α-Effect of an Organoiodinane Oxyanion Nucleophile: Absence of an Unusual Solvent Effect

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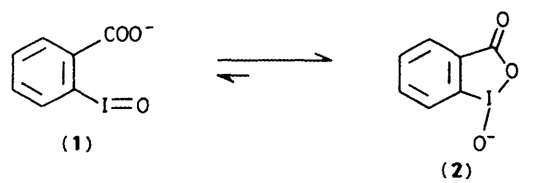
1-Oxido-1,2-benziodoxol-3(1*H*)-one (*o*-iodosylbenzoate) shows a significant α-effect in the cleavage of *p*-nitrophenyl acetate; however, unusual solvent effects are absent in dimethyl sulphoxide–water solvent mixtures.

In 1969, Jencks observed that 'the α-effect is not a single, distinct entity, and there are so many different factors influencing nucleophilic reactivity which are important in "α-effect" compounds that one is sometimes tempted to doubt the usefulness of the term.'[1] Time has not completely resolved this situation; several factors remain in contention,[2] of which stabilization of the reaction transition state by an additional pair of electrons on the atom α to the nucleophilic centre[3] and various solvent effects[4] currently receive the most attention.

The high esterolytic and phosphorolytic reactivity of *o*-iodosylbenzoate (**1**) in its preferred, valence tautomeric 1-oxido-1,2-benziodoxol-3(1*H*)-one form (**2**)[5] suggested that an α-effect might contribute to its nucleophilicity. In this connection, the recent report of Buncel and Um[6] could be taken to provide a simple operational criterion for the detection of such an effect. However, we report now that although (**2**) does indeed react with *p*-nitrophenyl acetate much more rapidly than *O*-nucleophiles of comparable basicity, unusual solvent effects in dimethyl sulphoxide–water blends are entirely absent.

We first determined the titrimetric pK_a of aqueous (**2**) as 7.1. An existing correlation of rate constants *vs.* pK_a for reactions of a series of phenoxides with *p*-nitrophenyl acetate (PNPA)[7] then allows us to extrapolate an expected second order rate constant for the cleavage of PNPA by (**2**) as *k ca.* 1 mol^{-1} dm^3 min^{-1} at 25 °C. In fact, under the conditions



(1) (2)

Table 1. Kinetic data for *p*-nitrophenylacetate with 1-oxido-1,2-benziodoxol-3(1*H*)-one (**2**) and *p*-chlorophenoxide (ArO⁻) in DMSO–water mixtures at 25 °C.[a]

Mol.% DMSO	k_2/ mol^{-1} dm^3 s^{-1}	k_{ArO^-}/ mol^{-1} dm^3 s^{-1} [b]	k_2/k_{ArO^-}
0	1.50	0.685	2.19
20	1.34	0.760	1.76
40	3.98	2.80	1.42
50	7.62	5.90	1.29
60	12.5	13.6	0.92
70	23.4	34.7	0.67
80	45.4	94.8	0.48
90	153	334	0.46
100	342		

[a] Rate constants were measured spectroscopically at 400 nm, following released *p*-nitrophenol–*p*-nitrophenoxide; estimated error <|3%|.
[b] From ref. 6.

employed by Hupe and Jencks[7] [0.05 M phosphate buffer, pH 8, ionic strength (μ) 1.0, KCl], we find the measured rate constant for this reaction to be 120 mol^{-1} dm^3 min^{-1}, more than a hundred times larger than the anticipated rate constant, indicating a significant α-effect.

To characterise further the nucleophilicity of (**2**) we compared it to the common nucleophiles, imidazole and hydroxide ion, using Swain–Scott nucleophilicity parameters[8] as a convenient measure. Second order rate constants for cleavages of aqueous PNPA by (**2**), imidazole, and hydroxide ion were spectroscopically determined at various temperatures between 17 °C and 40 °C, and then extrapolated to 0 °C (the standard reference temperature[8]) *via* the Arrhenius equation. We found the k_2 values (mol^{-1} dm^3 s^{-1}, corrected for ionization) to be 0.25 for (**2**), 0.11 (imidazole), and 0.67 (OH⁻). From the known[8] nucleophilicity constants, *n*, for imidazole (3.58) and hydroxide ion (4.23), and the corresponding experimental rate constants for PNPA cleavages, the Swain–Scott relation, in the form of equation (1), gave s = 1.21 for the susceptibility constant of substrate PNPA. With this value of s, and the rate constant for the reaction of (**2**) with PNPA (0.25 mol^{-1} dm^3 s^{-1}), we calculate n = 3.88 as the nucleophilicity parameter of (**2**). We see that (**2**) is very similar in its properties to imidazole;[9] it too provides unusually high nucleophilicity toward acyl substrates at an essentially neutral pH.

