

Carbodiimide-Promoted Olefin Epoxidation with Aqueous Hydrogen Peroxide^{†,‡}

George Majetich,* Rodgers Hicks, Guang-ri Sun, and Patrick McGill

Department of Chemistry, The University of Georgia, Athens, Georgia 30602

Received November 4, 1997

Commercially available carbodiimides in hydroxylic solvents containing hydrogen peroxide with mildly basic or acidic catalysts have been found to promote the epoxidation of olefins. A commercially available 30% aqueous solution of hydrogen peroxide serves as the oxidant for this process. The presumed reactive species is a peroxyisourea generated *in situ* by the addition of hydrogen peroxide to the carbodiimide.

Introduction and Background

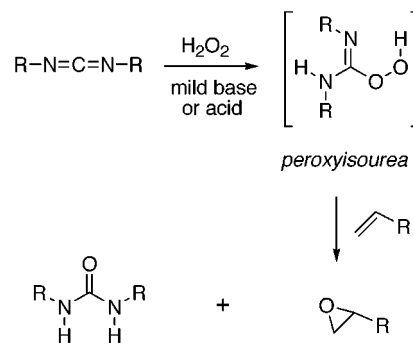
The epoxidation of olefins is one of the most widely studied reactions in organic chemistry.¹ Peroxyacids, the most common epoxidation reagents, are most often prepared by treating the corresponding acid with anhydrous hydrogen peroxide.² Unfortunately, anhydrous hydrogen peroxide is not readily available except as part of a stable complex.³ This, along with the diminishing availability of high quality *m*-CPBA, has stimulated the search for new epoxidizing agents.⁴

A dilute aqueous solution of H₂O₂ is the ideal oxygen source for olefin epoxidation: it is safe, readily available, and generates water as the sole byproduct.⁵ Only a few electron-rich olefins undergo epoxidation with H₂O₂ alone; either the presence of a polarized multiple bond or the addition of a promoter (such as a pertungstate salt⁶ or a metalloporphyrin⁷) is usually necessary. The epoxidation of olefins using H₂O₂ with selenic acids,⁸ hexafluoroacetone,⁹ organosilane derivatives,¹⁰ and alkoxysulfurans¹¹ has been reported. Hydrogen peroxide reacts

with formamide,¹² nitriles (Payne oxidation),¹³ or Vilsmeier reagents¹⁴ to generate oxidants *in situ*.

Since the transfer of an oxygen atom from a molecule of H₂O₂ to an olefin is a dehydration, numerous dehydrating agents have been used in epoxidation systems.^{15–19} In theory, the nucleophilic addition of hydroperoxide anion to the electrophilic carbon of a carbodiimide, a common dehydrating agent, would generate a peroxyisourea that is isoelectronic with a peroxyacid; the transfer of the electrophilic oxygen atom from this reactive intermediate to an olefin would produce an epoxide and a urea byproduct (Scheme 1).

Scheme 1



[†] A patent application [U.S. 08/813039] has been filed for this epoxidation procedure (March 6, 1997).

[‡] Dedicated with appreciation and best wishes to Professors N. L. Allinger and R. K. Hill on the occasion of their 70th birthdays.

(1) Rao, A. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ley, S. V., Eds.; Pergamon: Oxford, 1991; Vol. 7, pp 357–436.

(2) Fieser, M.; Fieser, L. F. *Reagents for Organic Synthesis* Wiley-Interscience: New York, 1967; Vol. 1, p 135.

(3) (a) Heaney, H. *Aldrichimica Acta* 1993, 26, 35. (b) Heaney, H. *Topics Current Chem.* 1993, 164, 1. (c) Cooper, M. S.; Heaney, H.; Newbold, A.; Sanderson, W. *Synlett* 1990, 533 and references therein. (d) Muzart, J. *Synthesis* 1995, 1325. (e) McKillop, A.; Sanderson, W. R. *Tetrahedron* 1995, 51, 6145.

(4) For recent epoxidation procedures, see: (a) Murray, R.; Singh, M.; Williams, B.; Moncrieff, H. *J. Org. Chem.* 1996, 61, 1830. (b) Yang, D.; Yip, Y.; Tang, M.; Wong, M.; Zheng, J.; Cheung, K. *J. Am. Chem. Soc.* 1996, 118, 491. (c) Zhang, W.; Loebach, J.; Wilson, S.; Jacobsen, E. *J. Am. Chem. Soc.* 1990, 112, 2801. (d) Jacobsen, E.; Zhang, W.; Muci, A.; Ecker, J.; Deng, L. *J. Am. Chem. Soc.* 1991, 113, 7063. (e) Zhang, W.; Jacobsen, E. *J. Org. Chem.* 1991, 56, 2296. (f) Sato, K.; Aoki, M.; Oagawa, M.; Hashimoto, T.; Noyori, R. *J. Org. Chem.* 1996, 61, 8310. (g) Sharpless, K. B.; Rudolph, J.; Reddy, K. L.; Chiang, J. P. *J. Am. Chem. Soc.* 1997, 119, 6189. (h) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *Ibid.* 1997, 119, 11224.

(5) Strukul, G., Ed. *Catalytic Oxidation with Hydrogen Peroxide as Oxidant*; Kluwer: Dordrecht, Netherlands, 1992.

(6) (a) Venturello, C.; Abneri, M.; Ricci, M. *J. Org. Chem.* 1983, 48, 3831. (b) Venturello, C.; D'Aloisio, R. *J. Org. Chem.* 1988, 53, 1553.

(7) Reynaud, J.; Battioni, P.; Bartoli, J.; Mansuy, D. *J. Chem. Soc., Chem. Commun.* 1985, 888.

(8) Grieco, P. A.; Yokoyama, Y.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* 1977, 42, 2034.

(9) Heggs, R. P.; Ganem, B. *J. Am. Chem. Soc.* 1979, 101, 2484.

However, previous investigations found that carbodiimides are not effective as epoxidation promoters. Hamilton and co-workers used nearly anhydrous H₂O₂ (98%), acetic acid, and diisopropylcarbodiimide (DIC) in ethyl acetate to epoxidize phenanthrene and pyrene with <3%

(10) (a) Ho, T. L. *Synth. Commun.* 1979, 37. (b) Rebek, J.; McCready, R. *Tetrahedron Lett.* 1979, 4337.

(11) Martin, L. D.; Martin, J. C. *J. Am. Chem. Soc.* 1977, 99, 3511.

(12) Chen, Y.; Reymond, J. *Tetrahedron Lett.* 1995, 36, 4015.

(13) (a) Payne, G.; Deming, P.; Williams, P. *J. Org. Chem.* 1961, 26, 659. (b) Payne, G. *Tetrahedron* 1962, 18, 763.

(14) (a) Dulcere, J.-P.; Rodriguez, J. *Tetrahedron Lett.* 1982, 23, 1887. (b) Rodriguez, J.; Dulcere, J.-P. *J. Org. Chem.* 1991, 56, 469.

