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POLYMER-BOUND IODOSOBENZOATE REAGENTS FOR THE CLEAVAGE OF REACTIVE PHOSPHATES

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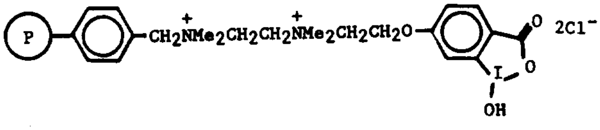
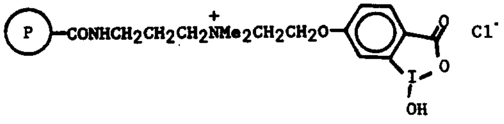
Summary. Two polymer-bound iodosobenzoate derivatives have been prepared and found to be phosphorolytically active against both p-nitrophenyldiphenyl phosphate and the nerve agent, Soman.

Since the discovery of their catalytic cleavage of activated esters and phosphates,[1] iodosobenzoates and closely related species have come under intense scrutiny as decontaminants for the destruction of toxic phosphates.[2-4] The reactivity of the iodosobenzoates is strongly potentiated by solubilization in cationic micellar surfactants.[1] Therefore, we prepared an iodosobenzoate-functionalized, cationic surfactant that proved to be a versatile micellar decontamination agent.[5] In turn, this focused our attention on the need for a solid decontaminant that would be easy to handle, and useful in the case of small "spills" of toxic agents. The concept of combining the catalytic properties of a functional surfactant with the stability of a polymer[6] lends itself naturally to the design of a cationic iodosobenzoate-functionalized polymer. We are pleased to report here the preparation and some kinetic properties of the first two representatives of this class of decontaminants.

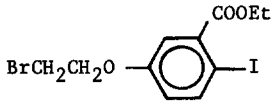
Polymers P-1 and P-2 were prepared. P-1 derived from a 3-step sequence in which tetramethylethylene diamine was first monoquaternized with bromide 1[5] (refluxing benzene, 19 h), and 3.5 mmol of the resulting quaternary salt[7] was then quaternized with 0.8 g (3.2 mequiv of CH_2Cl) of Polysciences 3% cross-linked, 20-60 mesh, 52% chloromethylated



P-1



P-2



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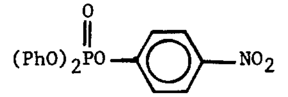
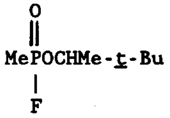


2 (PNPDPP)



$\mathrm{Me\overset{\overset{O}{\|}}{\underset{\underset{F}{|}}{P}}OCHMe\text{-}\underline{t}\text{-}Bu}$

3 (GD)

polystyrene ($CHCl_3$, 80°C, 4 days, stirring, sealed tube). After purification,[8] the bis-quaternary salt polymer was found to contain 2.5 mequiv/g of ionic halide (i.e., 1.25 mequiv/g of diquaternary side chains) by addition of $AgNO_3$, followed by electrochemical back titration with bromide, corresponding to 45% ring substitution. Elemental analyses for I and N gave values in accord with 40-44% ring substitution.

Conversion to the final, P-1 polymer was carried out by the chlorination/hydrolysis method[9] that, in this case, releases ethanol and directly[9] converts the iodo and ester groups to the iodosobenzoate in its (illustrated) 1-hydroxy-1,2-benziodoxolin-3-one form.[1,5] The ir spectrum of P-1 had lost the ester carbonyl at 1705 cm^{-1} in favor of a broad band near 1620 cm^{-1}, characteristic of iodosobenzoates.[10] Iodometric titration confirmed oxidizing power equivalent to 1.2 mequiv/g of iodoso groups (42% ring substitution of the phenyl groups of P-1).

Polymer P-2 was derived from Bio-Rad AG4-X4A, a copolymer of ethyl acrylate cross-linked with 4% divinylbenzene, in which ~82% of the ethyl carboxylate side chains have been converted into γ-dimethylaminopropioamide groups by aminolysis with γ-dimethylaminopropyl amine.[11] This polymer was quaternized with 0.70 equiv of bromide 1 (EtOH, 60-55°C, sealed tube, 5 days) to afford the o-iodoester precursor of P-2. After washing (EtOH, CH_3CN) and drying, the precursor polymer was characterized by separate titrations for free MeN, and ionic bromide, and by AgOAc exchange of acetate for bromide, followed by elemental analysis for I and N. These methods indicated ~1.3-1.5 mequiv/g or ~50% of quaternized side chains in the polymer.

