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CHEMISTRY OF AN ACYLOXYIODINANE, THE INTERMEDIATE IN IODOSOBENZOATE CATALYZED CLEAVAGE OF ACTIVE ESTERS

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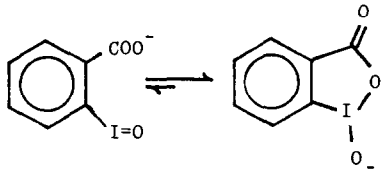
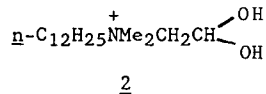
Summary: The 1-acetoxy-1,2-benziodoxol-3(1H)-one intermediate in the o-iodosobenzoate cleavage of p-nitrophenyl acetate can be directly observed in dimethyl sulfoxide.

Some current efforts to develop efficient catalysts for the decontamination of toxic phosphates focus[2] on o-iodosobenzoate (1) or its derivatives,[3] and on the hydrated surfactant-aldehyde 2.[4,5] Not only are these reagents potent O-nucleophiles in moderately basic aqueous cationic micellar solutions, but the O-phosphorylated or acylated intermediates derived from their attack on reactive phosphates or esters, rapidly hydrolyze and regenerate the initial catalysts. These features distinguish 1 and 2 from such nucleophilic decontamination reagents as peroxides,[6] benzimidazole,[7] oximates,[8] or



1 1a

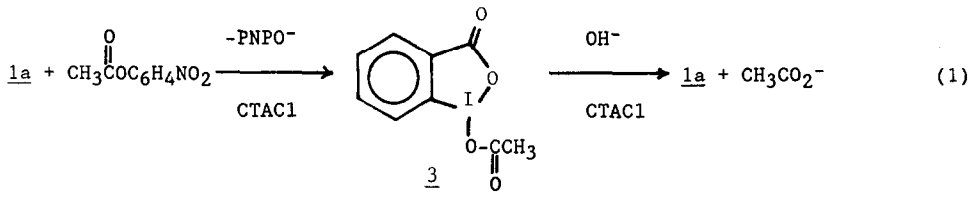


2

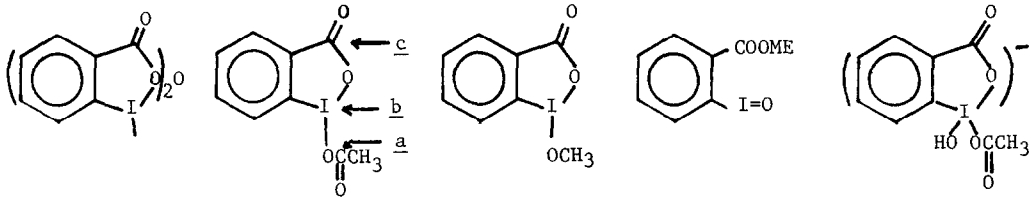
alkenylphosphonium ions[9] that require either strongly basic conditions, stoichiometric quantities, or turn over too slowly.[10] The mechanism by which acylated or phosphorylated 2 is hydrolyzed seems clear,[4] but for 1a, the reactive form of 1,[3] it is uncertain.[3c] Here we report new and elucidating mechanistic experiments.

In pH 8 aqueous micellar cetyltrimethylammonium chloride (CTACl) solution, o-iodosobenzoate (1), in its preferred 1-oxido-1,2-benziodoxol-3(1H)-one valence tautomeric form (1a),[11] cleaves p-nitrophenyl acetate (PNPA) with k_ψ = 0.018 s^{-1}, k_2 = 180 $M^{-1}s^{-1}$, eq. (1).[3a] Acetate 3 was proposed as an intermediate, but it did not accumulate under these conditions. Authentic 3, available from the reaction of 1a-OH and acetic anhydride,[12] hydrolyzes in pH 8 CTACl solution with k_ψ ~0.4 s^{-1}, about 20 times faster than 3 forms from 1a and PNPA.[3a]