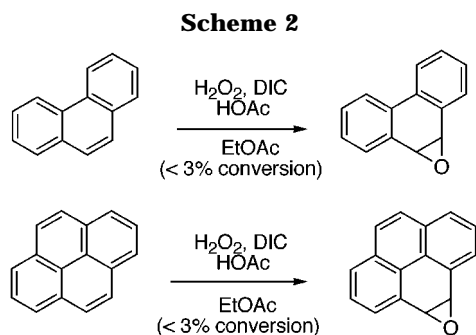
(15) (a) Rebek, J.; McCready, R.; Wolf, S.; Mossman, A. *J. Org. Chem.* 1979, 44, 1485. (b) Rebek, J.; Wolf, S.; Mossman, A. *J. Org. Chem.* 1978, 43, 180.

(16) R. McCready, Ph.D. Dissertation, University of Pittsburgh, 1980.

(17) S. Wolf, Ph.D. Dissertation, University of California, Los Angeles, 1977.

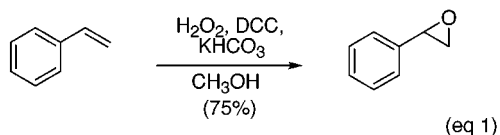
(18) Krishnan, S.; Kuhn, D.; Hamilton, G. *Tetrahedron Lett.* 1977, 1369.

(19) Rebek, J.; Wolf, S.; Mossman, A. *J. Chem. Soc., Chem. Commun.* 1974, 711.

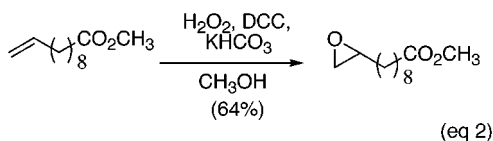


conversion (Scheme 2).¹⁸ Rebek and co-workers reported that the epoxidation of olefins using anhydrous H_2O_2 and a carbodiimide failed.^{19,20} The authors stated that "commercially available dicyclohexylcarbodiimide (DCC) failed to epoxidize cyclododecene in THF containing H_2O_2 even when acidic (HCl or HBF_4) or basic (NaHCO_3) catalysts were present".^{15a}

We discovered that treating styrene with a 10-fold molar excess of 30% aqueous H_2O_2 in methanol and 1 equiv of DCC and KHCO_3 at room temperature produced styrene oxide in 75% yield within 2 h (eq 1).²¹ When the reaction was run without the DCC, epoxidation occurred in 54% yield, although complete reaction required eighteen hours.



To rule out direct epoxidation by H_2O_2 , the less electron-rich substrate methyl 10-undecylenoate was treated under the same conditions used with styrene (eq 2). Although the epoxidation was incomplete even after 24 h, methyl oxirananonanoate was isolated in 64% yield. Repeating this reaction without DCC gave only unreacted olefin after 24 h.



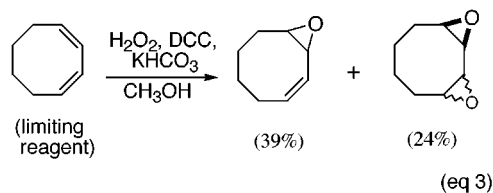
Optimization of The Aqueous H_2O_2 -Carbodiimide Epoxidation Process

Having found conditions that allowed carbodiimides to function as epoxidation promoters, we sought to optimize this new process and establish its scope and limitations. α -Pinene was used as a common substrate for these studies.

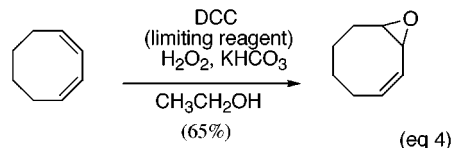
(a) Procedures A and B. Throughout this manuscript procedure A involves the use of 2 mol equiv of DCC and KHCO_3 relative to the olefin (typically 0.10 to 1.00 mmol) and 1 mL of a 30% aqueous solution of H_2O_2 (at least a 5-fold molar excess) in 5 mL of methanol or ethanol. The dicyclohexyl urea (DCU) byproduct is sparingly soluble in simple alcohols, making it easy to remove by filtration. The epoxide is isolated by ethereal workup. Adding sodium bisulfite to destroy the excess

H_2O_2 prior to workup resulted in the rapid decomposition of the epoxide. On the other hand, sodium sulfite, which is less acidic than sodium bisulfite, consumed any remaining H_2O_2 without causing problems. Nevertheless, this neutralization step is unnecessary for most oxidations. In a few cases the polarity of the epoxide and the unreacted DCC are similar, which makes chromatographic separation tedious. Instead, stirring an ethereal solution of the crude reaction mixture with 5% aqueous acetic acid for 20 min completely hydrolyzed any unreacted DCC without compromising the oxidation yield.

1,3-Cyclooctadiene was used to test the suitability of procedure A for the selective epoxidation of conjugated double bonds. Using these conditions, the mono- and bis-epoxides shown in eq 3 were isolated in 39% and 24% yield, respectively. To suppress the formation of the bis-



epoxide, 5 equiv of the diene relative to the carbodiimide were used. This ratio, referred to here as procedure B, produced the mono-epoxide in 65% yield as the only product (eq 4). This alternative procedure, wherein the carbodiimide is the limiting reagent, is preferred over procedure A for the epoxidation of alkenes that are inexpensive relative to the cost of the carbodiimide or for the monoepoxidation of conjugated dienes.



Other weak inorganic bases such as sodium bicarbonate, sodium carbonate, sodium phosphate (mono- or di- or tribasic), or their potassium equivalents can be substituted for potassium bicarbonate in procedures A or B without any loss of efficiency. Although epoxidation proceeds using only 0.1 mol equiv of the weak inorganic base versus carbodiimide, the rate and yield of the reaction are greatly improved if stoichiometric amounts of base and carbodiimide are used. Strong organic bases such as sodium ethoxide react with the nascent epoxide, thereby destroying it. Triethylamine, a weak organic base, does not promote epoxidation, because the amine undergoes rapid oxidation. In contrast, pyridine is an effective catalyst.

(b) Solvent Studies. Several reaction media were compared using procedure A and α -pinene. In general, the solvent system was chosen to dissolve, or at least partially dissolve, the reactant olefin and not to react with the carbodiimide, the H_2O_2 , or the product. While simple alcohols such as methanol or ethanol are the preferred solvents, 2-propanol or 1-butanol were also acceptable. Epoxidation occurred in aromatic alcohols, such as benzyl alcohol or phenol, but the lower volatility and lower water solubility of these alcohols made the isolation of the product difficult.

The choice of reaction solvent was always a compromise between the requisite protic character and the

(20) Rebek, J.; Wolf, S.; Mossman, A. Abstracts of the 172nd National Meeting of the American Chemical Society, ORGN 109, 1976.

