reflux, and borane–methyl sulfide complex in THF (6.0 mL of 2.0 M) was added dropwise. After addition was complete, the solvent was removed in vacuo, HCl (10 mL of 6 N) was added, and the mixture was heated at reflux for 1 h. The cooled reaction mixture was neutralized and extracted with ether, and the extract was dried ($MgSO_4$), filtered, concentrated, and distilled [Kugelrohr at 35 °C (3 mm)] to give 0.60 g (62%) of a mixture of **12a** and **12b**. The ^{13}C NMR spectrum showed signals of a major isomer identical with that of an authentic sample of δ-skytanthine (**12b**) available from earlier work:[3b] ^{1}H NMR ($CDCl_3$) δ 0.87 (d, 3 H, J = 7 Hz), 0.97 (d, 3 H, J = 7 Hz), 1.05–1.19 (m, 1 H), 1.38–1.73 (m, 5 H), 1.75–1.85 (m, 1 H), 1.88–2.01 (m, 1 H), 2.02–2.14 (m, 2 H), 2.23 (s, 3 H), 2.46–2.59 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 22.2 (t), 22.7 (q), 30.9 (d), 31.4 (t), 36.5 (d), 40.3 (d), 46.2 (q), 46.6 (d), 57.3 (t), 58.0 (t).

Substituted *o*-Iodoso- and *o*-Iodoxybenzoic Acids: Synthesis and Catalytic Activity in the Hydrolysis of Active Phosphorus Esters and Related Systems

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2-Iodoso- and 2-iodoxybenzoic acids containing alkyl, alkyloxy, nitro, carboxyl, and water-solubilizing substituents have been synthesized, and their influence on the rates of hydrolysis of *p*-nitrophenyl diphenyl phosphate (PNPDPP), *p*-nitrophenyl isopropylphenylphosphinate (NPIPP), and *p*-nitrophenyl hexanoate (PNPH) has been determined in the presence of added cetyltrimethylammonium chloride (CTAC). All the compounds are true catalysts, with rates increasing with increasing catalyst concentration. 2-Iodoxybenzoic acids possess 60–110% of the activity of their 2-iodosobenzoic acid analogues in 0.001 M CTAC. The effects of substituents of variable electronic and aqua/lipophilic character upon catalytic activity have been determined. Lipophilic substituents significantly enhanced the rates while simple ring substitutions with electron-releasing and -withdrawing and water-soluble groups had only moderate effects. Extraordinary rate enhancements were obtained with 5-(2-hydroxyethoxy)-2-iodoxybenzoic acid and 5-(alkyloxy)-2-iodosobenzoic acid and -2-iodoxybenzoic acid derivatives, giving second-order rate constants of 400–5000 M^{-1} s^{-1}. The efficient catalysis of the hydrolysis of active phosphorus derivatives renders these aromatic 2-iodoso- and 2-iodoxybenzoic acids potentially useful decontaminants.

Introduction

Fluorophosphate, fluorophosphonate, phosphate, phosphonate, and phosphinate esters are persistent acetylcholinesterase inhibitors[1] and neurotoxic agents. Many are, or have been, used as potent pesticides.[2] Their decomposition rates under various conditions are clearly of considerable importance, and effective methods for their detoxification have attracted the attention of numerous research groups over the past several years.[3]

Potentially significant applications of such detoxification methods are the cleanup of chemical spills and, in military

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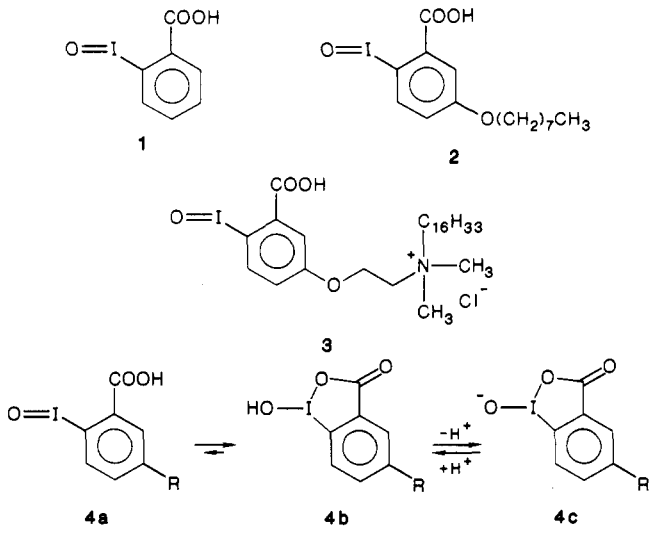
0022-3263/88/1953-3972$01.50/0

Scheme I



1 2 3 4a 4b 4c

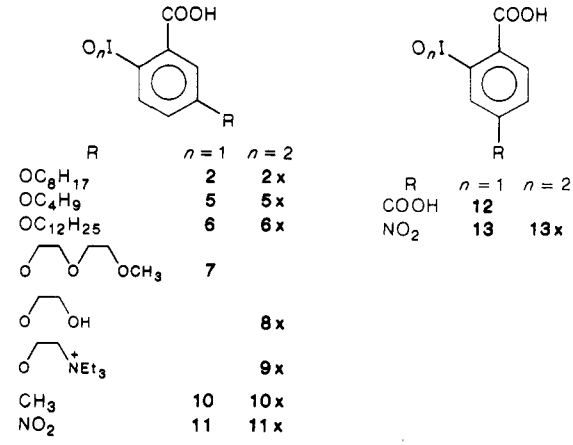
circles, the decontamination of equipment that has been exposed to chemical warfare agents. However, commonly used decontaminants suffer from a number of disadvantages.[4]

Most persistent phosphorus derivatives are only sparingly soluble in water; micellar and microemulsion media have often been employed.[5] Mechanistic investigations under these conditions have demonstrated enhancements in the rates of both solubilization and decomposition by enhanced hydrolysis rates.[6]

