Tetrahedron Letters, Vol. 34, No. 11, pp. 1729-1732, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

IODOSONAPHTHOATE CATALYSTS FOR THE CLEAVAGE OF A REACTIVE PHOSPHATE

Robert A. Moss,* Hongmei Zhang, Swati Chatterjee, and Karsten Krogh-Jespersen
Department of Chemistry, Rutgers, The State University of New Jersey
New Brunswick, New Jersey 08903

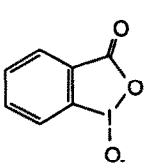
Summary. Iodosonaphthoates 3-5 are potent catalysts for the hydrolysis of p-nitrophenyldiphenyl phosphate.

o-Iodosobenzoate, 1, and its derivatives, are powerful catalysts for the hydrolysis of reactive phosphates and phosphonates in aqueous micellar solution.[1] Their potent nucleophilicity depends upon the negative charge at IO^-, which, in turn, requires maintenance of the closed, iodoxolone ring depicted in 1. However, both X-ray structural results[2] and ab initio calculations[3] indicate that the internal O-I bond is "long", so that a resonance hybrid representation of the iodoxolone ring should include "open" (iodoso) contributors, as shown in 2 (representing the parent 1-oxido-iodoxol-3(1H)-one[3]). To the extent that 2 relaxes toward the open iodosocarboxylate structure, the negative charge, nucleophilicity, and catalytic power at IO^- will decrease; the 3-center-4-electron O-I-O triad will "shuttle" negative charge from IO^- to the "carboxylate" group. On the other hand, if the iodoxolone ring could be "clamped" shut, the same interconnected properties at IO^- might be buttressed.

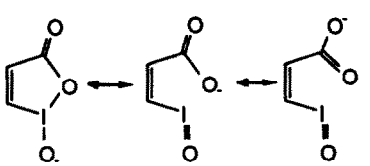
In planar iodosonaphthoates (naphthiodoxolones) 3 and 4, the van der Waals radii of the adjacent 8-peri-H atoms overlap those of the carbonyl oxygen of 3 or the O^- of 4; models indicate H/O separations of ~1.8 Å, whereas the sums of the van der Waals radii are ~2.6 Å. These interactions could be relieved if the iodoxolone rings were to close somewhat at the internal O-I bonds. Indeed, ab initio calculations[4] indicate that the iodoxolone O-I bond lengths decrease from 2.63 to 2.60 to 2.49 Å, and the negative charge at IO^- increases from -1.12 to -1.14 to -1.16, in the sequence 2, 1, 3.

Stimulated by these considerations, we prepared iodosonaphthoates 3-6, and determined their kinetic properties in the hydrolysis of the test substrate, p-nitrophenyldiphenyl phosphate (PNPDPP). Analogous data for 1, 2, and the recently described dibenzobarrelene iodosocarboxylate, 7,[5] are included for comparison. We are delighted to report that 3 and 4 are superior catalysts, but not necessarily for the anticipated reasons.

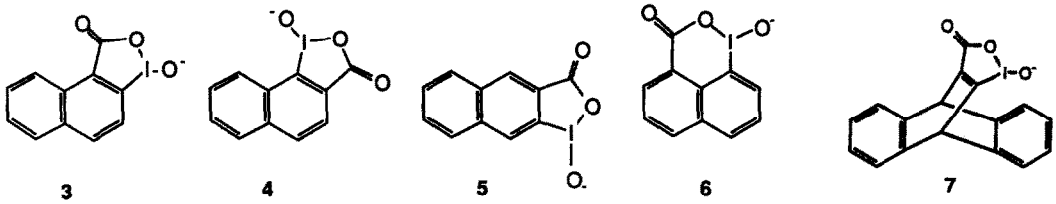
New iodosocarboxylates 3-6 were obtained by oxidations of the corresponding iodocarboxylates with either magnesium monoperoxyphthalate (3, 4)[6] or 35-40% peracetic