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

Table 1. The Epoxidation of α -Pinene with Procedure A in Different Solvent Systems

solvent	reaction time	% yield epoxide
2-propanol	24 h	40%
1-butanol	24 h	40%
C ₆ H ₅ CH ₂ OH/CH ₃ OH(1:1)	2 days	none
C ₆ H ₅ OH/CH ₃ OH(1:1)	2 days	20%
acetone	24 h	trace
DMF	24 h	trace
1,4-dioxane	24 h	trace
THF	4 days	trace
CH ₃ OH/EtOAc (1:1)	24 h	trace
CH ₃ CH ₂ OH/anhydrous H ₂ O ₂	48 h	28%
CH ₃ OH/H ₂ O (1:1)	24 h	35%

lipophilic character needed for substrate solubility. This led us to examine the feasibility of using water-miscible cosolvents for the oxidation. Unfortunately, the epoxidations of α -pinene in acetone, DMF, 1,4-dioxane, and THF were all unsatisfactory (Table 1).

Since carbodiimide-promoted olefin epoxidations require solvents having a hydroxyl group, we were curious whether the presence of water is essential for epoxidation. To answer this question an anhydrous ethereal solution of H₂O₂ was prepared²² and combined with absolute ethanol to give an anhydrous ethanolic solution 2.5 M in H₂O₂.²³ The epoxidation of α -pinene occurred in 28% yield using this solution as both the solvent and the H₂O₂ source. Comparing this result with the 68% yield obtained for this reaction in wet methanol and the 83% yield obtained in wet ethanol using procedure B, indicates that while water is not essential for epoxidation, its presence does increase the yield.

Solubility problems are often encountered when the water exceeds 50 volume % of the solvent. This was first observed when α -pinene was epoxidized in a 1:1 mixture of methanol and water (supplemented by the water contributed by the 30% aqueous H₂O₂). Under these conditions, the reaction mixture formed two immiscible phases and the yield decreased significantly. In light of this observation, the best solvent system should be homogeneous.

(c) Procedure C. The use of sodium phosphate to facilitate the addition of the hydroperoxide anion to the carbodiimide permitted the efficient epoxidation of α -pinene in a 1:1 mixture of methanol and ethyl acetate; no epoxidation was observed using this solvent system with KHCO₃. This result was unexpected since the tribasic phosphate initially formed an insoluble complex upon addition of aqueous H₂O₂. Nevertheless, after stirring the reaction mixture for 12 h at room temperature, workup afforded an 83% yield of epoxide. Further studies established that while acetone, 1,4-dioxane, and THF were useful cosolvents for this oxidation, no oxidation was observed when DMF was used. Moreover, sodium phosphate (mono- or dibasic), sodium carbonate, potassium phosphate, or potassium carbonate were acceptable catalysts. This modification of procedure A is designated as procedure C.

(d) Choice of the Carbodiimide. The waxy solid DCC is a potent allergen that crumbles and scatters easily during handling, making inadvertent skin contact

likely. These considerations prompted us to substitute diisopropylcarbodiimide (DIC), an easily handled liquid that is less allergenic than DCC, or ethyl(3-(dimethylamino)propyl)carbodiimide (EDC), a water-soluble carbodiimide, in the epoxidation. Both DIC and EDC were as effective dehydrating agents as DCC. However, DIC is easier to work with which makes it the carbodiimide of choice for large-scale epoxidations.

The epoxidation of oleic acid and vinylacetic acid, two water-soluble substrates, was attempted using the water-soluble carbodiimide EDC and water as the solvent. In both cases an insoluble gummy material formed, and workup of these reactions provided only the unreacted alkenes.

(e) Procedures D and E. Seeking an acid-catalyzed procedure to complement the base-initiated epoxidations, several acids were examined. Strong acids gave poor results. For example, using *p*-TsOH, the DCC-based epoxidation of 1-dodecene gave 1,2-epoxydodecane in 19% yield, while HCl (introduced as a 0.12 M solution in methanol) gave only a 7% conversion. Ion-exchange resins, such as Amberlite IR-120, also afforded low yields of 1,2-epoxydodecane (16%). We discovered that Amberlite IRC-50, a polymer-bound sulfonic acid, was a practical catalyst for this process. The use of 2 mol equiv of DCC relative to the olefin (typically 0.10 to 1.00 mmol) and 1 mL of a 30% aqueous solution of H₂O₂ in 5 mL of methanol and 10 mg of IRC-50 beads is called procedure D. A second set of acid-catalyzed conditions was established in which the carbodiimide is the limiting reagent and the alkene is in excess (procedure E). As one would expect, strongly acidic ion-exchange resins promote both epoxidation and the consumption of the oxidized product.

Transition metal and lanthanide-based Lewis acids were unsuitable as catalysts because they accelerated the decomposition of H₂O₂ instead of its addition to the carbodiimide. Other Lewis acids, such as triethylaluminum, zinc bromide, cerium chloride, and boron trifluoride etherate were also unsuitable as catalysts because they facilitated the rapid conversion of DCC to DCU.

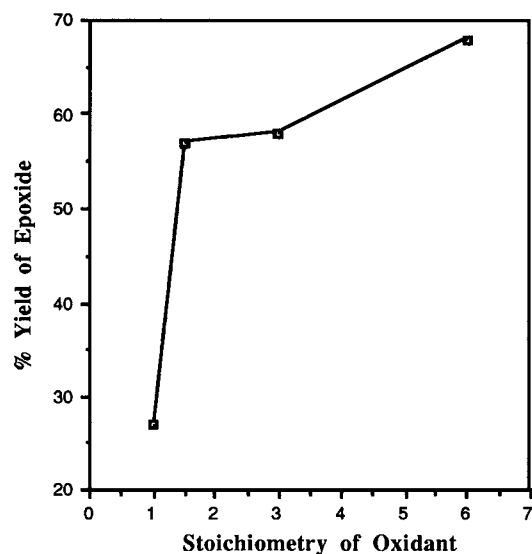
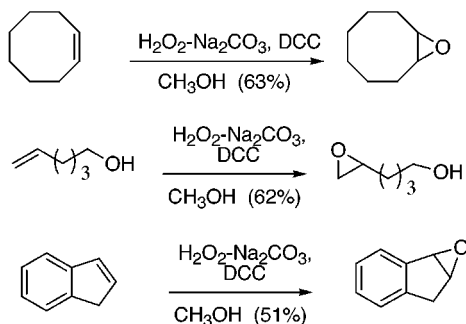
(f) Stoichiometry of the Oxidant. More than a 5-fold excess of H₂O₂ (relative to the limiting reagent) was used routinely throughout these studies. The epoxidation of α -pinene was carried out under conditions A at four different oxidant stoichiometries to determine the minimum amount of oxidant required. While an excess of H₂O₂ is clearly needed, the yield of epoxide only slightly improved when more than 3 equiv of H₂O₂ were used (cf. Chart 1). Even a 3% aqueous solution of H₂O₂ was effective as the source of oxidant—provided that at least 2 equiv of H₂O₂ were used and that the longer reaction times required were acceptable.