The iodoester polymer was ground in a mortar[12] and oxidized by the chlorination/hydrolysis method[9] to give iodosobenzoate polymer P-2, that was washed (H_2O, 0.1 M aq. NH_4Cl, 1:1 H_2O/CH_3CN, CH_3CN) and dried. P-2 had 0.32 mequiv/g of iodoso groups by iodometric titration, corresponding to the oxidation of ~20% of the iodo groups of its precursor.[13] Although the iodosobenzoate loading of P-2 is only ~25% that of P-1, both polymers are active in the cleavage of p-nitrophenyl diphenyl phosphate (PNPDPP, 2).

The cleavage of 0.062 μmol of PNPDPP by 5 mg of P-1 (6.0 μequiv of I-0) was followed in 2.5 ml aliquots of 0.02 M pH 8 phosphate buffer, $\mu = 0.1$ (KCl), by the 1 vial/1 kinetic point method, spectroscopically monitoring released p-nitrophenoxide ($PNPO^-$) at 400 nm.[14] A plot of $PNPO^-$ absorbance vs. time appears in Figure 1. The data obeys good first order kinetics and give $\underline{k}_\psi = 0.011\ s^{-1}$ ($\underline{r} = 0.999$). A duplicate run gave $\underline{k}_\psi = 0.010\ s^{-1}$. Importantly, the iodobenzoate precursor polymer was essentially inactive toward PNPDPP (see Figure). Similar kinetic experiments with P-2 and PNPDPP also led to first order kinetics with $\underline{k}_\psi = 0.011 \pm 0.002\ s^{-1}$ (3 runs). As with P-1, the polymeric iodobenzoate precursor of P-2 was effectively inactive against PNPDPP.

Correcting the pseudo first order rate constants for total iodosobenzoate present (as if it were all free and fully available in solution), we obtain "second order" rate constants for P-1 and P-2 of 4.6 and 17 L/M-s, respectively. These are to be compared with $\underline{k}_2 = 550$ L/M-s for the cleavage of PNPDPP by 5-methoxy-2-iodosobenzoate in 10^{-3} M CTACl micellar solution under similar conditions,[4] so that the polymer-immobilized catalysts are ~120 (P-1) or ~32 (P-2) times less reactive toward PNPDPP than a micelle-solubilized analogue. Lower activity of polymer-bound reagents, relative to their soluble analogues is not unusual.[15]

Most importantly, both P-1 and P-2 were active against the nerve agent Soman (GD), 3. Thus, $\tau_{1/2}$ for the OH^- mediated hydrolysis of GD in pH 8.0, 0.05 M phosphate buffer was 67 ± 0.5_2 min.[16] This was reduced to 18.1 min by P-1, when 5 µmol of GD cleaved with good first order kinetics in the presence of 100 mg (120 µequiv. of I=O) of P-1. Polymer P-2 was also active against GD, with $\tau_{1/2} = 41.4$ min in an analogous experiment using 25 mg (8 µequiv.) of polymer.[17]

Although the phophorolytic reactivity of these first polymer-bound iodosobenzoates is as yet far from optimized, we are confident that enhancements can be achieved by appropriate polymer "engineering". We are continuing our studies accordingly and are also studying the immobilization of iodosobenzoate derivatives on other solid supports.

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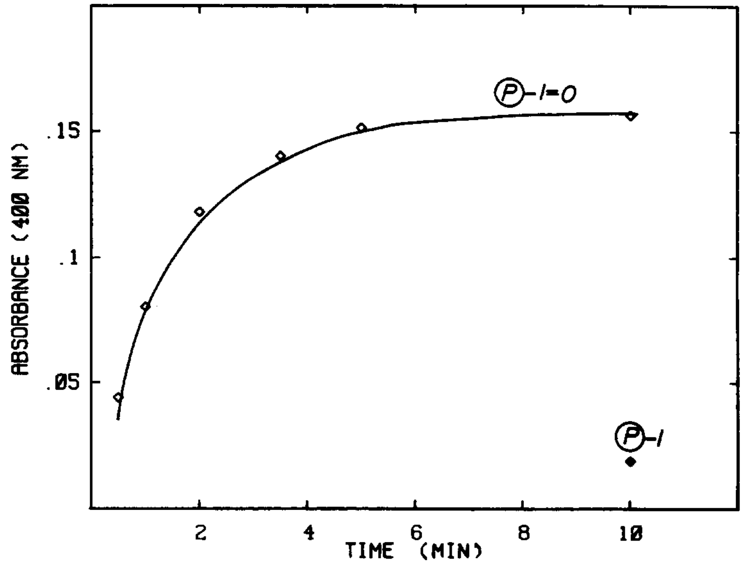