1



2



3 4 5 6 7

acid (5, 6).[7] Each iodoso compound exhibited >98% of I=O equivalence in the standard $KI/Na_2S_2O_3$ iodometric titration.[8]

Iodocarboxylates, 3-I - 6-I (i.e., the precursors of iodosocarboxylates 3-6) were synthesized as follows. 2-Iodo-1-naphthoic acid (3-I) was prepared by the directed iodination of 1-cyanonaphthalene at C_2 (lithium tetramethylpiperidide, THF; then I_2, -78°, 40%),[9] followed by hydrolysis to 2-iodo-1-naphthamide (aq. H_2SO_4, HOAc, refl. 16 h, 96%),[10] and deaminative hydrolysis[11] ($NaNO_2$, 70% aq. H_2SO_4, 25°, 71%) to 3-I, mp 188-190°C.[12]

1-Iodo-2-naphthoic acid (4-I) was prepared from 2-methylnaphthalene by nitration to 1-nitro-2-methylnaphthalene (fuming HNO_3 in HOAc, 39%),[13] followed by an "intramolecular" redox reaction, affording 1-amino-2-naphthoic acid (KOH, EtOH, refl., 16 h, 11%),[14] and diazotization/iodination to 4-I, mp 203-205°C (dec) ($NaNO_2$, aq. H_2SO_4, H_3PO_4, 0°; then conc. aq. KI, 8%).[15]

3-Iodo-2-naphthoic acid (5-I) and 8-iodo-1-naphthoic acid (6-I) were prepared from the corresponding 2,3- or 1,8-naphthalic anhydrides by decarboxylation/mercuration ($Hg(OAc)_2$, refl. HOAc, 98 h) to the anhydrohydroxymercurinaphthoic acids, followed by iodination (aq. KI and I_2, 100-110°, 24-48 h),[16] affording 5-I, 50%, mp 212-214°C (Lit.[17] mp 214°C) or 6-I, 50%, mp 162-164°C (Lit.[16b] mp 163.5-164.5°C).[18] Satisfactory NMR spectra and elemental analyses were obtained for compounds 3-I and 4-I.

The reactivites of the newly prepared iodosonaphthoates in CTACl micellar hydrolyses of PNPDPP were evaluated from full rate-constant-[CTACl] profiles for the cleavages of 1 x 10^{-5} M PNPDPP by 1 x 10^{-4} M iodosonaphthoate at various [CTACl] in 0.02 M pH 8 phosphate buffer.[19] We thus obtained k_ψ^{max}, the maximum pseudo-first-order rate constants for the PNPDPP cleavages, as well as the [CTACl] necessary to elicit k_ψ^{max}. The pK_a's of the iodosocarboxylates (1-hydroxyiodoxolones) were determined from discontinuities in their pH-rate constant profiles for cleavages of PNDPP in aqueous CTACl.[19] Correcting each k_ψ^{max} for the concentration and extent of ionization (at pH 8) of each catalyst, yielded estimated values of k_{cat}, the second order rate constant for PNDPP cleavage. Finally, we also determined the apparent catalytic "turnover" rate constant (k_{turn}) by running the micellar PNPDPP cleavage at a 2:1 substrate/catalyst ratio. Values of k_ψ^{max}, [CTACl], k_{cat}, and k_{turn} are collected in Table I, where the reproducibilities of the rate constants are ±4%.