(g) Alternate H₂O₂ Sources. Stable adducts of H₂O₂, such as sodium percarbonate [2Na₂CO₃·3H₂O]₂,^{3d,e} readily release H₂O₂ when exposed to water and can result in a violent exothermic reaction when used in the presence of an oxidizable substrate. We speculated that the decomposition of the adduct would be slower in methanol, thereby permitting it to serve as both the source of oxidant and as the base for the carbodiimide-promoted epoxidation process.²⁴ This conjecture proved to be valid as summarized in Scheme 3.

(22) Hudlicky, M. *Oxidations in Organic Chemistry*; ACS Monograph 186; American Chemical Society: Washington, DC, 1990; p 7. To prevent the accumulation of peroxides these solutions were prepared fresh for each use.

(23) (a) Kingzett, C. *J. Chem. Soc.* **1980**, 37, 792. (b) Schimpf, H. A *Manual of Volumetric Analysis*, Wiley: New York, 1909, p 214.

(24) Sodium percarbonate in acetic acid is not useful for epoxidations, see: Ohta, A.; Ohta, M. *Synthesis* **1985**, 216.

Chart 1. Epoxide Yield versus Stoichiometry of H₂O₂**Scheme 3**

(h) Effect of Heating Using Procedure A. The epoxidation of α -pinene in a 1:1 mixture of methanol and ethyl acetate was sluggish at room temperature; refluxing this reaction mixture for 3 h produced α -pinene epoxide in 71% yield. Unfortunately, this result is misleading because α -pinene epoxide is stable under these conditions. Further work showed that heating the reaction mixtures of more reactive epoxides gave low yields. Control experiments verified that the decomposition of the peroxyisourea to DCU and the rate of epoxide consumption by either the solvent (methanol) or the alkoxide are accelerated at higher temperatures. When styrene was reacted using procedure A under reflux only 2-methoxy-2-phenylethanol and 2-methoxy-1-phenylethanol were isolated. Thus, while some carbodiimide-promoted epoxidations may benefit from heating, in general it should be avoided.

(i) Procedures F and G. Standard *m*-CPBA and Payne oxidations are included for comparative purposes as procedures F and G, respectively. The seven sets of experimental conditions are summarized in Table 2.

Results

A variety of unactivated olefins (internal or terminal, acyclic or cyclic) were epoxidized using the five optimized H₂O₂-carbodiimide procedures (Tables 3, 4, and 5). Scrutiny of Table 3 reveals four trends: (1) olefins having at least two alkyl substituents give good yields of the epoxides; (2) tri- and tetrasubstituted allylic alcohols give

comparable yields under all the conditions employed; (3) monosubstituted olefins typically epoxidize in lower yield with both the H₂O₂-carbodiimide procedure and the Payne system than with the more robust oxidant *m*-CPBA; and (4) steric congestion near the double bond retards epoxidation with the carbodiimide-promoted procedures.

Tables 4 and 5 summarize the epoxidation of three rigid bicyclic alkenes and four conformationally flexible olefins, respectively. The carbodiimide-promoted epoxidations and the Payne oxidation display similar selectivity, and both processes were as facially selective as *m*-CPBA. Limonene, which has two double bonds with different degrees of substitution, gave a 1:1 mixture of isomeric epoxides **14a** and **14b** and trace amounts of the bis-epoxide with the Payne system, whereas the carbodiimide-promoted process displayed a modest preference for the oxidation of the trisubstituted endocyclic olefin (a 3:2 mixture of **14a** and **14b** and <2% of the bis-epoxide).

We have found that carbodiimide-promoted olefin epoxidations represent a practical way to prepare acid- and heat-sensitive epoxides. β -Pinene oxide or indene oxide are too acid-sensitive to be prepared by *m*-CPBA, but are easily prepared by using the H₂O₂-carbodiimide procedures (cf. substrates **8** and **10**, Tables 3 and 4, respectively).

The preparative capabilities of this protocol were also explored. In large-scale reactions rapidly mixing the reagents together was exothermic; hence, the slow addition of H₂O₂ with efficient cooling was required. Cyclooctene oxide and allylbenzene oxide were synthesized on a 20-g scale in 58% and 61% yield, respectively, using procedure A. The use of procedure B achieved the large-scale preparation of cyclooctene oxide and β -pinene oxide in 57% and 60% yield, respectively.

A neighboring group, or Henbest,²⁵ directing effect is possible when a coordinating group is present, as in the epoxidation of allylic alcohols. Thus five allylic or homoallylic alcohols were treated with H₂O₂ and DCC to look for a Henbest directing effect. These results, along with those obtained by using either Payne oxidation or metal-catalyzed epoxidation,²⁶ are presented in Table 6. For each substrate, each of the H₂O₂-carbodiimide procedures gave the same product distribution. The most pronounced directing effect was observed with the homoallylic alcohol terpinen-4-ol (**16**), which gave the syn epoxide independent of the choice of oxidant.²⁷ In contrast, the oxidation of homoallylic alcohol **18** gave a chromatographically inseparable mixture of **18a** and **18b**, with only a modest preference for the face with the hydroxyl group.²⁸ Significant Henbest directing effects were observed in the epoxidation of allylic alcohols **19** and **20**.

We foresaw that the epoxidation of α,β -unsaturated enones using base-catalyzed procedures would involve nucleophilic addition of a hydroperoxide anion²⁹ instead of the involvement of the peroxyisourea intermediate.

(25) Henbest, H.; Wilson, R. *J. Chem. Soc.* **1957**, 1958.

(26) (a) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, *101*, 159. (b) Finn, M.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J., Ed.; Academic Press: New York, 1985, Vol. 5, pp 247–308.

(27) Mitchell, P. *Org. Prep. Proceed. Int.* **1990**, *22*(4), 534.

(28) Barrelle, M.; Apparu, M. *Bull. Soc. Chim. Fr.* **1972**, 2016.

(29) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Reading, MA, **1972** and references therein.

Table 2. Standard Conditions for Epoxidations

method	olefin equiv	dehydrating agent (equiv)	oxygen source	promoting agent (equiv)	reaction time
A	1	DCC (2)	H ₂ O ₂	KHCO ₃ (2)	14–24 h
B	5	DCC (1)	H ₂ O ₂	KHCO ₃ (2)	24 h to 72 h
C	1	DCC (2)	H ₂ O ₂	Na ₃ PO ₄ ·12H ₂ O (2)	24 h
D	1	DCC (2)	H ₂ O ₂	catalytic Amberlite IRC-50	24 h
E	5	DCC (2)	H ₂ O ₂	catalytic Amberlite IRC-50	24 h
F	1	none	<i>m</i> -CPBA	none	30 min to 12 h
G	1	C ₆ H ₅ CN (1.5)	H ₂ O ₂	KHCO ₃ (1)	48 h

Indeed, cyclohexenone was completely converted to the corresponding epoxy ketone in only 20 min under procedure A without consumption of the DCC; under acidic conditions C, epoxidation of cyclohexenone was not observed.

