

Epoxidation of Alkenes with Bicarbonate-Activated Hydrogen Peroxide

Huirong Yao and David E. Richardson*

Center for Catalysis, Department of Chemistry
University of Florida, Gainesville, Florida 32611-7200

Received November 8, 1999

We describe here the discovery of the bicarbonate-catalyzed epoxidation of alkenes with aqueous hydrogen peroxide at near-neutral pH. For some substrates, the procedure is comparable in apparent synthetic utility to the best methods now available for H₂O₂-based alkene epoxidations that avoid extensive hydrolytic formation of diol (e.g., ligand-accelerated methyltrioxorhenium/H₂O₂¹). The new process features a stable *main group* catalyst/activator of unexpected simplicity (bicarbonate ion) and can be applied readily in water or mixed aqueous solutions under homogeneous conditions.

Hydrogen peroxide is a high oxygen content, environmentally friendly oxidant for which water is the sole byproduct in heterolytic oxidations,² but it is a slow oxidant in the absence of activation³ due to the poor leaving tendency of the hydroxide ion.⁴ Transition metal salts or complexes have been used as catalysts for alkene epoxidations with aqueous H₂O₂.^{5,6} Other methods for activation of H₂O₂ include forming reactive peroxyacids from carboxylic acids,⁷ forming peroxycarboximide acid from acetonitrile (Payne oxidation),⁸ generation of peroxyisourea,⁹ or using sodium perborate or sodium percarbonate (Na₂CO₃·1.5H₂O₂) in strongly basic solution.¹⁰ Such systems can have one or more disadvantages, such as toxic or rapidly decomposed metal catalysts, oxidative decomposition of organic ligands, organic byproducts, or strongly acidic or basic reaction conditions that decompose the desired epoxide product.

A method for activating hydrogen peroxide with bicarbonate ion was described by Drago and co-workers¹¹ and Richardson et al.¹² in their studies of sulfide oxidations in alcohol/water solvents. In the bicarbonate-activated peroxide (BAP) system,¹³ the active

* To whom correspondence should be addressed. Telephone: (352) 392-6736. Fax: (352) 392-3255. E-mail: der@chem.ufl.edu.

(1) (a) Rudolph, J.; Reddy, K. L.; Chiang, J. P.; Sharpless, K. B. *J. Am. Chem. Soc.* **1997**, *119*, 6189. (b) Herrmann, W. A.; Ding, H.; Kratzer, R. M.; Kühn, F. E.; Haider, J. J.; Fischer, R. W. *J. Organomet. Chem.* **1997**, *549*, 319.

(2) Sheldon, R. A. *Top. Curr. Chem.* **1993**, *164*, 21–34.

(3) (a) Strukul, G. *Catalytic Oxidation with Hydrogen Peroxide as Oxidant*; Kluwer: Dordrecht, 1992. (b) Mtochowski, J.; Said, S. B. *Pol. J. Chem.* **1997**, *71*, 149.

(4) Edwards, J. O. In *Peroxide Reaction Mechanisms*; Edwards, J. O., Ed.; Interscience: New York, 1962; pp 67–106.

(5) Jacobson, E. N. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G., Wilkinson, E., Eds.; Pergamon: New York, 1995; Vol. 12, p 1097.

(6) (a) Tetzlaff, H. R.; Espenson, J. H. *Inorg. Chem.* **1999**, *38*, 881. (b) Venturello, C.; Alneri, E.; Ricci, M. *J. Org. Chem.* **1983**, *48*, 3831. (c) De Vos, D. E.; Sels, B. F.; Reynaers, M.; Rao, Y. V. S.; Jacobs, P. A. *Tetrahedron Lett.* **1998**, *39*, 3221.

(7) (a) Swern, D. In *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. 2, p 355. (b) Lewis, S. H. In *Oxidation*; Augustine, R. L., Ed.; Marcel-Dekker: New York, 1969; Vol. 1, p 213.

(8) Payne, G. B.; Deming, P. H.; Williams, P. H. *J. Org. Chem.* **1961**, *26*, 659.

(9) Majetich, G.; Hicks, R. *Synlett* **1996**, 649.

(10) McKillop, A.; Sanderson, W. R. *Tetrahedron* **1995**, *51*, 6145.

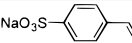
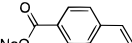

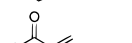
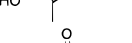
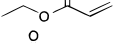
(11) Drago, R. S.; Frank, K. M.; Yang, Y.-C.; Wagner, G. W. *Proceedings of 1997 ERDEC Scientific Conference on Chemical and Biological Defense Research*; ERDEC, 1998.