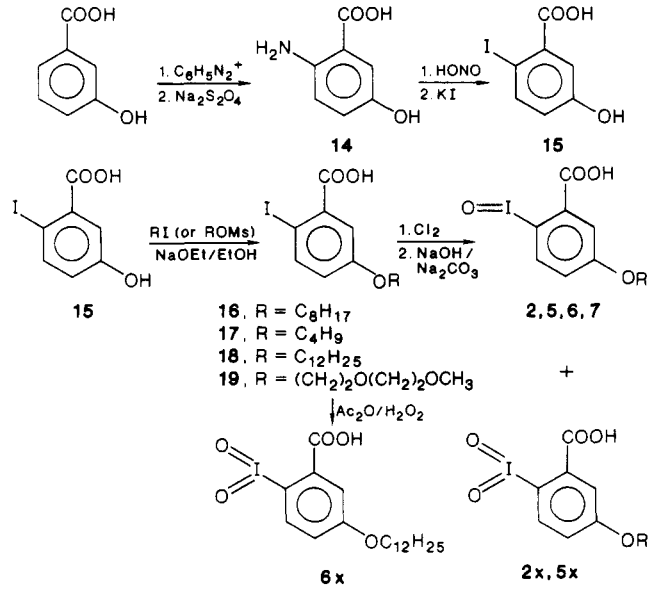
A particularly significant advance in this micellar approach was the introduction by Moss and co-workers of 2-iodosobenzoic acid (**1**, IBA) and its derivatives as nucleophilic catalysts in phosphate ester decomposition. *o*-Iodosobenzoic acids **1–3** (Scheme I) exist predominantly in the 1-hydroxy-1,2-benziodoxolin-3-one (alternatively denoted 1-hydroxy-1,2-benziodoxol-3(3*H*)-one) (**4b**) tautomeric form. They were shown to be powerful reagents for the cleavage of phosphates in an aqueous cetyltrimethylammonium chloride (CTAC) micellar medium.[7-9] Moss recently studied five further analogues of IBA, 5-methoxy-IBA, 5-nitro-IBA, and three compounds with modified iodoxole rings,[10] but all were less active than IBA itself. Significantly, all of the Moss IBA compounds accelerated the rate of ester decomposition without being consumed, at least in the CTAC micellar medium studied.

Our attention was recently drawn to the related 2-iodoxybenzoic acid (IBX), which also exists in a cyclic form[11] and is considerably more stable and easier to synthesize. Moss reported that 2-iodoxybenzoic acid was less active as a catalyst than the 2-iodoso- by a factor of 3.8, but analogues have apparently not been tested. In several reports,[8,9] Moss has speculated on the mechanism responsible for the extraordinary reactivity of IBA. The best evidence indicates that the cyclic IBA anion species (pK_a = 7.0) is the nucleophile which attacks phosphorus to form an "acyl" species, followed by hydroxide attack on this species to release the phosphoric acid derivative. All evidence from Moss's laboratory indicates that the first step is rate determining. To date, there is no evidence regarding the mechanism of IBX-catalyzed hydrolysis, although by analogy it probably resembles the IBA system. Indeed, the iodosobenzoate and iodoxybenzoate functionalities, although known in the literature for almost 100 years, have not been investigated synthetically with any vigor. In view of the great interest in these compounds and their derivatives as decontamination catalysts, we have synthesized a variety of IBA and IBX derivatives and measured their catalytic activity versus a number of standard simulants.

Scheme II



Scheme III



Synthesis

The IBA and IBX analogues prepared in this study are shown in Scheme II. The alkyloxy derivatives (compounds **2**, **2x**, **5**, **5x**, **6**, and **6x**) were studied to examine the effect of altering the chain length upon catalytic activity. Although Moss suggested that the octyl chain in **2** was responsible for an increased solubility in the micelles, and therefore a higher activity,[8] no published comparative work was previously available to examine that hypothesis. The

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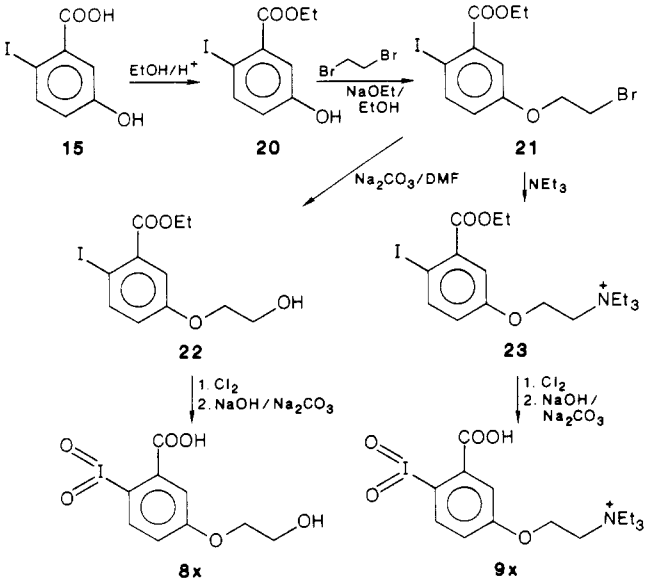
Scheme IV



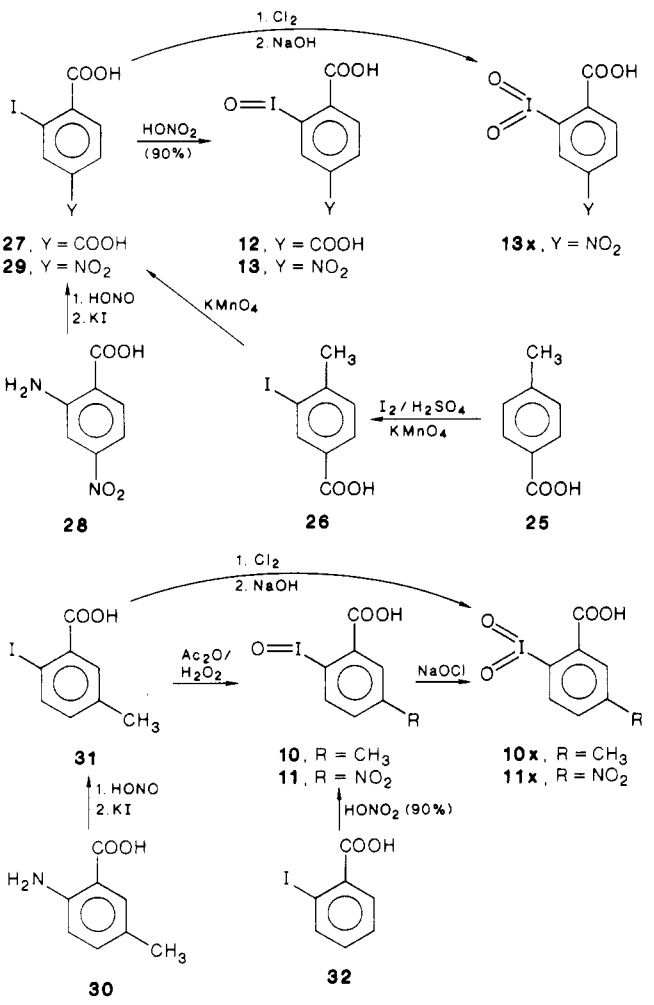
compounds were synthesized by following the general procedure developed by Moss (Scheme III) and gave the IBA compounds (**2**, **5**, **6**) in reasonable yields. The analogous IBX derivatives **2x** and **5x** were isolated from preparations of the corresponding IBA, whereas **6x** (5-dodecyloxy-IBX) was prepared directly from the iodo compound by using Ac_2O/H_2O_2.