Table 3. Epoxidation of a Variety of Olefins












Substrate	Yields Under Conditions						
	A	B	C	D	E	F	G
	74%	89%	85%	70%	72%	75%	47%
	65%	68%	64%	57%	60%	68%	67%
	67%	70%	77%	63%	65%	70%	64%
	59%	61%	39%	42%	54%	84%	41%
	40%	28%	52%	27%	32%	91%	36%
	75%	80%	75%	73%	39%	88%	68%
	48%	36%	0%	14%	19%	59%	15%
	69%	59%	47%	73%	98%	0%	42%

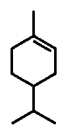
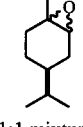
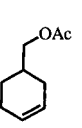
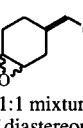
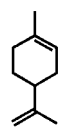
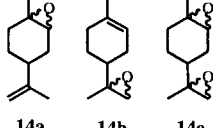
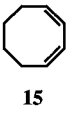
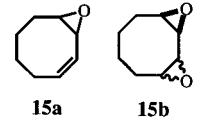
Table 4. Epoxidation of Bridged Bicyclic Olefins

Substrate	Yields Under Standard Conditions						
	A	B	C	D	E	F	G
	68%	83%	30%	73%	68%	74%	33%
	91%	60%	49%	48%	65%	0%	27%
	64%	61%	50%	68%	57%	79%	48%

Ketones can undergo acid-catalyzed Baeyer–Villiger oxidation with peroxyacids to generate esters, an undesired side-reaction in the epoxidation of nonconjugated enones. While control experiments showed that the peroxyisourea did not react with ketones, we found that treatment of 2-allylcyclohexanone or 2-prenylcyclohexanone for 48 h with H₂O₂ and DCC under either basic or acidic conditions produced complex mixtures. These results contrast with the selectivity possible using a peroxycarboximide intermediate (Payne oxidation) or a peracid.

Although the carbodiimide-based process takes place under rather mild conditions, limitations do exist. For example, the reaction of homoallylic alcohol **22** with procedure A gave a complex mixture of products (Figure 1). However, if the hydroxyl group was protected (cf. acetate **13**, Table 5), an epoxide could be isolated. Allylic alcohols **23** and **24** also gave unknown products with the H₂O₂-carbodiimide procedure.

Table 5. Epoxidation of Conformationally Flexible Cyclic Olefins

Substrate	Products	Percent Yield Under Standard Conditions	
	 1:1 mixture of diastereomers	A: 83 B: 61 C: 74 D: 38 E: 44 F: 73 G: 63	
	 1:1 mixture of diastereomers	A: 62 B: 68 C: 86 D: 29 E: 62 F: 75 G: 52	
	 1:1 mixture of diastereomers	A: 35 a & b B: 85 a & b C: 39 a & b D: 49 a & b E: 75 a & b F: 75 a & b G: 70 a & b	10 c 2 c 0 c 15 c 1 c 11 c 16 c
		A: 39 a B: 65 a C: 45 a D: 18 a E: 12 a F: 80 a G: 46 a	24 b 0 b 14 b 17 b 0 b 0 b 13 b

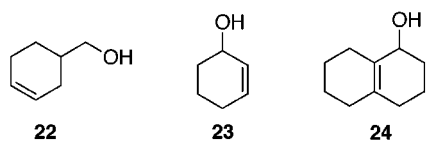
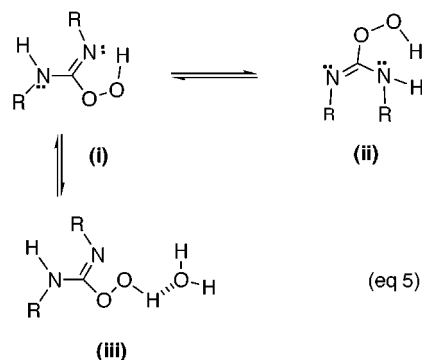


Figure 1.

Discussion and Mechanistic Considerations

Hydroxylic solvents permitted epoxidation, whereas no oxidation was observed in aprotic solvents or under anhydrous conditions. Thus, hydrogen bonding must stabilize both the peroxyisourea intermediate and the transition state leading to its formation. The decline in yield observed when too much water is present in the reaction medium can be attributed to the lower solubilities of DCC and the reactant olefin in the medium: too much water would also affect the solvation of the peroxyisourea. We believe that an equilibrium exists between two intramolecularly associated forms of the peroxyisourea which lead to epoxidation (cf. **i** and **ii**, eq 5) and an open, solvated form (cf. **iii**) whereby the electrophilic oxygen atom is shielded. This solvation prevents this conformer from reacting with the olefin and leads to the unwanted consumption of the peroxyisourea. This equilibrium is highly influenced by the composition of the solvent. Once the concentration of water in the reaction media exceeds 50%, the equilibrium favors the open form of the peroxyisourea (cf. **iii**).



A similar, albeit less dramatic, rate reduction is observed for peroxyacid epoxidations in solvents that can function as Lewis bases.³⁰ For example, the rate constant for the epoxidation of cyclohexene with *m*-CPBA at 20 °C drops from $2.25 \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ in dichloromethane^{30a} to $2.5 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ in *tert*-butyl alcohol.^{30b}

Presumably, oleic and vinylacetic acids fail to react in water, despite the use of water-soluble carbodiimides, because the hydrocarbon chains of these substrates cluster together to form micelles, leaving the alkene moiety inaccessible for oxidation.

The structure of the intramolecular hydrogen-bonded peroxyisourea reagent dictates that this reactive intermediate cannot exhibit a steric preference (cf. Figure 2). The cyclic nature of this form of the peroxyisourea orients the alkyl substituent attached to the imine nitrogen away from the electrophilic oxygen atom. To avoid eclipsing the C–O and C=N bonds, the remaining alkyl group attached to the amide nitrogen is directed out of the plane of the hydrogen-bonded chelate. Thus, both alkyl substituents are poorly situated to interact sterically with an olefin approaching the electrophilic oxygen. Similar arguments hold for oxidations using peroxyacids and peroxycarboximidic acids. Thus, when facial specificity is observed, as with the bridged bicyclic olefins **9**, **10**, and **11** (Table 4), it is due to the steric interactions between the olefin and the electrophilic oxygen atoms of the reagents rather than the steric influences of their substituents.

Table 6. Henbest Directing Effect Studies

Substrate	Products	Reagent ^a and Chemical Yield	% Cis Epoxide
		A (80%) B (74%)	100 100
		A (68%) B (65%)	75 ^b 75 ^b
	 	A (50%) B (52%) C (76%)	60 60 100
	 	A (76%) B (76%) C (75%)	>99 >99 100
	 	A (54%) B (66%) C (23%)	88 89 43

^a A: peroxyisourea; B: Peroxycarboximidic acid;
C: Vanadium Complex

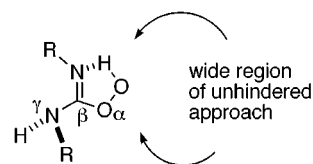


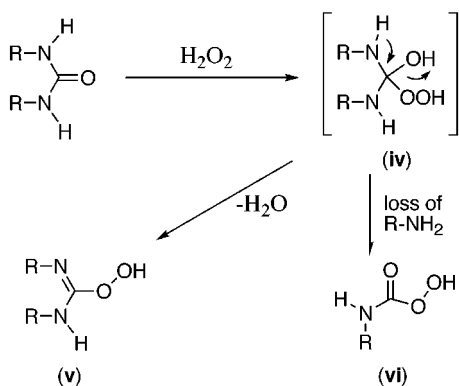
Figure 2.