When we now carry out the reaction of 1a and PNPA in DMSO,[13] monitoring by nmr (DMSO-d_6), we observe the formation of 3 (δ_{Me} 2.25) and acetate (δ_{Me} 1.80), coincident with the



disappearance of PNPA (δ_{Me} 2.32). Most importantly, in DMSO where no OH^- is present to destroy 3, this species largely accumulates. It is, however, attacked by iodosobenzoate 1a with the formation of acetate and anhydride 4. The products can be controlled by manipulating the reactant concentrations: with excess 1a, 3 builds up and then decays as 1a converts it to 4[14] and acetate (Figure 1); with excess PNPA, 3 is relatively stable and acetate formation is minimized (Figure 1, inset).[15]



4 3′ 5 6 7

Nucleophilic attack on 3 might occur at any of three sites (cf., 3′). The formation of 4 from 1a and 3 points to direct attack at iodine (b). In agreement, we find that the reaction of 3 with NaOMe/DMSO-d_6 rapidly affords ether 5 (δ_{Me} 4.17) and acetate. A similar reaction occurs with methanol, but much more slowly.[16] The absence of methyl acetate (δ_{Me} 1.99, δ_{MeO} 3.56) in the methoxide reaction excludes pathway a.

Although the conversion of 3 to 5 is readily understood in terms of direct attack at iodine (3′, b), we cannot completely exclude attack of methoxide at the lactone carbonyl (c), affording ester 6 with loss of acetate. Ester 6 could then react with methoxide at I=O, subsequently reforming lactone ether 5 with expulsion of the ester methoxyl group.[17] In a cogent experiment that bears on the conversion of 3 to 1a with OH^-, we find that reaction of 0.1 mmol of 3 with 1 ml of 22.06 atom-% $H_2{}^{18}O$ (containing 7 mg of NaOH) in 3 ml of DMSO gives 1/1a with 21.64 atom-% ^{18}O in the iodoso position and only 2.00 atom-% ^{18}O in the lactone group.[18] Indeed, so reactive are the iodine atoms of these iodinanes toward nucleophiles, that even iodosobenzoate (1a) itself exchanges with $H_2{}^{18}O$ in an identical experiment.[19]

These findings strongly imply that path b is the dominant, if not exclusive route for nucleophilic attack on 3, with subsequent conversion to 1a, 4, or 5 (for nucleophiles OH^-, 1a, or MeO^-, respectively).[20] The most reasonable mechanism for the turnover of acetylated (or phosphorylated) iodosobenzoate catalysts under aqueous micellar conditions is therefore

hydroxide attack at iodine, with the formation of an anionic 12-I-4[11,21] intermediate (e.g, 7) that subsequently loses acetate (or phosphate).[22] In basic CTACl solution, where [OH^-] is high at the cationic micellar surface, intermediates such as 3 are very rapidly hydrolyzed via 7, regenerating 1/1a, so that the overall cleavage of reactive esters (or phosphates) becomes catalytic. In DMSO, the reaction is merely stoichiometric in iodosobenzoate so that, with the substrate in excess, an intermediate like 3 accumulates.

Finally, we see now why micellar iodosobenzoates are such remarkably efficient esterolytic catalysts. The hypervalent[11] iodine atom plays a double role. Its special bonding[23] creates a highly polarized I^+-O^- bond in 1a, where the substantial negative charge on oxygen confers potent nucleophilicity for the substrate cleavage step. Secondly, the ability of the resulting 10-I-3 intermediate (e.g., 3) to associate with an additional anionic ligand, affording for example the 12-I-4 species 7, provides a facile mechanism for turnover and completion of the catalytic cycle, particularly in aqueous micellar solution.