Although the alkyloxy compounds have a high catalytic activity, their solubility in water is rather low. Increased water solubility was considered likely to lead to increased activity and greater convenience for practical use. We therefore prepared compounds with a glycol chain attached to the IBA (IBX) nucleus (compounds **7** and **8x**). The route shown in Scheme III, utilizing the mesylate of diethylene glycol monomethyl ether[12] (prepared by standard methods from the alcohol) as alkylating agent, gave **7**. Several attempts to prepare the analogous hydroxy derivative (R = $OCH_2CH_2OCH_2CH_2OH$) by the same methodology failed; therefore, 5-hydroxy-2-iodobenzoic acid (**15**) was esterified and then alkylated with 1,2-dibromoethane, as described by Moss,[9] to give **21**, which, upon hydrolysis and oxidation, gave hydroxyethyl IBX **8x** (Scheme IV).

To improve the water solubility, we also synthesized compounds in which a charged group was attached to the aromatic nucleus. With ammonium salt **9x**, this was simply accomplished by treatment of **21** with triethylamine, followed by chlorination and hydrolysis (Scheme IV). An alternative route involved synthesis of terephthalic IBA derivative **12** from toluic acid, via iodination, followed by oxidation, first with permanganate (to produce **27**) and then with fuming nitric acid to afford **12** (Scheme V). At the pH commonly used in the hydrolytic runs (8.5), one of the carboxylic acid groups in **12** would be ionized, which should lead to increased water solubility.

A further approach to the solubility problem involved shortening the alkyl tail attached to the IBA (or IBX) nucleus. Thus, 5-methyl-IBA (**10**) was prepared from 5-methyl-2-aminobenzoic acid (**30**; Aldrich) by diazotization, iodination (to give **31**), and oxidation with Ac_2O/H_2O_2. 5-Methyl-IBX (**10x**) was made from **31** via chlorination/hydrolysis (Scheme V).

Scheme V



To determine the effect of an electron-withdrawing group on catalytic activity, we synthesized nitro derivatives **11**, **11x**, **13**, and **13x** (Scheme V). Compound **13** was prepared from 2-amino-4-nitrobenzoic acid (**28**; Aldrich) by diazotization, iodination (to give **29**), and oxidation with fuming nitric acid. Iodoxy analogue **13x** was prepared by chlorination/hydrolysis of **29**. Synthesis of **11** was easily accomplished by treatment of 2-iodobenzoic acid (**32**) with fuming nitric acid by the method of Morrison and Hooz.[13] Iodoxy derivative **11x** was synthesized from **13** by oxidation with sodium hypochlorite solution.[14]

Aside from the determination of the effects of methyl and nitro groups on catalytic activity, **10** (**10x**), **11** (**11x**), and **13** (**13x**) were also of interest because of their relatively straightforward syntheses. The anthranilic acid precursors for these compounds are commercially available; thus large-scale synthesis of each should be easy.

Kinetic Methodology

The minimal requirement for evaluation of the catalyst systems from the user (field) standpoint was that a good decontamination formulation should provide at least 10 half-lives ($t_{1/2}$) of reaction in 10 min under field conditions ("Mackay's criterion").[4] In other words, $t_{1/2} \leq 1$ min.

p-Nitrophenyl diphenyl phosphate (PNPDPP) and *p*-nitrophenyl isopropylphenylphosphinate (NPIPP) were utilized as phosphorus substrates for the kinetic mea-

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Table I. Second-Order Rate Constants (M^{-1} s^{-1}) for 2-Iodoxybenzoic Acid vs 2-Iodosobenzoic Acid Cleavages in 1 mM and 5 mM CTAC at pH 8.5

	vs NPIPP			vs PNPDPP			vs PNPH		
catalyst[a]	k^X	k^I	k^X/k^I	k^X	k^I	k^X/k^I	k^X	k^I	k^X/k^I
5-H		31			260			182	
(1)		(66)			(277)			(238)	
5-butoxy[c,b]	433	406	1.07	4450	4575	0.97	2805	2504	1.12
(5, 5x)	(245)	(257)	(0.95)	(976)	(1089)	(0.90)	(804)	(917)	(0.88)
5-octyloxy[c,c]	256	461	0.56	4494	4526	0.99	2794	3611	0.77
(2, 2x)	(186)	(200)	(0.93)	(953)	(966)	(0.99)	(807)	(807)	(1.00)
5-dodecyloxy[b,c]	300	361	0.83	4012	4864	0.82	1777	3176	0.56
(6, 6x)	(138)	(156)	0.88)	(913)	(1007)	(0.91)	(743)	(887)	(0.84)
4-nitro[c,d]	66	66	1.00	1089	1032	1.06	1056	416	2.54
(13, 13x)	(75)	(92)	(0.82)	(538)	(647)	(0.83)	(225)	(304)	(0.74)
5-nitro[e]	35	34	1.03	494	588	0.84	181	212	0.85
(11, 11x)	(48)	(49)	(0.98)	(344)	(381)	(0.90)	(160)	(157)	(1.02)
5-methyl[c,b]	64	90	0.71	564	774	0.73	381	579	0.66
(10, 10x)	(67)	(138)	(0.49)	(307)	(583)	(0.53)	(221)	(516)	(0.43)
4-COOH[d]		4			146			89	
(12)		(7)			(110)			(92)	
5-DEG-OMe[c]		28			463			246	
(7)		(92)			(380)			(272)	
5-OCH_2CH_2OH[c]	600			3218			2130		
(8x)	(391)			(1009)			(886)		
5-$OCH_2CH_2N^+Et_3$[c]	30								
(9x)									

[a] Footnotes denote the synthetic procedures used to prepare the IBX or IBA compounds, respectively, from the corresponding 2-iodobenzoic acid. The quantity k_2[IBX]/k_2[IBA] represents the kinetic advantage of the IBX over the IBA derivative. Unparenthesized values were obtained at 1 mM CTAC; values in parentheses are for 5 mM CTAC. [b] (1) Ac_2O/H_2O_2, (2) H_2O. [c] Chlorination/hydrolysis. [d] Fuming nitric acid. [e] 11 prepared from 2-iodobenzoic acid with fuming nitric acid; 11x prepared from 11 with NaOCl.

surement. *p*-Nitrophenyl hexanoate (PNPH) was similarly used as a carboxylate ester substrate. PNPDPP and PNPH have been used extensively as standard reference substrates for the kinetic evaluation of phosphate hydrolysis catalysts and thus provide a good data base for comparing our compounds to other systems. NPIPP, a new *p*-nitrophenolate-releasing simulant introduced in this study, was utilized because the effects of catalysts on its rate of hydrolysis correlate well with those for fluoride-releasing agents.

Kinetics were carried out in both 0.001 and 0.005 M CTAC at pH 8.5 (borate buffer) and were monitored spectrophotometrically for the appearance of *p*-nitrophenolate anion at 402 nm. Substrate concentration in all runs was 5.0×10^{-5} M, and the concentration of catalyst ranged between 0.1 and 1.0 mM, with the exception of the turnover experiment where [cat.] = 0.05 mM. Second-order rate constants were determined from rate measurements at several (usually seven) concentrations of catalyst (IBA or IBX).