$$\log k_{OH^-} - \log k_{im} = s[n(OH^-) - n(im)] \qquad (1)$$

Recently, Buncel and Um reported that the cleavage of PNPA by the α-nucleophile butane-2,3-dione mono-oximate, when compared with the normal nucleophile *p*-chlorophenoxide (ArO⁻), exhibited a pronounced maximum in rate enhancement (α-effect) in dimethyl sulphoxide (DMSO)–water mixtures as the medium composition was varied.[6] Although they clearly indicated that a complete interpretation of their results would require a kinetic and thermodynamic dissection into initial and transition state contributions,[6] we wondered whether the observed behaviour was general and might be diagnostic for α-effect *O*-nucleophiles. Accordingly, we determined rate constants for the cleavages of PNPA by (**2**) in DMSO–water blends. The results are presented in Table 1, where they are compared to analogous data for the non-α-effect *p*-chlorophenoxide nucleophile.[6,10]†

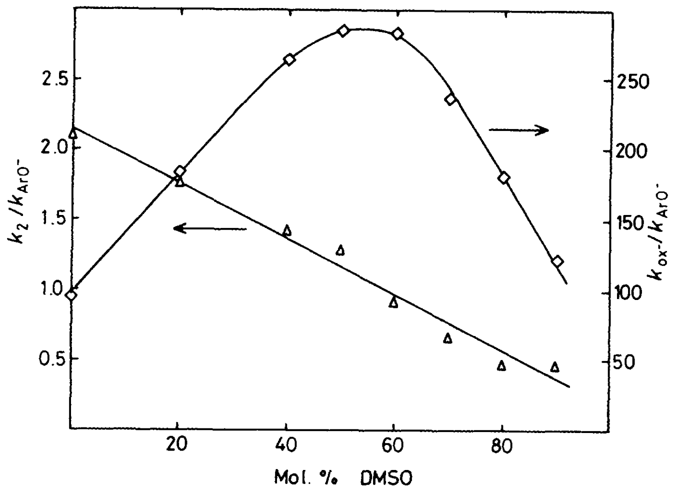


Figure 1. Relative reactivities, k_2/k_{ArO^-} (△) or k_{ox^-}/k_{ArO^-} (◇,) *vs.* mol.% DMSO in water. The data for k_2 are in Table 1; the k_{ox^-} data are taken from ref. 6.

Although the reactivities of both (**2**) and ArO⁻ are enhanced by the incremental solvent changes from water toward DMSO, the phenoxide is affected more strongly. For example, the reported enhancement in *k* over the range 0—90 mol. % DMSO solvent is a factor of 488 for ArO⁻,[6] but we find only 102 for (**2**), so that the relative rate constant, k_2/k_{ArO^-} actually decreases from 2.19 to 0.46 over this solvent interval (Table 1). Most importantly, k_2/k_{ArO^-} is linear (correlation coefficient 0.992) in mol. % DMSO (Figure 1), and contrasts strikingly with the behaviour of k_{ox^-}/k_{ArO^-}, where k_{ox^-} is the second order rate constant for the cleavage of PNPA by the α-nucleophile butane-2,3-dione mono-oximate.[6] The marked enhancement of relative nucleophilicity in solvent mixtures of intermediate composition, abundantly evident with the oximate nucleophile, is entirely ***absent*** with (**2**). Clearly, an unusual solvent effect on the α-effect does not operate with (**2**); such an effect does not appear to be general for oxygen α-nucleophiles.

The origin of the α-effect of (**2**) remains unclear. A reasonable bonding scheme for (protonated) (**2**) features a planar, nearly linear (*ca.* 166°), hypervalent three-centre-four-electron O–I–O unit, with two lone pairs in iodine 5s and 5p orbitals, where the latter orbital is perpendicular to the molecular plane.[11] The α-effect could therefore arise from stabilization of the (**2**) + PNPA transition state by the iodine p electrons.[3] However, the necessary overlap between the iodine 5p orbital and the 2p orbital on the adjacent nucleophilic oxygen atom is likely to be poor, so that electronic stabilization as the origin of the α-effect of (**2**) must be considered provisional in the absence of appropriate calculations.

A solvent effect is not completely precluded. If the large, hydrophobic I–O⁻ moiety of (**2**) is not strongly hydrated in water, it might be unusually nucleophilic compared with

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† The pK_a values of (**2**) (S. Swarup, unpublished work) and *p*-chlorophenoxide[10] vary in a similar way with DMSO–water composition, so that trends in rate differences do not originate in ΔpK_a.

phenoxides of similar basicity. The observed behaviour of k_2/k_{ArO^-}, for PNPA cleavage in going from water to DMSO (Figure 1), suggests that the accompanying dehydration of ArO^- is more important than the dehydration of (**2**). This explains how the reactivity enhancements conferred upon (**2**) in the protic, methanol-like[12] Stern layers of cationic micelles exceed those experienced by for example, the phenoxide ion.‡

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‡ We determined maximum micellar enhancements of 230 and 1180, respectively, in the second order rate constants for cleavages by (**2**) of PNPA or 2,4-dinitrofluorobenzene (DNFB) in 2.5—5.0 × 10^{-3} M aqueous micellar cetyltrimethylammonium bromide (relative to aqueous buffers). Corresponding maximum micellar enhancements for phenoxide ion were 24 (PNPA) and 350 (DNFB).