A basic premise throughout this study is that the oxidant is a peroxyisourea. While this is a reasonable assumption to make, we have been unable to verify its formation experimentally. This prompted us to evaluate the possibility of other oxidizing species.

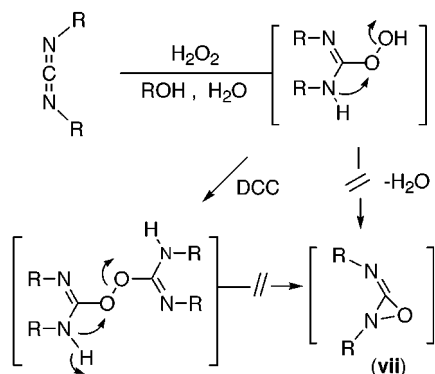
Only two alternative oxidants can be postulated for the base-promoted epoxidations. First, hydroperoxide ion can add to the carbonyl group of the dicyclohexyl urea, which becomes part of the reaction mixture once either epoxidation or singlet oxygen generation begins.¹⁷ This adduct (**iv**) can form either a peroxyisourea (**v**) or a

(30) (a) Paquette, L.; Barrett, J. *Org. Synth.* **1969**, *49*, 62. (b) Renolen, P.; Ugelstad, J. *J. Chim. Phys.* **1960**, *57*, 634. (c) Curci, R.; DiPrete, R.; Edwards, J.; Modena, G. *J. Org. Chem.* **1970**, *35*, 740. (d) Kavcic, R.; Plesnicar, B. *J. Org. Chem.* **1970**, *35*, 2033.

Scheme 4

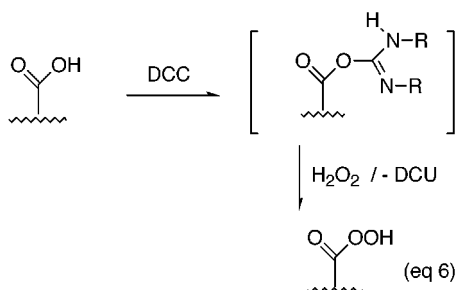


Scheme 5

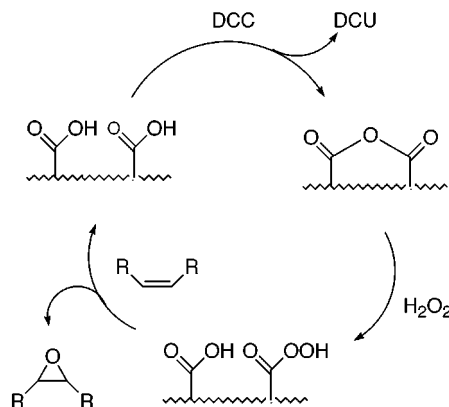


peroxyacid (**vi**) as shown in Scheme 4; either of which could act as the oxygen transfer agent. To test this, α -pinene was treated using procedure A with DCU as the dehydrating agent instead of DCC. Only a trace of α -pinene oxide was detected after 48 h. This result is not surprising since the carbonyl of a urea is less electrophilic than that of formamide. Alternatively, the formation of an azaoxirane (**vii**) can be postulated via the pathways shown in Scheme 5. This oxidant can be discounted because such a highly strained species could not survive in the protic reaction medium and because the byproduct of the epoxidation would be a carbodiimide, not the urea observed.

The acid-catalyzed procedures C and D require a weakly acidic ion-exchange resin to assist the nucleophilic addition of H_2O_2 to the carbodiimide. If a peroxyisourea is not involved in these oxidations, then the catalyst itself must play an active role. Toward this end we can speculate that a resin-bound oxidant is involved. More specifically, if the DCC reacts first with the polymer-bound carboxylic acid units, and then with the H_2O_2 present, a peroxyacid would be produced (eq 6). Alternatively, adjacent carboxylic acid moieties can be dehydrated by the DCC to form a polymer-bound anhydride³¹



Scheme 6



which can then react with H_2O_2 (Scheme 6). The transfer of the electrophilic oxygen from the peroxyacid to an olefin would achieve epoxidation and make both processes catalytic.

Table 7. Epoxidation of **25**

reagent	solvent	promoting agent	% axial attack
polymer-bound peroxyacid	CH_3OH	none	68
H_2O_2 -DCC (procedure A)	CH_3OH	KHCO_3	29
H_2O_2 -DCC (procedure B)	$\text{CH}_3\text{CH}_2\text{OH}$	KHCO_3	32
H_2O_2 -DCC (procedure C)	THF/EtOAc	Na_3PO_4	27
H_2O_2 -DCC (procedure D)	CH_3OH	IRC-50	28
H_2O_2 -DCC (procedure E)	$\text{CH}_3\text{CH}_2\text{OH}$	IRC-50	32
<i>m</i> -CPBA (procedure F)	CH_2Cl_2	KHCO_3	71
<i>m</i> -CPBA	CH_3OH	none	78
H_2O_2 -benzonitrile (procedure G)	CH_3OH	KHCO_3	30

A series of experiments were carried out to test if resin-bound peroxyacids were actually involved in the epoxidation. 1-*tert*-Butyl-4-methylenecyclohexane (**25**) is an useful substrate for testing the selectivity of peroxyisoureas and peroxyacids because it gives widely varying ratios of O-axial and O-equatorial epoxides depending on the oxidant used.³² When olefin **25** was treated with the polymer-bound peroxyacid (produced by treating IRC-50 with methanesulfonic acid and H_2O_2 ³³) in methanol, the percent of axial attack was consistent with that produced by peroxyacids in methanol. In contrast, the product distributions obtained with the five H_2O_2 -carbodiimide procedures are similar to those obtained using an H_2O_2 -benzonitrile system (Table 7). These observations argue against a polymer-bound peroxyacid as the oxidizing species and dictate the involvement of a common intermediate in both the acid and base-catalyzed H_2O_2 -carbodiimide epoxidations. Given all of these considerations, the oxygen transfer agent is most likely a peroxyisourea.

Summary

We have developed a practical method for the epoxidation of olefins that uses solutions of 30% aqueous H_2O_2 as the oxidant. The best solvent system consists of a

(31) For the preparation of polymer-bound anhydrides, see: Scott, L.; Rebek, J.; Oysyanko, L.; Sims, C. *J. Am. Chem. Soc.* **1974**, *96*, 1606.