The results in Table I reveal that iodosonaphthoates 3 and 4 are the most reactive iodosocarboxylates yet developed for the micellar cleavage of PNPDPP. They are 4-6 times

Table I. Kinetics of Iodosocarboxylate Cleavages of p-Nitrophenyldiphenyl Phosphate[a]

Catalyst	pK_a[b]	k_ψ^{max}, s^{-1} [c]	10^3[CTACl], M[d]	k_{cat}, $M^{-1}s^{-1}$ [e]	k_{turn}, s^{-1} [f]	Ref.
2	7.78	0.010	3.00	160	----	3
1	7.25[g]	0.064	1.00	759	0.024[h]	1a,b
3	7.70	0.31	0.50	4660	0.10	i
4	7.20	0.36	0.50	4190	0.23	i
5	7.10	0.26	0.50	2950	0.16	i
6	7.51	0.079	0.50	1040	0.027[j]	i
7	7.35	0.34	0.50	4150	0.13	5

[a]Conditions: 0.02 M pH 8.0 phosphate buffer, μ = 0.08 (NaCl), 25±0.5°C, [PNPDPP]=1 x 10^{-5} M, [catalyst] = 1 x 10^{-4} M, 1.0 vol-% DMF, 0.33 vol-% MeCN. The formation of p-nitrophenylate ion was followed at 400 nm. [b]Determined from pH-rate constant profiles for the cleavage of PNPDPP in micellar CTACl; see refs. 1b and 3 for examples. [c]Maximum pseudo-first-order rate constant for PNPDPP cleavage taken from rate constant/[CTACl] profile. [d]Concentration of CTACl at which k_ψ^{max} was observed. [e]$k_{cat} = k_\psi^{max}$/[catalyst], corrected for 100% ionization to IO^-; pK_a values are given in the Table. [f]Pseudo-first-order rate constant for cleavage of 2-fold excess PNPDPP in 1 x 10^{-3} M CTACl; other conditions as in note a. [g]p-Nitrophenyl acetate was the substrate.[1a] [h]5-fold excess PNPDPP, 1 x 10^{-2} M CTACl.[1a] [i]This work. [j][CTACl] = 5 x 10^{-4} M.

more reactive than iodosobenzoate (1) in the phosphorolytic step, and also more reactive in the subsequent turnover step (i.e., hydrolysis of the O-phosphorylated catalyst). Indeed, k_{turn} for 3-5 > 0.1 s^{-1}, which suggests that they would be practical decontaminants for fluorophosphonate nerve agents.[1d]

Relative to 1 or 2 the most likely source of the kinetic superiority of iodosonaphthoates 3-5 is their greater hydrophobicity, which leads to enhanced binding to the CTACl micelles and, consequently, more efficient reaction with the hydrophobic, micelle-bound PNPDPP. In support of this idea, note that k_ψ^{max} increases, and $[CTACl]_{max}$ decreases, with each added aromatic ring in the catalyst sequence: 2, 1, 3 - 5. Thus, the kinetic parameters are all comparable for the iodosocarboxylates that feature 2 aromatic rings, including not only the iodosonaphthoates 3 - 5, but also their structurally distinct relative, 7.

The binding of 1,8-iodosonaphthoate 6 is likely to be equally strong ($[CTACl]_{max}$ = 5 x 10^{-4} M), but k_ψ^{max} is intrinsically lower because the iodinane ring of 6 is 6-membered, rather than 5-membered (as in 3 - 5 or 7). An analogous reactivity decrease associated with expansion of the iodinane ring was previously manifested in the benzo series of catalysts.[20]

Despite the catalytic power of the new iodosonaphthoates, there are, at most, only minor reactivity-enhancing effects of the steric congestion built into the angularly fused

catalysts 3 and 4.[21] These are less than twice as reactive as 5, where the congestion is absent, representing a disappointing experimental sequel to the theoretical analysis presented above. Perhaps a larger or different 8-substituent is required to enforce iodoxolone ring closure, or, possibly, the net gain in negative charge at the oxido oxygen of 3 is insufficient to evoke a major augmentation of the nucleophilic character and reactivity.

Acknowledgments. We are grateful to Drs. T. Emge and S. Ginell for X-ray analysis of 2-iodo-1-naphthoic acid. We thank the U.S. Army Research Office for financial support.

