for purity by TLC and mass spectrometry (samples introduced by direct probe). Mass spectra of ^{18}O- and deuterium-labeled compounds whose preparations are described below were identical with the exception of isotopic mass shifts to those from the unlabeled materials; peaks due to impurities or starting materials were absent.

Uridine-O^2-^{18}O (5). A solution of O^2,5′-anhydrouridine (6)[15] (180 mg) in $H_2{}^{18}O$ (99%) (250 μL) and concentrated HCl (25 μL) was heated at 90 °C for 1.5 h. The reaction mixture was cooled and applied to three 20 × 20 cm preparative TLC plates (2000 μm). The band corresponding to uridine was scraped from the plate and eluted with MeOH until no more UV-absorbing fractions were eluted. The MeOH was evaporated in vacuo. The residue was crystallized from aqueous EtOH (99%) to give 80 mg (40%) of **5**. Mass spectral analysis showed 90% incorporation of ^{18}O (correction for dilution of the $H_2{}^{18}O$ by $H_2{}^{16}O$ of the HCl showed quantitative incorporation of ^{18}O).

5-Iodouridine-O^2-^{18}O (10). A solution of dioxane (9 mL) and 0.5 N HNO_3 (1 mL) containing I_2 (160 mg) and **5** (80 mg) was refluxed for 3 h.[25] The reaction mixture was cooled and applied to a 20 × 20 cm preparative TLC plate. The plate was developed and scraped, and the band corresponding to **10** was eluted with MeOH. After evaporation of the MeOH, the residue was crystallized from EtOH to give 60 mg (50%) of **10**.

O^6,5′-Anhydrouridine-O^2-^{18}O (7). A solution of **10** (60 mg) in dry Me_2SO (10 mL) was added rapidly to a solution of potassium *tert*-butoxide in dry *tert*-butyl alcohol (10 mL) under nitrogen.[5,6] The solution was stirred for 24 h at 70 °C and excess potassium *tert*-butoxide was destroyed with water. The reaction mixture was applied to water-washed Dowex-50 (H^+) (3 mL) and washed with water until no more UV-absorbing fractions were eluted. The eluate was taken to dryness in vacuo and the residue crystallized from EtOH to give 18 mg (46%) of **7**.

5-iodouridine-O^4-^{18}O (11). Prepared like **10** above except that uridine-O^4-^{18}O (90% ^{18}O)[14] (80 mg) was used as starting material, yield 60 mg (50%).

O^6,5′-Anhydrouridine-O^4-^{18}O (3). Prepared like **7** above using **11** (60 mg) as starting material, yield 20 mg (51%).

Uridine-5′-*d* (12). A solution of 2′,3′-*O*-isopropylideneuridine-5′-aldehyde (9)[16] (1.6 g) in EtOH (50 mL) and sodium borodeuteride (99%) was stirred at room temperature for 1 h. The solvent was evaporated in vacuo and the residue extracted with hot acetone (3 × 25 mL). The residue, after evaporation of the acetone under reduced pressure, was covered with aqueous trifluoroacetic acid (10 mL) and stirred at room temperature for 10 min.[18] Trifluoroacetic acid was removed under reduced pressure and the oil residue was triturated with ether until an off-white solid was obtained. After decantation of the ether, the solid was crystallized from EtOH to give 750 mg (54%) of **12** from **9**. Mass spectral analysis showed 95% incorporation of deuterium at the 5′ position.

5-Iodouridine-5′-*d* (13). Prepared like **10** above except **12** (100 mg) was used as starting material, yield 70 mg (51%).

O^6-5′-Anhydrouridine-5′-*d* (8). Prepared like **7** above except **13** (78 mg) was the starting material, yield 24 mg (47%).

Acknowledgments. The authors are indebted to the National Institutes of Health for support of this work (CA 18024, GM 13901). K.H.S. was recipient of an National Institutes of Health Postdoctoral Fellowship (CA 02466).

Registry No.—**3**, 64235-90-1; **5**, 64235-89-8; **6**, 22329-20-0; **7**, 64252-84-2; **8**, 64235-87-6; **9**, 27999-65-1; **10**, 64235-86-5; **11**, 64235-85-4; **12**, 64235-88-7; **13**, 64235-84-3.