(32) (a) Carlson, R.; Behn, N. *J. Org. Chem.* **1967**, *32*, 1363. (b) Vedejs, E.; Dent, W.; Kendall, J.; Oliver, P. *J. Am. Chem. Soc.* **1996**, *118*, 3556.

single phase with a simple alcohol and less than 50 volume percent of water. The yields of epoxide obtained with this method are comparable to those produced by the Payne oxidation and are only slightly lower than those available by using high quality *m*-CPBA. Finally, we postulate that the most likely reactive species is a peroxyisourea.

Experimental Section

General. All reactions were carried out on a 0.10 to 1.00 mmol scale under an atmosphere of nitrogen and monitored by TLC analysis until the starting material was completely consumed. Unless otherwise indicated, ethereal workup consisted of the following procedure: the reaction was quenched at room temperature with saturated aqueous ammonium chloride. The organic solvent was removed under reduced pressure on a rotary evaporator, and the residue was taken up in ether, washed with brine and dried over anhydrous MgSO_4 . Filtration, followed by concentration at reduced pressure on a rotary evaporator and at 1 Torr to a constant weight, afforded a crude residue which was purified by flash chromatography using NM silica gel 60 (230–400 mesh ASTM) and distilled reagent grade solvents. Microanalysis was performed by Atlantic Microlab, Inc., Atlanta, GA. ^1H NMR spectra were obtained in CDCl_3 and were calibrated using trace CHCl_3 present (δ 7.26) as an internal reference.

1-Cyclohexene-1-methanol (**2**), 2-methyl-1-cyclohexene-1-methanol (**3**), and 3-cyclohexene-1-methanol (cf. **13**) were obtained from stocks maintained in our inventory. Other olefinic substrates were obtained from commercial sources. The A.C.S. reagent grade H_2O_2 used was obtained from J. T. Baker as a 30% w/v aqueous solution, signifying that 100 mL of solution contains 30 g of H_2O_2 . Since commercial 30% aqueous solutions of H_2O_2 lose oxygen over time, even recently purchased bottles of this reagent may contain varying amounts of oxidants. Because of this, the H_2O_2 concentration of each bottle was determined via titration.²³

Complete chromatographic separation of unreacted DCC from epoxides containing no other polar functional groups is often tedious. Except in cases of extremely acid-sensitive products such as β -pinene oxide, the remaining DCC can be hydrolyzed by stirring an ethereal solution of the crude epoxide with 5% aqueous acetic acid for 20 min. The ethereal phase is then washed with sat. NaHCO_3 , dried over anhydrous MgSO_4 , and concentrated. Complete chromatographic separation of the epoxide from DCU is straightforward.

On occasion, sufficient solid sodium sulfite was added in small portions to neutralize (based on iodide starch paper) any excess H_2O_2 prior to standard ethereal workup.

The authors have provided Chemical Abstracts Service (CAS) registry numbers for known reaction products. Spectral data are provided for new compounds. The following abbreviations are used throughout this section: hexanes (H) and diethyl ether (E).

This section has been organized as follows: (a) General Epoxidation Procedures; (b) Epoxidation of Various Substrates; and (c) Large-scale Epoxidations. In addition to these experimentals, detailed experimental descriptions of the various carbodiimide-based epoxidations we discussed within the text can be found in the Supporting Information section of this article.

(a) General Epoxidation Procedures. Procedure A: Epoxidation with Excess DCC. Solid KHCO_3 (2.00 mol equiv relative to the olefin) was suspended in a solution of the olefin (100 mg) and DCC (2.00 mol equiv relative to the olefin) in 5 mL of methanol. Hydrogen peroxide (1 mL of a 30% solution, 8.80 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. During workup, the solids were removed by filtration and the filtrate was subjected to ethereal workup.

Procedure B: Epoxidation with a Limited Quantity of DCC. Solid KHCO_3 (73 mg, 0.73 mmol) was suspended in a solution of the olefin (5.00 mol equiv relative to DCC) and DCC (150 mg, 0.73 mmol) in 5 mL of ethanol. Hydrogen peroxide (1 mL of a 30% solution, 8.80 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. During the workup, the solids were removed by filtration, and the filtrate was subjected to ethereal workup.

Procedure C: Epoxidation with Sodium Phosphate in Methanol/Ethyl Acetate. Solid $\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O}$ (2.00 mol equiv relative to the olefin) was suspended in a solution of the olefin (100 mg) and DCC (2.00 mol equiv relative to the olefin) in 2.5 mL of methanol and 2.5 mL of ethyl acetate. Hydrogen peroxide (1 mL of a 30% solution, 8.80 mmol) was added, and the reaction mixture was stirred at room temperature for 24 h. During workup, the solids were removed by filtration, and the filtrate was subjected to ethereal workup.

Procedure D: Acid-Catalyzed Epoxidation with Excess DCC. Amberlite IRC-50 (10 mg) was suspended in a solution of the olefin (100 mg) and DCC (2.00 mol equiv relative to the olefin) in 5 mL of methanol. Hydrogen peroxide (1 mL of a 30% solution, 8.80 mmol) was added, and the mixture was stirred at room temperature for 24 h. During the workup, the solids were removed by filtration, and the filtrate was subjected to ethereal workup.

Procedure E: Acid-Catalyzed Epoxidation with a Limited Quantity of DCC. Amberlite IRC-50 (10 mg) was suspended in a solution of the olefin (5.00 mol equiv relative to DCC) and DCC (150 mg, 0.73 mmol) in 5 mL of ethanol. Hydrogen peroxide (1 mL of a 30% solution, 8.80 mmol) was added, and the mixture was stirred at room temperature for 24 h. During the workup, the solids were removed by filtration, and the filtrate was subjected to ethereal workup.

Procedure F: Epoxidation with *m*-CPBA. To a 0 °C solution of 100 mg of the olefin in CH_2Cl_2 was added a solution of *m*-CPBA (1.30 mol equiv relative to the olefin) in CH_2Cl_2 . The mixture was slowly warmed to room temperature, stirred, and monitored by TLC analysis prior to ethereal workup.

Procedure G: A Payne Epoxidation. Solid KHCO_3 (1.00 mol equiv relative to the olefin) was suspended in a solution of the olefin (100 mg) and benzonitrile (1.50 mol equiv relative to the olefin) in 1 mL of methanol. Hydrogen peroxide (a 30% solution, 1.5 mol equiv relative to the olefin) was added, and the mixture was stirred at room temperature for 48 h. The solvent was removed at reduced pressure, and the resulting residue was purified by chromatography.

(b) Epoxidation of Substrates: Epoxidation of Methylenecyclohexene (1). Methylenecyclohexene (100 mg, 1.04 mmol) was converted to 6-oxaspiro[2.5]octane [75934-94-0] in 74% yield using procedure A, in 89% yield using procedure B, in 85% using procedure C, in 70% yield using procedure D, in 72% yield using procedure E, in 75% yield using procedure F, and in 47% yield using procedure G.