References and Notes

(1) (a) R.A. Moss, K.W. Alwis, and G. Bizzigotti, J. Am. Chem. Soc., 105, 681 (1983). (b) R.A. Moss, K.W. Alwis, and J-S. Shin, ibid., 106, 2651 (1984). (c) R.A. Moss, K.Y. Kim, and S. Swarup, ibid., 108, 788 (1986). (d) P.S. Hammond, J.S. Forster, C.N. Lieske, and H.D. Durst, ibid., 111, 7860 (1989). (e) A.R. Katritzky, B.L. Duell, H.D. Durst, and B.L. Knier, J. Org. Chem., 53, 3972 (1988).

(2) A.R. Katritzky, G.P. Savage, G.J. Palenik, K. Qian, Z. Zhang, and H.D. Durst, J. Chem. Soc. Perkin Trans. 2, 1657 (1990).

(3) R.A. Moss, B. Wilk, K. Krogh-Jespersen, J.T. Blair, and J.D. Westbrook, J. Am. Chem. Soc., 111, 250 (1989).

(4) The calculations were analogous to those described in ref. 3. Effective core potentials and split valence basis sets were utilized on all non-H atoms. Geometries were fully optimized at the Hartree-Fock level (assuming planarity) and the net atomic charges were obtained from a natural orbital population analysis.

(5) R.A. Moss and H. Zhang, Tetrahedron Lett., 33, 4291 (1992).

(6) P. Brougham, M.S. Cooper, D.A. Cummerson, H. Heaney, and N. Thompson, Synthesis, 1015 (1987).

(7) J.G. Sharefkin and H. Saltzman, Anal. Chem., 35, 1428 (1963).

(8) H.J. Lucas, E.R. Kennedy, and M.W. Formo, in "Organic Synthesis," E.C. Horning, Ed., Wiley, New York, 1955, Collect. Vol. 3, p. 483.

(9) R.R. Fracer and S. Savard, Can. J. Chem., 64, 621 (1986).

(10) K.A. Cirigottis, E. Ritchie, and W.C. Taylor, Austral. J. Chem., 27, 2209 (1974).

(11) S. Sarel and M.S. Newman, J. Am. Chem. Soc., 78, 5416 (1956).

(12) The structure of 2-iodo-1-naphthoic acid was verified by an X-ray crystal structure carried out by Drs. T.J. Emge and S. Ginell of this department. Of interest was a 73° twist of the carboxyl group out of the naphthalene plane, indicative of the 8-peri-H/1-carboxyl and 2-iodo/1-carboxyl interactions. Details of the structure will appear in the Ph.D. Dissertation of H. Zhang, Rutgers University, 1993.

(13) W.W. Hartman and L.A. Smith in "Organic Syntheses", A.H. Blatt, Ed., Wiley, New York, 1943, Collect. Vol. 2, p. 438.

(14) M.S. Reddy and C.V. Ratnam, Bull. Chem. Soc. Jpn., 58, 2449 (1985).

(15) H.A.J. Schoutissen, J. Am. Chem. Soc., 55, 4531 (1933).

(16) (a) G.J. Leuck, R.P. Perkins, and F.C. Whitmore, J. Am. Chem. Soc., 51, 1831 (1929). (b) R.J. Bailey, P.J. Card, and H. Shechter, ibid., 105, 6096 (1983).

(17) H. Goldstein and E. Cornamusaz, Helv. Chim. Acta, 14, 200 (1931).

(18) Application of this reaction sequence to 1,2-naphthalic anhydride gave 4-I, identical to the material prepared from 2-methylnaphthalene (see above). We originally considered the naphthalic anhydride product to be 3-I; cf., S. Chatterjee, Ph.D. Dissertation, Rutgers University, 1990.

(19) See references 1b, 3, and 5 for examples.

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

(21) Interestingly, steric congestion between the 8-peri-H and IO^- of 4 does not appear to hinder its reactivity, relative to the isomeric 3.

(Received in USA 8 December 1992)