References and Notes

(1) (a) University of Utah. (b) Baylor College of Medicine.
(2) M. Ikehara, *Acc. Chem. Res.*, **2**, 47 (1969).
(3) J. J. Fox, *Pure Appl. Chem.*, **18**, 223 (1969).
(4) M. Ikeda, Y. Tamura, and M. Ikehara, *J. Heterocycl. Chem.*, **7**, 1377 (1970).
(5) D. Lipkin and J. A. Rabi, *J. Am. Chem. Soc.*, **93**, 3309 (1971).
(6) S. Tsuboyama and J. A. McCloskey, *J. Org. Chem.*, **37**, 166 (1972).
(7) J. B. Westmore, D. C. K. Lin, K. K. Ogilvie, H. Wayborn and J. Berestiansky, *Org. Mass Spectrom.*, **6**, 1243 (1972).
(8) E. G. Lovett and K. Lipkin, *J. Am. Chem. Soc.*, **95**, 2312 (1973).
(9) D. C. K. Lin, L. Slotin, K. K. Ogilvie, and J. B. Westmore, *J. Org. Chem.*, **38**, 1118 (1973).
(10) M. Ikehara and M. Muraoka, *Chem. Pharm. Bull.*, **24**, 672 (1976).
(11) C. Hignite, in "Biochemical Applications of Mass Spectrometry", G. R. Waller, Ed., Wiley-Interscience, New York, N.Y., 1972, Chapter 16.
(12) J. A. McCloskey, in "Basic Principles in Nucleic Acid Chemistry", Vol. I, P. O. P. Ts'o, Ed., Academic Press, New York, N.Y., 1974, Chapter 3.
(13) S. J. Shaw, D. M. Desiderio, K. Tsuboyama, and J. A. McCloskey, *J. Am. Chem. Soc.*, **92**, 2510 (1970).
(14) G. Puzo, K. H. Schram, and J. A. McCloskey, *Nucleic Acids Res.*, **4**, 2075 (1977).
(15) S. Shibuya, A. Kuninaka, and H. Yoshino, *Chem. Pharm. Bull.*, **22**, 719 (1974).
(16) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5661 (1965).
(17) J. A. Rabi and J. J. Fox, *J. Org. Chem.*, **37**, 3898 (1972).
(18) J. E. Christensen and L. Goodman, *Carbohydr. Res.*, **7**, 510 (1968).
(19) We are grateful to Drs. T. C. Thurber and L. B. Townsend, University of Utah, for a gift of this material.
(20) J. A. McCloskey and K. Biemann, *J. Am. Chem. Soc.*, **84**, 2005 (1962).
(21) J. M. Rice, G. O. Dudek, and M. Barber, *J. Am. Chem. Soc.*, **87**, 4569 (1965).
(22) The structure shown in ref 8 has a mass of 111 amu and is evidently a typographical error. The structure presently shown as h is based on text and related structures in ref 8.
(23) H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965).
(24) M. Barber and R. M. Elliott, 12th Annual Conference on Mass Spectrometry and Allied Topics, Dallas, Texas, June, 1964, p 150.
(25) H. Pischel, A. Holy, G. Wagner, and D. Cech, *Collect. Czech. Chem. Commun.*, **40**, 2689 (1975).

Enhanced Nucleophilic Reactivity (α Effect) in the Reaction of Peroxobenzoate Anions with *p*-Nitrophenyl Acetate[1]

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Received June 13, 1977

Progress in the experimental study of enhanced nucleophilic reactivity (α effect) and the theoretical interpretation of the phenomenon has recently been reviewed by Hudson.[2] Although peroxo anions are recognized as α nucleophiles,[3] few species of this type have been studied,[4,5] probably as a result of the difficulties in preparing the materials, and no systematic investigation of structure–nucleophilic reactivity relationships has been reported. The present work forms part of a study of oxidations by peroxo acids in aqueous solution, relating particularly to hydroperoxidase enzyme systems,[6] in which nucleophilic attack by the peroxo anion may be an important component of the oxidation pathway. We report studies of the nucleophilic reactivity of the peroxobenzoate anion and nine substituted peroxobenzoate anions toward *p*-nitrophenyl acetate, a choice of substrate which permits comparison with a wide range of data in the literature.[4,7]