Figure 1. Absorbance of released p-nitrophenoxide vs. time in the pH 8 cleavage of 2 by iodosobenzoate polymer P-1. The corresponding behavior of the iodobenzoate precursor polymer at 10 min reaction time is shown at the lower right of the Figure. See text for details.

References and Notes

(1) R.A. Moss, K.W. Alwis, and G.D. Bizzigotti, J. Am. Chem. Soc., 105, 681 (1983); R.A. Moss, K.W. Alwis, and J-S. Shin, ibid., 106, 2651 (1984).

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

(3) A.R. Katritzky, B.L. Duell, H.D. Durst, and B. Knier, Tetrahedron Lett., 28, 3899 (1987).

(4) R.A. Moss, S. Chatterjee, and B. Wilk, J. Org. Chem., 51, 4303 (1986).

(5) R.A. Moss, K.Y. Kim, and S. Swarup, J. Am. Chem. Soc., 108, 788 (1986).

(6) P. Hodge and D.C. Sherrington, Ed., "Polymer-supported Reactions in Organic Synthesis," Wiley, New York, 1980.

(7) $Me_2NCH_2CH_2N^+Me_2CH_2CH_2OC_6H_3ICOOEt,Br^-$ was recrystallized twice from 2:1 $C_6H_6/CHCl_3$. It had mp 166-168°C, and gave an appropriate ^{1}H nmr spectrum and a satisfactory (C,H,N) elemental analysis.

(8) After an appropriate washing cycle (3 x 15 ml each of $CHCl_3$, THF, 1:1 THF/water, water, THF) we obtained 1.88 g of polymer that was dried at 0.1 mm-Hg, 5 h, 25°C. Ir (nujol) showed 1705 cm^{-1} (strong, ester).

(9) R.A. Moss, P. Scrimin, S. Bhattacharya, and S. Chatterjee, Tetrahedron Lett., 28, 5005 (1987). Details of the procedure as applied in the present case are available upon request.

(10) G.P. Baker, F.G. Mann, N. Sheppard, and A.J. Tetlow, J. Chem. Soc., 3721 (1965).

(11) The polymer carried 5.4 mequiv/g of NMe_2 as determined by titration with excess aq. HCl, followed by back titration with aq. NaOH.

(12) Unground polymer did not undergo satisfactory I → I=O oxidation.

(13) Alternative oxidation methods ($Cl_2/MeOH$, Cl_2/H_2O, 30% H_2O_2, peracetic acid) did not improve this conversion; the majority of the precursor polymers iodo groups seem to be unavailable to the oxidants. Note that the free NMe_2 groups are not converted to reactive groups by the chlorination[9] procedure. In a control experiment, AG4-X4 polymer was 50% quaternized with isobutyl bromide and then subjected to chlorination/hydrolysis. The resulting polymer was inactive against PNPDPP (see below).

(14) P-1 strongly adsorbed $PNPO^-$, so that after each aliquot was filtered, the recovered P-1 was ground in a mortar with 2.5 ml of 0.1 M aq. $NaClO_4$ solution to leach $PNPO^-$. $PNPO^-$ absorbance was determined on combined filtrate and leachate (5.0 ml). P-2 bound $PNPO^-$ less strongly, so that leaching required stirring only, not grinding.

(15) S.L. Regen and J.L. Besse, J. Am. Chem. Soc., 101, 4059 (1979). Also, the iodosobenzoate groups of P-1 and P-2 may not be as strongly activated in the polymers as in cationic CTACl micelles. However, the positive charges on the polymer side chains may serve to mimic the micellar milieu.

(16) GD cleavage was continuously monitored at 25°C by F^- release as measured with a (calibrated) Orion model 960900 Combination Fluoride Electrode and a Fisher Accumet model 825 MD pH meter/Ionanalyzer. Rate constants and half-lives were generated from $[F^-]$ vs. time by standard computational methods.

(17) The iodo precursor of P-2 (45 mg) afforded $\tau_{1/2} = 51.2$ min in a control hydrolysis of GD.

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