The decomposition of substrate (NPIPP, PNPDPP, or PNPH) in aqueous or largely aqueous media should follow a rate law of the form

$$\text{rate} = k_{hyd}[\text{NPIPP}] + k_{OH}[OH^-][\text{NPIPP}] + k_2[\text{IBA}][\text{NPIPP}] = \{k_{hyd} + k_{OH}[OH^-] + k_2[\text{IBA}]\}[\text{NPIPP}] \quad (1)$$

where the term k_{hyd}[NPIPP] represents the hydroxide-independent "background" reaction, the $k_{OH}[OH^-]$[NPIPP] term represents the second-order reaction between OH^- and substrate, and the k_2[IBA][NPIPP] term is the rate enhancement resulting from the addition of catalyst to the system.

The hydrolysis reactions were all run at the same buffered pH value (borate, pH 8.5). Under these conditions the first two terms of eq 1 ($k_{hyd} + k_{OH}[OH^-]$) are constant. If the catalyst is in large excess over substrate ([IBA] ≫ [NPIPP]) (or if catalyst is not consumed in the reaction), then the third term is also essentially constant. Under these conditions, eq 1 reduces to a description of an experimentally first order process:

$$\text{rate} = k_{obsd}[\text{NPIPP}] \quad (2)$$

where

$$k_{obsd} = k_{hyd} + k_{OH}[OH^-] + k_2[\text{IBA}] \quad (3)$$

Equation 3 forms the basis of the kinetic analysis and the data presented in Table I. Typically, several (usually seven) values of k_{obsd} were determined at different catalyst concentrations and constant pH (pH was routinely measured before and after each reaction to ensure it remained unchanged). These data were plotted as k_{obsd} vs [IBA]. In all cases the plots were consistent with the linear relation predicted by eq 3. A linear least-squares routine was used to determine the statistically most valid slope (k_2) and intercept ($k_{hyd} + k_{OH}[OH^-]$) for each data set.

Figure 1 (supplementary material) shows a typical plot of absorbance vs time data in the hydrolysis of NPIPP. The line drawn through the points is a theoretical line assuming simple first-order kinetics, as in eq 2. Figure 2 (supplementary material) shows the same data plotted as log ($A_\infty - A_t$) vs time. Such linearity was normally observed for 5 or more half-lives (i.e., >96% reaction). All kinetic runs were performed by utilizing this regime.

A point of interest was whether the catalysts were consumed (or otherwise stoichiometrically degraded) as the reaction proceeded or were regenerated and were indeed "true" catalysts. Because of the predicted instability of the most likely intermediate (a 1-(acyloxy)-1,2-benziodoxol-3(3*H*)-one), this question was addressed directly. Several kinetic runs were performed with 5-alkyloxy-IBAs **2**, **5**, and **6** vs PNPDPP in 0.001 M CTAC where the substrate was in large excess ([PNPDPP] = 5×10^{-5} M; [PNPDPP]/[IBA] = 50–100). The reactions were allowed to go to completion. With such a small proportion of the catalyst, the kinetics could only be first order if the catalyst was not consumed during the course of the reaction (i.e., [IBA] = constant). The experimental data fitted first-order kinetic analysis and yielded a k_{obsd} value consistent

with data collected at higher concentrations of catalyst (i.e., under "enforced" pseudo-first-order conditions). These observations provide strong evidence that the substituted IBA compounds are *not* consumed (i.e., "turn over") in the reaction and indeed funtion as true catalysts.

Details of the kinetics procedures have been reported elsewhere.[6,15]

Results and Discussion

Hydrolyses in Micellar Media. The results are summarized in Table I. In absolute terms, the most efficient catalyst vs NPIPP at 0.001 M CTAC was **8x** (5-(2-hydroxyethoxy)-IBX; k_2 = 600). 5-Octyloxy-IBA (**2**) and 5-butoxy-IBX (**5x**) were nearly as effective, with k_2 = 461 and 433, respectively. Hydrolysis of PNPDPP was best catalyzed by 5-dodecyloxy-IBA (**6**; k_2 = 4864) followed by 5-butoxy-IBA (k_2 = 4575) and 5-octyloxy-IBA (k_2 = 4526). 5-Octyloxy-IBX was also quite effective, giving k_2 = 4494. The alkyloxy derivatives were also the most effective vs PNPH, in the order 5-octyloxy-IBA, 5-dodecyloxy-IBA, and 5-butoxy-IBX (k_2 = 3611, 3176, and 2805, respectively). The high activity of the alkyloxy compounds verifies Moss's earlier work with 5-octyloxy-IBA and other IBAs, which indicated that substrates possessing groups that increase solubility in the micelles should increase the reactivity.[8,10] However, lengthening the tail did not markedly increase the rate and thus would appear to be of limited value in these systems.

With the exception of **8x**, the other derivatives were significantly less effective than the alkyloxys in hydrolyzing any of the substrates tested. Of these, the 4-nitro and 5-methyl compounds were the best, being 2–3 times more active than IBA itself, but 5–7 times less active than the alkyloxy analogues (Table I). Although presumably more water soluble, 4-carboxy-IBA (**12**) and diethylene glycol IBA (**7**) were less effective than IBA, probably because of a low solubility in the micelle. Solubility problems prevented a complete investigation of quaternary salt **9x**.

Most surprising was the high activity of the IBX derivatives tested (relative to the IBAs). These possessed from 56% (5-octyloxy-IBX) to 107% (5-butoxy-IBX) of the catalytic efficiency of the corresponding IBA compounds in the hydrolysis of NPIPP and PNPDPP. 5-Octyloxy-IBX had k_2 = 4494 vs PNPDPP, which was 99% of the iodoso activity. 5-Butoxy-IBX was nearly as efficient, with k_2 = 4450, and 97% of the iodoso activity. However, 4-nitro-IBX showed the greatest kinetic advantage vs PNPDPP compared to the iodoso, at 106%. In the hydrolysis of NPIPP, 5-(2-hydroxyethoxy)-IBX was most efficient in overall rate (k_2 = 600), while 5-butoxy-IBX (k_2 = 433) possessed the greatest advantage over the iodoso (107%). 5-Dodecyloxy- and 5-octyloxy-IBX had the next highest efficiencies (k_2 = 300 and 256, respectively), but with significantly lower activities than the IBA derivatives (83% and 56%, respectively). 4-Nitro-IBX, although about 4 times less active than the 5-octyloxy, possessed 100% of the activity of the corresponding iodoso compound. 5-Methyl-IBX was equally as good, although with somewhat lower activity than 5-methyl-IBA (71%).

Interestingly, increasing the concentration of CTAC from 1 to 5 mM markedly improved the catalytic efficiency of the nitro and methyl derivatives vs NPIPP. The alkyloxy compounds, on the other hand, decreased in efficiency. Rate vs [CTAC] profiles typically increase rapidly to a maximum as the cmc is approached and then decrease slowly with increasing surfactant concentration.[7-9] 5-Octyloxy-IBA, for example, possesses a maximum rate at 0.20 mM and IBA at 1.00 mM CTAC.[8] The rate–[surfactant] profiles for the nitro and methyl derivatives probably increase more gradually, so that the measurements at 1 mM and 5 mM both fall on the upward portion of the curve. Practically, this is advantageous, because, by increasing surfactant concentration, one can increase the capacity of the system without a concomitant decrease in catalyst reactivity.