Experimental Section

Kinetic measurements were made using procedures described in the literature[4] (pseudo-first-order conditions; initial [peroxo acid]/[*p*-nitrophenyl acetate] was >10:1; pH 10 ($NaHCO_3/Na_2CO_3$ buffer); ionic strength 0.1 mol L^{-1} ($NaNO_3$); 25 ± 0.2 °C), recording the release of the *p*-nitrophenolate ion at 402 nm. Peroxobenzoic acid and *m*-chloroperoxobenzoic acid were recrystallized (3:1 v/v, petroleum ether/diethyl ether) to give materials of purity >99%. Other peroxobenzoic acids were ~85% pure, the only significant impurity being the respective parent carboxylic acid. The pK_a values (Table I) were determined by potentiometric titration[8] (25 °C, ionic strength approximately constant at 0.1 mol L^{-1} ($NaNO_3$)). Solutions were checked cerimetrically to ensure that no hydrogen peroxide was present. Calculated second-order rate constants (Table I) were corrected for the "blank rate" in buffer solution alone. EDTA (5×10^{-4} mol L^{-1}) was added in a number of experiments but had no influence on the rate.

Results and Discussion

The nucleophilic reactivity of the meta- and para-substituted peroxobenzoate anions varies systematically with basicity, giving a Brønsted slope of 0.38 (Figure 1, a). The data for *o*-chloroperoxobenzoate falls on the line described by the meta- and para-substituted analogues, whereas *o*-nitro- and

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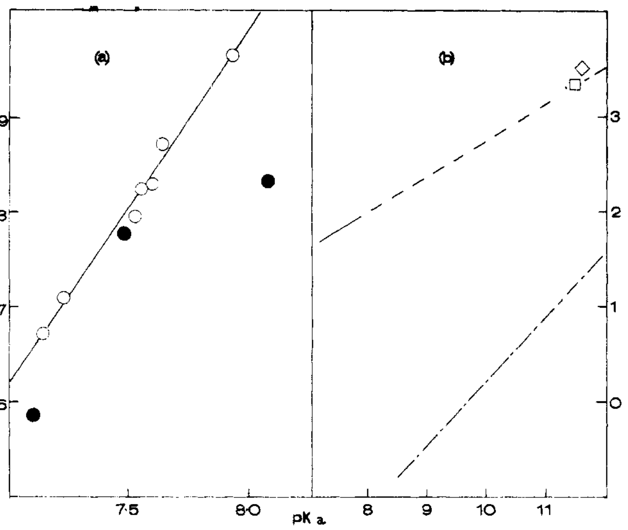

Figure 1. Brønsted-type correlations of log k_2 vs. pK_a for the reaction of oxygen nucleophiles with p-nitrophenyl acetate: (a) ○, meta- and para-substituted peroxobenzoic acids, ●, ortho-substituted peroxobenzoic acids; (b) – – –, data described in this work; - - -, data of ref 6 for phenoxides and alkoxides; ◇, HOO^- (ref 3); □, CH_3OO^- (ref 3).

Table I. Nucleophilic Reactivities of Peroxobenzoate Anions (PBA) toward *p*-Nitrophenyl Acetate[a]

Anion	Registry no.	pK_a[b]	k_2,[c] L mol^{-1} s^{-1}
p-OMe-PBA	64235-66-1	7.93	92.4
PBA	35683-46-6	7.64	74.7
p-Cl-PBA	64235-65-0	7.60	67.9
p-SO_3^--PBA	64235-73-0	7.56	67.1
m-Cl-PBA	64235-64-9	7.53	62.6
m-NO_2-PBA	64235-63-8	7.23	51.5
p-NO_2-PBA	64235-62-7	7.14	47.1
o-CO_2^--PBA	7770-90-3	8.08	68.3
o-Cl-PBA	64235-61-6	7.48	60.0
o-NO_2-PBA	64235-60-5	7.10	38.7

[a] Registry no.: p-nitrophenyl acetate, 830-03-5. [b] Measured at ionic strength 0.1 mol L^{-1} (sodium nitrate as added electrolyte), 25 °C. [c] At 25 °C, ionic strength 0.1 mol L^{-1}, pH 10 ($NaHCO_3$/Na_2CO_3 buffers).

o-carboxyperoxobenzoate, which may exhibit steric effects and pK_a values influenced by intramolecular H bonding, show experimental values below the line. Comparison of the pK_a values of the meta- and para-substituted peroxobenzoic acids with those of their parent benzoic acids gives a Hammett ρ value of 0.67.