(12) Richardson, D. E.; Yao, H.; Xu, C.; Drago, R. S.; Frank, K. M.; Wagner, G. W.; Yang, Y.-C. *Proceedings of 1998 ERDEC Scientific Conference on Chemical and Biological Defense Research*; ECBC, 1999.

(13) Richardson, D. E.; Yao, H.; Frank, K. M.; Bennett, D. *J. Am. Chem. Soc.* **2000**, *122*, in press.

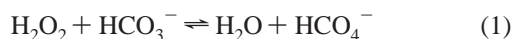
(14) (a) Flanagan, J.; Jones, D. P.; Griffith, W. P.; Skapski, A. C.; West, A. P. *J. Chem. Soc., Chem. Commun.* **1986**, 20–21. (b) Jones, D. P.; Griffith, W. P. *J. Chem. Soc., Dalton Trans.* **1980**, 2526–2532. (c) Adam, A.; Mehta, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1387–1388.

Table 1. Oxidation of Water-Soluble Alkenes by Hydrogen Peroxide in Sodium Bicarbonate (1 M) Solutions in D₂O (25 °C)^a

Substrate	Alkene : H ₂ O ₂ : HCO ₃ ⁻	Time	Conv. (%)	Product(s) (%)
	1 : 1.5 : 10	15 h	>99	epoxide (90) diol (5)
	1 : 3 : 10	4 h	95	epoxide (>99)
	1 : 1.5 : 10	3 h	70	epoxide (>99)
	1 : 6 : 20	24 h	78	epoxide (97)
	1 : 6 : 20	24 h	40	epoxide(70) diol (20)
	1 : 6 : 20	24 h	80	epoxide (45) diol (45)

^a Product analysis by ¹H NMR. All reactions without bicarbonate gave no detectable epoxide products after 24 h. Dibasic ammonium phosphate was employed to maintain similar ionic strength and pH of reaction media in the control reactions.

oxidant peroxymonocarbonate ion, HCO₄⁻, is formed with *t*_{1/2} ≈ 5 min (eq 1), presumably via the perhydration of CO₂



Peroxymonocarbonate is an anionic peracid with structure HOOCO₂⁻.¹⁴ Kinetic and thermodynamic investigations of eq 1 give a value of *E*⁰ (HCO₄⁻/HCO₃⁻). 1.8 V (vs NHE), and HCO₄⁻ is therefore a potent oxidant in aqueous solution. The maximum catalytic efficiency for oxidation of organic sulfides is observed in the pH range from 7 to 9, and the oxidation reactions are accelerated by increasing solvent water content.¹⁵ The reactivity of HCO₄⁻ toward sulfides suggested to us that it may also be useful in the preparation of epoxides in water and mixed solvents, and this was confirmed in the work described below.

The oxidation of water-soluble alkenes was carried out in D₂O in an NMR tube with a stoichiometric excess of H₂O₂ (1.5–6.0 equiv). For example, 1 mL of 0.1 M 4-vinylbenzenesulfonate with 1 M NaHCO₃ was prepared in D₂O, and 30% H₂O₂ was added (final [H₂O₂] = 0.15 M, pH 8). ¹H NMR studies gave a *t*_{1/2} value of 1.5 h for the initial disappearance of alkene, and after 15 h, the starting material was converted to epoxide (90%), diol (5%), and other byproducts (5%). The same procedure was applied to several other water-soluble alkenes (Table 1). In all cases, reactions without added bicarbonate salt are negligible after 24 h under similar conditions (as a control, replacement of NaHCO₃ by (NH₄)₂HPO₄ provided comparable ionic strength and pH). The water-soluble alkenes in Table 1 are mostly terminal alkenes with nearby electron-withdrawing groups. The low electron density of these alkenes usually reduces their nucleophilicity toward electrophilic oxygen of peroxyacids.¹⁶ The last two entries in Table 1 show that under the aqueous conditions of these reactions, readily hydrolyzed epoxides are partially converted to diols. This hydrolysis can be suppressed by using solvents with lower water content.¹⁷




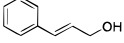
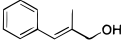


We found that the BAP system can be applied to a variety of homogeneous alkene oxidations (including epoxidation of terminal

(15) Although used in large concentrations, bicarbonate is a catalyst so the oxidations described here are low *E* factor reactions, in contrast to stoichiometric activators where a leaving group becomes a byproduct. See Sheldon, R. A. *J. Chem. Technol. Biotechnol.* **1997**, *68*, 381.