The surprising catalytic efficiency of the iodoxy analogues of iodoso compounds previously found to be effective catalysts, in addition to its theoretical significance, is of considerable practical importance because the stability of the iodoxy derivatives is far higher than that of their iodoso analogues.[16,17] One of the iodoso derivatives prepared by Moss lost activity over a period of time, and it is likely that other iodosobenzoates present similar stability problems.[18] Moreover, iodoxy compounds are often simpler to prepare than the iodoso derivatives.

Selected results of hydrolyses of fluoride-releasing substrates under micellar conditions demonstrated that 5-octyloxy-IBA was the most efficient (at both 0.001 M and 0.005 M CTAC), with 4-nitro- and 5-methyl-IBA being comparable in activity in the 0.005 M solutions.

Hydrolyses in Microemulsion Media. Although k_2 values for hydrolyses of fluorophosphates under micellar conditions were high, one cannot load significant amounts of substrate into the system to achieve an effective decontamination formulation. Thus, selected catalysts were tested in a microemulsion medium. Utilizing a high concentration of CTAC (ca. 20% (1 M)) with a cosurfactant such as Bu_4NBr or 1-butanol in aqueous bicarbonate, we obtained excellent rates of reaction. At concentrations of 1–10 mM, 5-nitro-IBA (**11**) hydrolyzed fluoride-releasing agents with $k_2 \sim 50$, which far exceeds Mackay's criterion and provides a system that gives essentially instantaneous decomposition of these toxic compounds.

Experimental Section

Methods. All melting points are uncorrected and were taken in open glass capillary tubes with a Thomas-Hoover melting point apparatus. IR spectra were obtained on a Perkin-Elmer 283B infrared spectrophotometer. ^1H NMR spectra were obtained at 60 MHz on a Varian EM 360L NMR spectrometer, with TMS as internal standard. ^{13}C NMR spectra were obtained at 25 MHz on a JEOL FX-100 NMR spectrometer, referenced either to solvent (δ_{CDCl_3} 77.0; δ_{DMSO}-d_6 39.5) or, when D_2O was utilized, to added DMSO (δ 40.4) or dioxane (δ 67.4), as noted. With mixtures of $CDCl_3$ and DMSO-d_6, $CDCl_3$ was used as reference. Low- and high-resolution mass spectra were obtained on an AEI MS30 mass spectrometer. Microanalyses were performed either in house, on a Carlo Erba 1106 elemental analyzer, or by Atlantic Microlabs, Atlanta, GA.

Materials. Commercially available reagent grade solvents and reagents were used without further purification. Silica gel filtrations utilized either E. M. Merck or MCB silica gel 60 (230–400 mesh). 2-Iodosylbenzoic acid (**1**) was purchased from Sigma Chemical Co. 2-Iodoxybenzoic acid (**1x**),[19] 5-(octyloxy)-2-iodosylbenzoic acid (**2**),[8] 2-iodosyl-1,4-benzenedicarboxylic acid (**10**),[20] 2-iodosyl-5-nitrobenzoic acid (**9**),[13] 2-iodo-5-methylbenzoic

(15) Mackay, R. A.; Longo, F. R.; Knier, B. L.; Durst, H. D. *J. Phys. Chem.* **1987**, *91*, 861.

(16) Examples are presented in the following: Banks, D. F. *Chem. Rev.* **1966**, *66*, 243.

(17) In ref 9, Moss reported that IBX possessed only 28% of the activity of IBA.

(18) Reference 9. We have observed a comparable decrease of catalytic activity in other substituted IBAs in CTAC microemulsions.

(19) Greenbaum, F. R. *Am. J. Pharm.* **1936**, *108*, 17; *Chem. Abstr.* **1936**, *30*, 2559[5].

(20) Baker, G. P.; Mann, G.; Sheppard, N.; Tetlow, A. J. *J. Chem. Soc.* **1965**, 3721.

acid (**31**),[21] and 2-iodoxy-5-nitrobenzoic acid (**11x**)[14] were prepared according to literature methods. 2-Iodosyl-4-nitrobenzoic acid (**13**)[23] was prepared by oxidation with fuming nitric acid[13] and 2-iodoxy-4-nitrobenzoic acid (**18x**)[23] by chlorination/hydrolysis.

5-(Alkyloxy)-2-iodobenzoic acids **17–19** were prepared from 5-hydroxy-2-iodobenzoic acid (**15**) and the appropriate alkyl iodide (or mesylate,[12] for **19**) according to the procedure given by Moss et al.[8] and purified by column chromatography (silica gel/CH_2Cl_2). Iodoso- and iodoxybenzoic acids were prepared from the corresponding iodo compounds by either chlorination/hydrolysis or Ac_2O/H_2O_2. General procedures are given below. 2-Iodosyl-5-methylbenzoic acid has been previously reported,[22] but the synthesis and properties are described here since the melting points were significantly different.

The properties and spectra of all new compounds are reported. Recrystallization solvents are given in parentheses.

5-Butoxy-2-iodobenzoic acid (17): yield, 67%; mp 88–91 °C; ^{13}C NMR ($CDCl_3$) δ 13.7 (Bu-C_4), 19.1 (Bu-C_3), 31.0 (Bu-C_2), 68.0 (Bu-C_1), 82.8 (Ar-C_2), 117.9 (Ar-C_6), 120.8 (Ar-C_4), 133.7 (Ar-C_1), 142.4 (Ar-C_3), 159.0 (Ar-C_5), 171.3 (C=O); IR ($CHBr_3$) 3300–2500 (br, s), 2950 (s), 2920 (s), 2860, 1690 (s), 1580, 1565, 1460, 1420, 1410, 1380, 1270 (br, s), 1220 (s), 1060 (w), 1025 (w), 1005, 865 (w), 820, 755, 720 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}IO_3$: C, 41.27; H, 4.09. Found: C, 41.69; H, 4.09.

5-(Dodecyloxy)-2-iodobenzoic acid (18): yield, 81%; light brown microcrystals; mp 54–58 °C; ^{13}C NMR ($CDCl_3$) δ 14.6 (Dod-C_{12}), 22.7 (Dod-C_{11}), 25.9 (Dod-C_3), 29.0–29.6 (Dod-C_2, -C_{4-9}), 31.9 (Dod-C_{10}), 68.4 (Dod-C_1), 82.8 (Ar-C_2), 117.9 (Ar-C_6), 120.9 (Ar-C_4), 133.7 (Ar-C_1), 142.4 (Ar-C_3), 159.1 (Ar-C_5), 171.5 (C=O); IR ($CHBr_3$) 3300–2500 (br, s), 2920 (s), 2850 (s), 1695 (s), 1585, 1560, 1460, 1420, 1410, 1380 (w), 1275 (br, s), 1230, 1190 (s), 1060 (w), 1005, 865 (w), 820 (w), 785, 755, 720 cm^{-1}.