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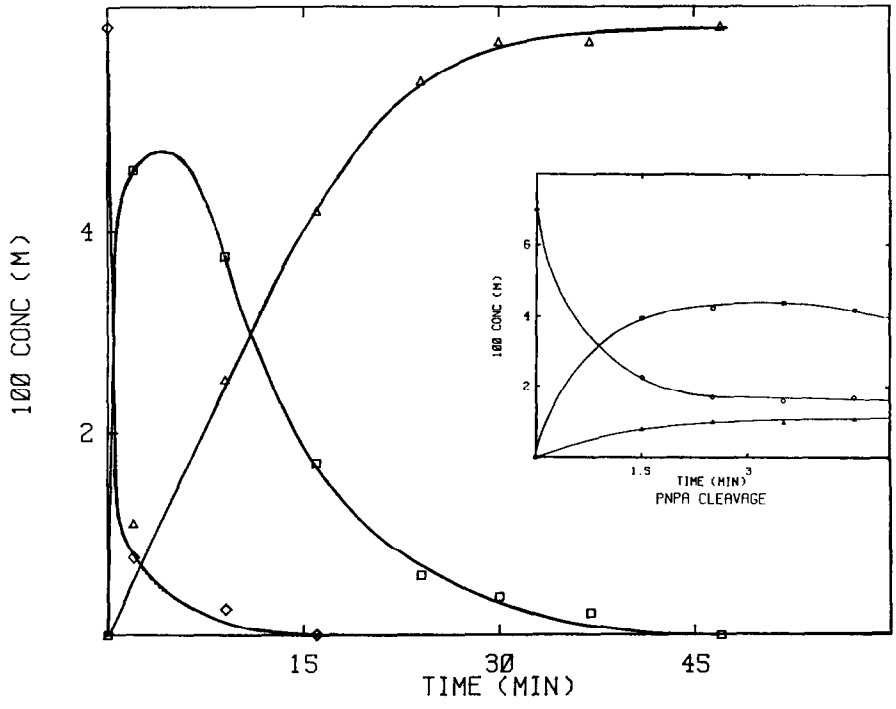

Figure 1. Concentration vs. time profile for cleavage of PNPA by o-iodosobenzoate sodium salt (1a) in DMSO-d_6; [PNPA] = 6 x 10^{-2} M; [1a] = 1.2 x 10^{-1} M. Inset. The same reaction, but with [PNPA] = 7 x 10^{-2} M and [1a] = 5.6 x 10^{-2} M. In both cases, ◇ = PNPA, □ = 3, Δ = $CH_3COO^-Na^+$. The solid lines have been arbitrarily drawn.

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(13) DMSO has a dielectric constant of 49, similar to the estimated value of ~36 for the Stern layers of cationic micelles: cf., Fendler, J.H. "Membrane Mimetic Chemistry," Wiley, New York, 1982, pp. 19,20.

(14) Anhydride 4 (mp 227°C dec.; lit.[12] mp 225°C dec.) forms in 80% yield from the reaction of 0.48 mmol of 1a with 0.24 mmol of PNPA in 3 ml of DMSO. Its ir carbonyl band (1680 cm^{-1}) is in accord with the lit. value.[12]

(15) Anhydride 4 does not form under pH 8 micellar conditions because the rapid destruction of 3 by OH^- supercedes the reaction of 3 with 1a. Cleavage of 4 under micellar condition is slow (k_ψ ~4.6 x 10^{-5} s^{-1}) and it would accumulate if it were formed.

(16) Ether 5 was previously prepared by methanolysis of 3;[12] our sample was identical (mp, ir) to the literature description.

(17) Indeed, an attempt to prepare 6 by Cl_2/OH^- oxidation of o-iodo methyl benzoate led only to 1/1a.

(18) ^{18}O analyses employed a VG 7070 (United Kingdom) mass spectrometer. For analysis minus iodoso oxygen, chemical ionization (isobutane) was used. Ethanolamine-modified isobutane chemical ionization was used to detect the radical molecular ion of the entire molecule; cf., Bowen, D.V.; Field, F.H. Org. Mass. Spec. 1974, 9, 195.

(19) The recovered 1a had 14.22 atom-% ^{18}O at iodoso oxygen and 2.30 atom-% ^{18}O at the lactone oxygens. Iodosobenzene has been reported to exchange with basic alcoholic $H_2{}^{18}O$; Gragerov, I.P.; Levit, A.F. J. Org. Chem. USSR 1963, 33, 544.

(20) The minimal lactone ^{18}O incorporation could reflect either a poorly competitive incursion of pathway c, or mechanistically irrelevant lactone carbonyl exchange that is not associated with acetate expulsion.

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(22) The facile ^{18}O exchange of 1a suggests that a 12-I-4 intermediate with two hydroxide ligands (i.e., 7 with OH in place of $OCOCH_3$) may also be encountered.

(23) See ref. 11a, pp. 739, 740.

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