The Brønsted correlation may be extrapolated to comprehend the activities of hydroperoxide and methyl hydroperoxide anions (Figure 1, b). Jencks and Gilchrist[7] have shown that, when data for "normal" oxygen anion nucleophiles over a wide range of basicity are considered, the Brønsted plots are nonlinear, the slope varying from 1.0 for nucleophiles which are less basic than the leaving group to a limiting value of about 0.3 for nucleophiles of high basicity. They have classified the reactions into two limiting types on the basis of this behavior. In these terms, the sensitivity to basicity of peroxo anion nucleophiles approaches limiting type I behavior, although normal nucleophiles show a much greater sensitivity in this range of basicity.

A variety of bases for quantitation of the α effect have been employed. In most recent experimental and theoretical work,[2] the comparison is made between an α nucleophile and a normal nucleophile of similar basicity (phenoxides and alkoxides in the case of oxygen anion nucleophiles). As shown in Figure 1 (b), this basis of comparison yields α effects of 10^2–10^3, increasing with decreasing nucleophile basicity in accord with the general decrease in the α effect with increasing pK_a of oxime nucleophiles in alkylation, acylation, and phosphorylation, as noted by Hudson.[2]

References and Notes

(1) We are indebted to Laporte Industries Ltd. for support of this research and to the Science Research Council for a studentship (D.M.D.).
(2) R. F. Hudson, "Chemical Reactivity and Reaction Paths", G. Klopman, Ed., Wiley, New York, N.Y., 1974, pp 167–252.
(3) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).
(4) W. P. Jencks and J. Carriulo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).
(5) E. J. Behrman, J. E. McIsaac, L. R. Subbaraman, J. Subbaraman, and H. A. Malhausen, *J. Org. Chem.*, **37**, 1037 (1972).
(6) P. Jones and D. N. Middlemiss, *Biochem. J.*, **130**, 411 (1972); **143**, 473 (1974); D. M. Davies, P. Jones, and D. Mantle, *ibid.*, **157**, 247 (1976).
(7) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **90**, 2622 (1968).
(8) A. J. Everett and G. J. Minkoff, *Trans. Faraday Soc.*, **49**, 410 (1953).

The Chemistry of Benzyl Hydroperoxide

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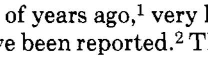
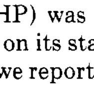
Received July 25, 1977

Although benzyl hydroperoxide (BHP) was synthesized a number of years ago,[1] very little data on its stability in solution have been reported.[2] Therefore, we report here the results of a study of BHP, including its rate of decomposition in an inert solvent and in styrene, the rate of polymerization of styrene initiated by benzyl hydroperoxide, and the chain-transfer constant of BHP in styrene.

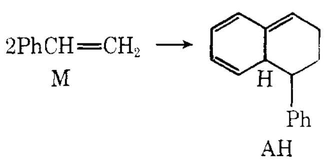


BHP



MCH

Our interest in BHP derives from a study underway in our laboratory of the chemistry of 5-methylene-1,3-cyclohexadiene (MCH). We are studying MCH as a model for the Diels–Alder dimer of styrene, AH, a molecule that is postulated[3] to be responsible for the initiation of the polymerization of styrene by a molecule-assisted homolysis[4] of a C–H bond (eq 1–3).[3b] We have studied the initiation of polymerization



(1)

$$AH + M \longrightarrow A\cdot + HM\cdot \qquad (2)$$

$$A\cdot(HM\cdot) + M \longrightarrow M_n\cdot \qquad (3)$$

of styrene by MCH,[5] and, since benzyl hydroperoxide is a potential impurity in MCH, we found it necessary to measure the dependence of the rate of polymerization of styrene on BHP as well.

We have observed that BHP is formed by air oxidation of MCH at room temperature in $CHCl_3$ solvent. Although we have not studied this process in detail, the mechanism may proceed with an initiation reaction involving MCH and oxygen