Anal. Calcd for $C_{19}H_{29}IO_3$: C, 52.78; H, 6.76. Found: C, 53.09; H, 6.84.

2-Iodo-5-[2-(2-methoxyethoxy)ethoxy]benzoic acid (19): yield, 45%; yellow oil; ^{13}C NMR ($CDCl_3$) δ 58.8 (CH_3), 67.5, 69.3, 70.4, 71.6 (CH_2), 83.0 (Ar-C_2), 117.6 (Ar-C_6), 120.2 (Ar-C_4), 134.3 (Ar-C_1), 142.1 (Ar-C_3), 158.4 (Ar-C_5), 169.0 (C=O); IR (thin film) 3600–2300 (br, s), 2920 (s), 2880 (s), 1710 (br, s), 1590 (s), 1560 (s), 1465 (s), 1455 (s), 1420 (s), 1280 (br, s), 1230 (br, s), 1130 (s), 1100 (s), 1060 (s), 1010, 960, 925, 870, 820, 780, 755, 740 cm^{-1}.

Anal. Calcd for $C_{12}H_{15}IO_5 \cdot 0.5H_2O$: C, 38.42; H, 4.30. Found: C, 38.19; H, 3.78.

General Procedure for Chlorination/Hydrolysis. 5-Butoxy-2-iodosylbenzoic Acid (5). Cl_2 gas (dried by passing through anhydrous $CaSO_4$) was bubbled into an ice-cooled solution of **17** (0.90 g, 2.81 mmol) in $CHCl_3$ (7 mL) for 30 min. The solvent was evaporated with a stream of dry argon and the resulting solid transferred to a mortar. Ice (5 g) and Na_2CO_3 (1.3 g) were added, and the mixture was crushed to a paste. NaOH (1.0 N, 14 mL) was added and the slurry stirred at 15–20 °C for 2 h, diluted with water (10 mL), and filtered. The filtrate was acidified with 4 N HCl and the solid collected, washed with water, and dried. The resulting material was washed with two small portions of EtOAc and once with ether and dried in vacuo to give 0.62 g (66%) of **5** as beige microcrystals: mp 200–200.5 °C dec; ^{13}C NMR (DMSO-d_6) δ 13.6 (Bu-C_4), 18.6 (Bu-C_3), 30.5 (Bu-C_2), 68.0 (Bu-C_1), 108.8 (Ar-C_2), 115.4 (Ar-C_6), 121.9 (Ar-C_4), 127.1 (Ar-C_3), 132.9 (Ar-C_1), 160.9 (Ar-C_5), 167.5 (C=O); IR ($CHBr_3$) 3200–2500 (br, s), 2960 (s), 2940 (s), 2880, 1600 (s), 1555 (br, s), 1450 (s), 1420, 1330, 1260, 1220, 1110, 1065, 1040, 1030, 1010, 790 (s), 725 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}IO_4$: C, 39.31; H, 3.90. Found: C, 39.58; H, 3.66.

5-Butoxy-2-iodoxybenzoic Acid (5x). Evaporation of the ethyl acetate/ether washes from above and recrystallization from acetone gave **5x** (6%). A second recrystallization gave an analytical sample, as colorless needles: mp 190–190.5 °C; ^{13}C NMR (DMSO-d_6) δ 13.7 (Bu-C_4), 18.6 (Bu-C_3), 30.5 (Bu-C_2), 67.6 (Bu-C_1), 82.1 (Ar-C_2), 116.2 (Ar-C_6), 119.2 (Ar-C_4), 137.8 (Ar-C_1), 141.2 (Ar-C_3), 158.5 (Ar-C_5), 167.8 (C=O); IR ($CHBr_3$) 3060, 2960, 2930, 2870, 1670 (s), 1580, 1450, 1320, 1280 (s), 1240, 1110, 1000 (w), 880, 830, 780, 770 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}IO_5$: C, 37.52; H, 3.72. Found: C, 37.43; H, 3.37.

5-(Octyloxy)-2-iodoxybenzoic acid (2x): obtained as by-product of chlorination/hydrolysis of **16**; yield, 26%; colorless plates (acetone); mp 113–115 °C; ^{13}C NMR (DMSO-d_6) δ 13.9 (Oct-C_8), 22.1 (Oct-C_7), 25.4 (Oct-C_3), 28.4–28.6 (Oct-C_2, -C_4, -C_5), 31.3 (Oct-C_6), 67.9 (Oct-C_1), 82.1 (Ar-C_2), 116.3 (Ar-C_6), 119.1 (Ar-C_4), 137.7 (Ar-C_1), 141.2 (Ar-C_3), 158.5 (Ar-C_5), 167.7 (C=O); IR ($CHBr_3$) 3080, 3065, 2950, 2940 (s), 2920 (s), 2850 (s), 1670 (s), 1650 (s), 1580, 1460 (s), 1420, 1390 (w), 1325 (s), 1280 (s), 1240 (s), 1110 (s), 1030, 1000, 920, 880, 820, 790, 775, 720 (w) cm^{-1}.

Anal. Calcd for $C_{15}H_{21}IO_5$: C, 44.13; H, 5.18. Found: C, 44.03; H, 4.94.

5-(Dodecyloxy)-2-iodosylbenzoic acid (6): prepared by chlorination/hydrolysis; yield, 33%. The sample was recrystallized from acetone, as colorless microcrystals: mp 121–123 °C dec; ^{13}C NMR ($CDCl_3/CD_3OD$) δ 14.0 (Dod-C_{12}), 22.6 (Dod-C_{11}), 25.8 (Dod-C_3), 28.8–29.5 (Dod-C_2, -C_{4-9}), 31.8 (Dod-C_{10}), 69.2 (Dod-C_1), 104.7 (Ar-C_2), 116.7 (Ar-C_6), 124.8 (Ar-C_4), 127.4 (Ar-C_3), 129.9 (Ar-C_1), 162.6 (Ar-C_5), 167.5 (C=O); IR ($CHBr_3$) 3080, 3070, 2960, 2940, 2920 (s), 2890, 2850 (s), 1650 (s), 1580, 1550, 1455 (s), 1420, 1410, 1390 (w), 1325 (s), 1310, 1290, 1280 (s), 1240, 1130 (s), 1110 (s), 1090, 1020 (s), 1000, 920, 880, 820, 790, 775, 725 cm^{-1}.

Anal. Calcd for $C_{19}H_{29}IO_4 \cdot 1.0H_2O$: C, 48.93; H, 6.70. Found: C, 48.57; H, 6.32.