(16) (a) Prat, D.; Lett, R. *Tetrahedron Lett.* **1986**, *27*, 707. (b) Prat, D.; Delpech, B. Lett, R. *Tetrahedron Lett.* **1986**, *27*, 711. (c) Stevens, H. C.; Kamen, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 734.

(17) Conversion rates are lower in mixed organic/aqueous solvents, in part because bicarbonate solubility decreases and less catalyst can be used; however, bicarbonate salts with alkylated ammonium cations can be used to increase catalyst solubility (Yao, H.; Richardson, D. E., work in progress).

Table 2. Epoxidation^a of Alkenes by Hydrogen Peroxide with Ammonium Bicarbonate in CD₃CN/D₂O (3:2, v:v)^b

Substrate	Time	Conv. (%)	Product(s) (%)
	24 h	40	epoxide(>99)
	24 h	50	epoxide(90) diol(10)
	24 h	90	exo epoxide (>95)
	24 h 48 h	35 50	epoxide (>99) ^c epoxide (>99) ^c
	24 h 48 h	20 35	epoxide (>99) ^c epoxide (>99) ^c
	10 h 24 h	35 70	epoxide (80) ^d epoxide (60) ^d
	24 h 48 h	40 50	epoxides (>99) ^e epoxides (>99) ^e

^a Stoichiometry: alkene ~0.05 M, hydrogen peroxide ~0.3 M and ammonium bicarbonate ~0.2 M; 25 °C. ^b All reactions without bicarbonate gave negligible epoxide products after 24 h, except for 3-methyl-2-buten-1-ol (10% conversion to epoxide in 24 h). Dibasic ammonium phosphate was employed in controls to maintain similar ionic strength and pH of reaction media. ^c All allylic epoxides rearranged to form terminal epoxides as the major product. ^d The epoxide was not stable; decomposition products not identified. ^e Mixture of statistically distributed epoxide products.

alkenes, internal alkenes, and allylic alcohols) if a mixed solvent system is used. By using acetonitrile/water (3:2 v:v), epoxidations of hydrophobic alkenes were accomplished with H₂O₂ and NH₄HCO₃ (~0.2 M) at room temperature (Table 2).

Oxidation of styrene was followed in CD₃CN/D₂O (3:2, v:v) by using NMR. Addition of styrene (0.05 M) to a solution of H₂O₂ (0.3 M) and NH₄HCO₃ (0.2 M) yielded styrene oxide (40%) as the only product after 24 h. Because of peroxide disproportionation, excess hydrogen peroxide is needed to give a high yield of epoxide, and the epoxidation reaction was attempted preparatively in CH₃CN/H₂O (3:2, v:v). With 0.19 M NH₄HCO₃, 10 equiv of 30% aqueous H₂O₂ gave styrene oxide in 75% distilled yield.¹⁸ Other unfunctionalized alkenes in Table 2 (α -methylstyrene and norbornene) form epoxide as the major product. The rate of alkene oxidation decreases significantly by replacement of acetonitrile with alcohol, e.g., ethanol or *tert*-butyl alcohol. For example, only trace oxidation products were detected for styrene after heating to 45 °C for 2 days in *d*₆-EtOH/D₂O (3:2, v:v) with H₂O₂ (0.3 M) and NH₄HCO₃ (0.2 M).¹⁹

BAP oxidations of various allylic alcohols were also investigated. Allyl alcohol (0.1 M) and 2-cyclohexen-1-ol (0.1 M) have the least reactive double bonds, and only trace oxidation products are observed for dilute H₂O₂ (0.3 M) with NH₄HCO₃ (0.2 M) in CD₃CN/D₂O after 24 h. Allylic alcohols with more substituted double bonds are epoxidized by the BAP system under similar conditions (Table 2). For all of the allylic alcohols epoxidation is strongly preferred over alcohol oxidation. In the case of geraniol, both allylic and remote alkene are oxidized with comparable rates. A striking feature in the BAP oxidation of these

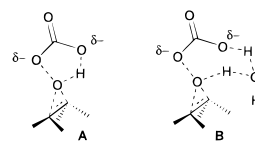
(18) Procedure: 6.30 g of NH₄HCO₃ (79 mmol) and 38 mL of H₂O₂ (30%, 360 mmol) were dissolved in 130 mL water, mixed with 240 mL of acetonitrile, and 4 mL of styrene (35 mmol) was added. The rt reaction was allowed to proceed in the dark without stirring for 24 h. The reaction mixture was diluted with 200 mL of water and extracted with chloroform (5 × 200 mL). The filtrate was washed with water (2 × 40 mL), dried, and concentrated by removal of solvent. Fractional distillation of the crude product gave 3.1 g of styrene oxide (75%).