General Procedure for Ac_2O/H_2O_2 Oxidation. 5-(Dodecyloxy)-2-iodoxybenzoic Acid (6x). Acetic anhydride (1 mL) and 30% H_2O_2 (0.25 mL) were stirred at exactly 40 °C for 4 h, and then 5-(dodecyloxy)-2-iodobenzoic acid (0.22 g, 0.50 mmol) was added and the mixture stirred at exactly 40 °C for 20 h. The slurry was poured into water (10 mL) and stirred at room temperature for 1 h. The solid was collected, washed, and dried to give 0.19 g (85%) of **6x**, as colorless microcrystals: mp 172–175 °C dec; ^{13}C NMR ($CDCl_3/CD_3OD$) δ 12.7 (Dod-C_{12}), 21.0 (Dod-C_{11}), 24.3 (Dod-C_3), 27.4–27.9 (Dod-C_2, -C_{4-9}), 30.2 (Dod-C_{10}), 66.7 (Dod-C_1), 80.4 (Ar-C_2), 115.4 (Ar-C_6), 117.7 (Ar-C_4), 135.7 (Ar-C_1), 140.0 (Ar-C_3), 157.4 (Ar-C_5), 166.4 (C=O); IR ($CHBr_3$) 2920 (s), 2850 (s), 1685, 1570 (br), 1450 (s), 1420, 1320, 1280 (s), 1235, 1100, 1010 (w), 870, 820, 790, 720 cm^{-1}.

Anal. Calcd for $C_{19}H_{29}IO_5$: C, 49.15; H, 6.29. Found: C, 50.39; H, 6.32.

2-Iodosyl-5-[2-(2-methoxyethoxy)ethoxy]benzoic acid (7): prepared by chlorination/hydrolysis; yield, 38%; yellow microcrystals: mp 104–106 °C; ^{13}C NMR ($CDCl_3$) δ 58.8 (CH_3), 68.5, 69.2, 70.5, 71.7 (CH_2), 105.3 (Ar-C_2), 116.7 (Ar-C_6), 124.6 (Ar-C_4), 127.5 (Ar-C_3), 130.0 (Ar-C_1), 162.0 (Ar-C_5), 167.1 (C=O).

Anal. Calcd for $C_{12}H_{15}IO_6 \cdot 1.0H_2O$: C, 36.02; H, 4.28. Found: C, 35.55; H, 3.25.

Ethyl 5-(2-Hydroxyethoxy)-2-iodobenzoate (22). Ethyl 5-(2-bromoethoxy)-2-iodobenzoate (**21**) (0.20 g, 0.50 mmol),[9] DMF (0.7 mL), and saturated $NaHCO_3$ (0.5 mL) were heated with stirring at 110 °C for 20 h. The mixture was poured into ice water (5 mL), acidified, and extracted with $CHCl_3$ (1 × 3 mL). The extract was dried ($MgSO_4$) and evaporated. Water (5 mL) was added and the mixture extracted with 3:1 ether/ethanol (2 × 6 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give 0.11 g (65%) of **22** as a colorless glass: ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 60.9 (CH_2OH), 61.7 (OCH_2CH_3), 69.4 (CH_2OAr), 82.6 (Ar-C_2), 117.0 (Ar-C_6), 119.3 (Ar-C_4), 136.1 (Ar-C_1), 141.7 (Ar-C_3), 158.4 (Ar-C_5), 166.1 (C=O); IR (thin film) 3600–3300, 3030 (w), 2980, 2920, 1720 (s), 1590, 1560, 1460, 1405, 1365, 1290 (s), 1250 (s), 1220 (s), 1140, 1100, 1050, 1010, 955, 895, 810, 770, 730 cm^{-1}; mass spectrum, m/e (relative intensity) 337 (12), 336 (100), 292 (50), 291 (18), 264 (32), 248 (11), 247 (71), 121 (13), 92 (21), 75 (15), 73 (13), 65 (17), 63 (23), 45 (56); high-resolution mass spectrum m/e calcd 335.986, found 335.989 (standard deviation 0.003).

5-(2-Hydroxyethoxy)-2-iodoxybenzoic acid (8x): prepared by chlorination/hydrolysis; yield, 61%; pale yellow microcrystals (EtOH); mp 168–169 °C dec; ^{13}C NMR ($CDCl_3$/DMSO-d_6) δ 59.2 (CH_2OH), 68.9 (Ch_2OAr), 81.2 (Ar-C_2), 116.1 (Ar-C_6), 118.5 (Ar-C_4), 135.8 (Ar-C_1), 140.6 (Ar-C_3), 157.9 (Ar-C_5), 166.9 (C=O); IR

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($CHBr_3$) 3420, 2920, 1680 (s), 1660 (s), 1580, 1460, 1440, 1315, 1290 (s), 1275 (s), 1080, 1040, 890, 850, 820, 810, 770 cm^{-1}.

Anal. Calcd for $C_9H_9IO_6$: C, 31.77; H, 2.67. Found: C, 32.22; H, 2.26.

[2-[3-(Ethoxycarbonyl)-4-iodophenoxy]ethyl]triethylammonium Bromide (23). Ethyl 5-(2-bromoethoxy)-2-iodobenzoate (**21**) (1.00 g; 2.51 mmol)[9] and triethylamine (8 mL) were heated at 110 °C with stirring in a Fisher–Porter tube for 3 days. The triethylamine was evaporated with a stream of nitrogen, ether (20 mL) added, and the mixture stirred for 30 min. The solid was collected, washed, and dried to give 0.83 g (66%) of **23** as beige microcrystals: mp 176–179 °C dec; ^{13}C NMR ($CDCl_3$) δ 8.0 (NCH_2CH_3), 14.0 (OCH_2CH_3), 54.2 (NCH_2CH_3), 56.4 (OCH_2CH_2N), 61.7, 62.1 (OCH_2CH_3, OCH_2CH_2N), 83.6 (Ar-C_2), 117.2 (Ar-C_6), 119.0 (Ar-C_4), 136.5 (Ar-C_1), 141.8 (Ar-C_3), 156.8 (Ar-C_5), 165.9 (C=O); IR ($CHBr_3$) 2980, 2920 (s), 1720 (s), 1590, 1560, 1460 (s), 1400, 1360, 1290 (s), 1250 (s), 1220 (s), 1100, 1060, 1010, 850 (w), 780, 725 cm^{-1}.

Anal. Calcd for $C_{17}H_{27}BrINO_3 \cdot 1.0H_2O$: C, 39.40; H, 5.64; N, 2.70. Found: C, 39.31; H, 5.19; N, 2.63.

[2-(3-Carboxy-4-iodoxyphenoxy)ethyl]triethylammonium Chloride (9x). Chlorination/hydrolysis of **23** (0.26 g, 0.50 mmol) followed by extraction of the acidified aqueous mixture with CH_2Cl_2 (2 × 5 mL), drying ($MgSO_4$), and evaporation gave a yellow solid (the ester of **9x** (**24**)), which was hydrolyzed by refluxing with 2.5 N NaOH (0.3 mL) and methanol (3 mL) for 3 h. The mixture was acidified (6 N HCl) and evaporated. The resulting solid was triturated with absolute EtOH (3 mL), filtered, and evaporated to give 0.11 g (51%) of **9x** as an amber glass: ^{13}C NMR ($CDCl_3/CD_3OD$) δ 7.3 (NCH_2CH_3), 53.8 (NCH_2CH_3), 55.8 (OCH_2CH_2N), 61.5 (OCH_2CH_2N), 83.6 (Ar-C_2), 116.7 (Ar-C_6), 118.9 (Ar-C_4), 136.2 (Ar-C_1), 141.7 (Ar-C_3), 156.6 (Ar-C_5), 167.4 (C=O); IR ($CHBr_3$) 3600–2300 (br), 3400 (s), 2980 (s), 2920 (s), 1710 (s), 1590, 1560, 1460 (s), 1390, 1365, 1270 (s), 1230 (br, s), 1100, 1065, 1000 (s), 960, 880, 860, 810, 780, 740 cm^{-1}.

Anal. Calcd for $C_{15}H_{23}ClINO_5 \cdot 1.5H_2O$: C, 37.01; H, 5.38; N, 2.88. Found: C, 37.06; H, 5.12; N, 2.93.

2-Iodosyl-5-methylbenzoic acid (10):[22] prepared by Ac_2O/H_2O_2; yield, 85%; colorless microcrystals; mp 248–250 °C (lit.[22] mp 210–212 °C); ^{13}C NMR (DMSO-d_6) δ 20.2 (CH_3), 116.7 (Ar-C_2), 126.0 (Ar-C_3), 131.5 (Ar-C_1, -C_6), 135.2 (Ar-C_4), 140.5 (Ar-C_5), 167.8 (C=O); IR ($CHBr_3$) 3400–2400 (br), 1610 (br, s), 1560 (br, s), 1450, 1400, 1310 (s), 1250, 1210, 1180, 1120, 1040 (w), 1005 (w), 905, 820, 790, 780 cm^{-1}.

Anal. Calcd for $C_8H_7IO_3$: C, 34.56; H, 2.54. Found: C, 34.68; H, 2.16.

2-Iodoxy-5-methylbenzoic acid (10x): prepared by chlorination/hydrolysis; yield, 86%; colorless needles (acetone); mp 199–201 °C; ^{13}C NMR ($CDCl_3/CD_3OD$/DMSO-d_6) δ 20.3 (CH_3), 89.5 (Ar-C_2), 131.4 (Ar-C_6), 133.2 (Ar-C_4), 134.9 (Ar-C_5), 137.7 (Ar-C_1), 140.6 (Ar-C_3), 168.1 (C=O); IR ($CHBr_3$) 3080, 2920, 1700 (s), 1685 (s), 1660 (s), 1590, 1450, 1400, 1280 (s), 1250 (s), 1200, 1040 (w), 1010 (w), 900 (w), 870 (w), 810, 780, 770, 720 cm^{-1}.

Anal. Calcd for $C_8H_7IO_4$: C, 32.68; H, 2.40. Found: C, 32.94; H, 2.00.

Registry No. 1, 304-91-6; **2**, 112391-40-9; **2x**, 112391-41-0; **4b** (R = H), 131-62-4; **4b** (R = OC_8H_{17}), 114185-69-2; **4b** (R = OC_4H_9), 114185-71-6; **4b** (R = $OC_{12}H_{25}$), 114185-73-8; **4b** (R = $O(CH_2)_2O(CH_2)_2OCH_3$), 114185-75-0; **4b** (R = CH_3), 114185-78-3; **4b** (R = NO_2), 1830-16-6; **5**, 112391-38-5; **5x**, 112391-39-6; **6**, 112391-36-3; **6x**, 112391-37-4; **7**, 114185-64-7; **8x**, 114185-66-9; **9x**, 114185-68-1; **10**, 90500-13-3; **10x**, 112391-33-0; **11**, 23330-00-9; **11x**, 64297-68-3; **12**, 64297-89-8; **13**, 112391-34-1; **13x**, 112391-35-2; **15**, 57772-57-3; **16**, 89031-97-0; **17**, 114185-61-4; **18**, 114185-62-5; **19**, 114185-63-6; **21**, 99665-71-1; **22**, 114185-65-8; **23**, 114185-67-0; **31**, 52548-14-8; PNPDPP, 10359-36-1; NPIPP, 80751-39-9; PNPH, 956-75-2; 5-(octyloxy)-1-hydroxy-1,2-benziodoxoline, 114185-70-5; 1,3-dione, 114185-70-5; 5-butoxy-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-72-7; 5-(dodecyloxy)-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-74-9; 5-(2-hydroxyethoxy)-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-76-1; 1-hydroxy-5-(2-triethylammoniumethoxy)-1,2-benziodoxoline-1,3-dione chloride, 114185-77-2; 5-methyl-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-79-4; 5-nitro-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-80-7; 1-hydroxy-6-carboxy-1,2-benziodoxolin-3-one, 1829-20-5; 6-nitro-1-hydroxy-1,2-benziodoxoline-3-one, 1830-20-2; 6-nitro-1-hydroxy-1,2-benziodoxoline-1,3-dione, 114185-81-8; butyl iodide, 542-69-8; dodecyl iodide, 4292-19-7; 2-(2-methoxyethoxy)ethyl mesylate, 60696-83-5.

Supplementary Material Available: Plots of absorbance (402 nm) vs time and log ($A_\infty - A_t$) vs time for the hydrolysis of NPIPP (2 pages). Ordering information is given on any current masthead page.

Alkylaminonitrobenzenes by Vicarious Nucleophilic Amination with 4-(Alkylamino)-1,2,4-triazoles

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A series of 4-(alkylamino)-1,2,4-triazoles transfer the alkylamino group to the 4-position of nitrobenzene and various 3-substituted nitrobenzenes, with no detectable ortho substitution. By contrast 2-nitrothiophene reacts in the 3-position and 2-nitronaphthalene in the 1-position; 1-nitronaphthalene gives a mixture of products derived from dominant 2- with some 4-substitution. The orientations are discussed and rationalized.

We recently reported[1] that nitrobenzene and a variety of 3-substituted nitrobenzenes could be efficiently aminated in the 4-position by 4-amino-1,2,4-triazole (**1**) in an extension of Makosza's vicarious substitution sequence. We now report extensions of this work in various directions.

Preparation of 4-(Alkylamino)-1,2,4-triazoles 3. We followed two literature methods: in the first,[2] the methyl *p*-toluenesulfonates of cation **4a** and of the ethyl analogue **4b** were prepared and rearranged into the corresponding 4-(methylamino)- (**3a**, 56%) and 4-(ethylamino)-1,2,4-triazoles (**3b**, 76%) (for the designation of various compounds of type **3** see Table I).

The second method for the preparation of compounds **3** is the reduction of imines **2**; the *N*-benzyl derivative **3d** was previously so obtained.[3] Reacting 4-amino-1,2,4-

(1) Katritzky, A. R.; Laurenzo, K. S. *J. Org. Chem.* **1986**, *51*, 5039.

(2) Becker, H. G. O.; Timpe, H.-J. *J. Prakt. Chem.* **1969**, *311*, 9.

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