(19) The observations of solvent dependence in the BAP epoxidations contrast with those for the H₂O₂/dicyclohexylcarbodiimide (DCC) system reported by Majetich and co-workers.⁹ The best solvents for the DCC-activated epoxidation are hydroxylic ones such as methanol, ethanol or 2-propanol (except pure water).

allylic alcohols is that the major products are usually the rearranged epoxides, i.e., terminal epoxides.

It is necessary to distinguish the mechanism of alkene oxidations with the BAP system in CH₃CN/H₂O from that of Payne's procedure⁸ in alcoholic solvent. Payne oxidations employ a slight excess of stoichiometric acetonitrile in alkaline hydrogen peroxide solution to produce a peroxy-carboximidic acid, which oxidizes alkenes. The byproduct acetamide is obtained stoichiometrically from the reaction of peroxy-carboximidic acid with alkene or hydrogen peroxide. In our study, oxidation of 4-vinylbenzene-sulfonate with the BAP system in the presence of a stoichiometric amount of acetonitrile in D₂O was investigated by using ¹H NMR. Over 90% of the alkene was converted to its epoxide product in 24 h, but no acetamide was detected in the ¹H NMR spectrum. In contrast, replacement of NaHCO₃ (pH. 8.4) or NH₄HCO₃ (pH. 8.0) by Na₂CO₃ (pH. 10.5) gave no oxidation products of the alkene after 24 h, but acetamide was formed. We conclude that the role of acetonitrile in the BAP system is to provide for substrate solubility and maintain high solvent polarity, favoring epoxidation by HCO₄⁻.²⁰

The mechanism for HCO₄⁻ epoxidation may be closely related to that for typical peracids, i.e., the generally accepted butterfly transition state,²¹ except that the proton transfer is to a carbonate-leaving group (A) rather than to a carboxylate. Since the BAP reactions here are in aqueous or mixed aqueous solution, the intramolecular proton transfer that reduces charge separation in the transition state could also occur by solvent participation (e.g., B). Further studies on the detailed mechanism are in progress.



Our ¹³C NMR studies on H¹³CO₄⁻ formation from H¹³CO₃⁻ with 2 M H₂O₂ in CH₃CN/H₂O (3:2, v:v) indicate K_{eq} (eq 1) \equiv [HCO₄⁻][H₂O]/[HCO₃⁻][H₂O₂] \approx 35 (25 °C) with a $t_{1/2}$ < 5 min (pH = 7.4). After 20 h, ~50% of H₂O₂ is consumed by decomposition based on the integration ratio of H¹³CO₃⁻ and H¹³CO₄⁻ in the spectrum. Therefore, decomposition of hydrogen peroxide in acetonitrile is relatively slow compared to the formation of HCO₄⁻. Oxidation reactions of alkenes with moderate reactivity can be achieved by forming HCO₄⁻ with a small excess of H₂O₂ despite the accompanying decomposition of H₂O₂ in the presence of CH₃CN as a cosolvent.²² Catalyst lifetime is not a major concern given the low cost and high stability of bicarbonate ion.

We believe BAP oxidations can be useful when a mild, low environmental impact oxidation method is desirable.^{23,24} Some limits to the utility of the method remain to be overcome (e.g., low conversions for less nucleophilic substrates, hydrolysis of sensitive epoxides). Kinetic studies and development of optimal catalysts and synthetic methods for alkenes and other substrates are in progress.

JA993935S

(20) In addition, the same reaction was carried out in mixed CD₃CN/D₂O (1:7, v:v) solvent that was buffered with (NH₄)₂HPO₄ to maintain similar pH and ionic strength compared to a bicarbonate solution, and only 5% of alkene conversion was observed after 24 h. In contrast to the simplicity of the homogeneous BAP procedure, the Payne procedure requires stirring and continuous addition of peroxide and base.

(21) See Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C. *J. Am. Chem. Soc.* **1998**, *120*, 9902–9910 and references therein.

(22) As was found in Payne's study, decomposition of H₂O₂ is significantly accelerated in the higher pH media of CH₃CN/H₂O with added Na₂CO₃, and acetamide byproduct is observed.

(23) Bolm, C.; Beckman, O.; Dabard, O. A. G. *Angew. Chem., Int. Ed.* **1999**, *38*, 907.

(24) Dartt, C. B.; Davis, M. E. *Ind. Eng. Chem. Res.* **1994**, *33*, 2887.