Epoxidation of 1-Cyclohexenylmethanol (2). 1-Cyclohexenylmethanol (100 mg, 0.89 mmol) was converted to 7-oxabicyclo[4.1.0]heptane-1-methanol [17550-61-7] in 65% yield using procedure A, in 68% yield using procedure B, in 64% using procedure C, in 57% yield using procedure D, in 60% yield using procedure E, in 68% yield using procedure F, and in 67% yield using procedure G.

Epoxidation of (2-Methylcyclohex-1-enyl)methanol (3). (2-Methylcyclohex-1-enyl)methanol (100 mg, 0.79 mmol) was converted to 2,3-oxa-3-methylbicyclo[4.1.0]heptane-1-methanol in 67% yield using procedure A, in 70% yield using procedure B, in 77% using procedure C, in 63% yield using procedure D, in 65% yield using procedure E, in 70% yield using procedure F, and in 64% yield using procedure G. This epoxide has the following spectral data/physical properties: ^1H NMR (250 MHz) 1.15–1.59 (m, 4 H), 1.38 (s, 3 H), 1.61–2.00 (m, 4 H), 3.60–3.79 (m, 2 H); ^{13}C (62.7 MHz) 64.8 (t), 64.5 (s), 62.8 (s), 31.7 (t), 26.6 (t), 20.7 (t), 20.1 (t), 19.9 (q) ppm; IR (film) 3400 br., 2934, 1434, 1031, 833 cm^{-1} . Anal. for $\text{C}_8\text{H}_{14}\text{O}_2$. Calcd: C, 67.56%; H, 9.93%. Found: C, 67.75%; H, 9.68%.

Epoxidation of Prop-2-enylbenzene (4). Prop-2-enylbenzene (100 mg, 1.69 mmol) was converted to phenylmethy-

(33) Harrison, C.; Hodge, P. *J. Chem. Soc., Perkin Trans. 1* **1976**, 605.

loxirane [4436-24-1] in 59% yield using procedure A, in 61% yield using procedure B, in 39% using procedure C, in 42% yield using procedure D, in 54% yield using procedure E, in 84% yield using procedure F, and in 41% yield using procedure G.

Epoxidation of 1-Dodecene (5). 1-Dodecene (100 mg, 0.59 mmol) was converted to 1,2-dodecylloxirane [2855-19-8] in 40% yield using procedure A, in 28% yield using procedure B, in 52% using procedure C, in 27% yield using procedure D, in 32% yield using procedure E, in 91% yield using procedure F, and in 36% yield using procedure G.

Epoxidation of Styrene (6). Styrene (100 mg, 0.96 mmol) was converted to styrene oxide [96-09-03] in 75% yield using procedure A (cf. initial observations), in 80% yield using procedure B, in 75% using procedure C, in 73% yield using procedure D, in 39% yield using procedure E, in 88% yield using procedure F, and in 68% yield using general procedure G.

Epoxidation of (*E*)-2,2-Dimethylhept-3-ene (7). (*E*)-2,2-Dimethylhept-3-ene (100 mg, 0.79 mmol) was converted to (*E*)-3,4-oxa-2,2-dimethylheptane in 48% yield using procedure A, in 36% yield using procedure B, in 0% using procedure C, in 14% yield using procedure D, in 19% yield using procedure E, in 59% yield using procedure F, and in 15% yield using procedure G. This epoxide has the following spectral data/physical properties: $^1\text{H NMR}$ (250 MHz) 0.91 (s, 9 H), 0.96 (t, 3 H, $J = 7.1$ Hz), 1.33–1.65 (m, 4 H), 2.46 (d, 1 H, $J = 2.4$ Hz), 2.75–2.85 (m, 1H); ^{13}C (62.7 MHz) 66.9 (d), 55.3 (d), 34.3 (t), 30.6 (s), 25.8 (q), 19.4 (t), 13.9 (q) ppm; IR (film) 2958, 1363, 909 cm^{-1} . Anal. for $\text{C}_9\text{H}_{18}\text{O}$. Calcd: C, 75.98%; H, 12.76%. Found: C, 75.85%; H, 12.71%.

Epoxidation of Indene (8). Indene (100 mg, 0.86 mmol) was converted to indene oxide in 69% yield using procedure A, in 59% yield using procedure B, in 47% using procedure C, in 73% yield using procedure D, in 98% yield using procedure E, in 0% yield using procedure F, and in 42% yield using procedure G.

Epoxidation of α -Pinene (9). α -Pinene (100 mg, 0.73 mmol) was converted to α -pinene oxide [1686-14-2] in 68% yield using procedure A, in 83% yield using procedure B, in 30% using procedure C, in 73% yield using procedure D, in 68% yield using procedure E, in 74% yield using procedure F, and in 33% yield using procedure G.

Epoxidation of β -Pinene (10). β -Pinene (100 mg, 0.73 mmol) was converted to β -pinene oxide [6931-54-01] in 91% yield using procedure A, in 60% yield using procedure B, in 49% using procedure C, in 48% yield using procedure D, in 65% yield using procedure E, in 0% yield using procedure F, and in 27% yield using procedure G.

Epoxidation of Bicyclo[2.2.1]hept-2-ene (11). Olefin 11 (100 mg, 1.06 mmol) was converted to 3-oxatricyclo[3.2.1.0^{2,4}]-octane [278-74-0] in 64% yield using procedure A, in 61% yield using procedure B, in 50% using procedure C, in 68% yield using procedure D, in 57% yield using procedure E, in 79% yield using procedure F, and in 48% yield using procedure G.

Epoxidation of 1-Methyl-4-isopropylcyclohexene (12). Olefin 12 (100 mg, 0.72 mmol) was converted to 1-methyl-4-(1-methylethyl)-7-oxabicyclo[4.1.0]heptane [3626-19-5] as a 1:1 mixture of diastereomers in 83% yield using procedure A, in 61% yield using procedure B, in 74% using procedure C, in 38% yield using procedure D, in 44% yield using procedure E, in 73% yield using procedure F, and in 63% yield using procedure G.

Epoxidation of Cyclohexene-4-carbinol Acetate (13). Olefin 13 (100 mg, 0.65 mmol) was converted to 7-oxabicyclo[4.1.0]heptane-3-methanol acetate in 62% yield as a 1:1 mixture of diastereomers, (1 α , 3 α , 6 α) [81370-41-4] and (1 α , 3 β , 6 α) [81370-42-5], using procedure A, in 68% yield using procedure B, in a 86% yield using procedure C, in 29% yield using procedure D, in 62% yield using procedure E, in 75% yield using procedure F, and in 52% yield using procedure G.

Epoxidation of Limonene (14). Using procedure A limonene (100 mg, 0.73 mmol) was converted to an inseparable mixture (1:1) of 1-methyl-4-(1-methylethenyl)-7-oxabicyclo[4.1.0]heptane (**14a**) [1195-92-2] and 2-methyl-2-(4-methyl-3-

cyclohexen-1-yl)oxirane [31684-93-2] (**14b**) in 35% yield. A 10% yield of 1-methyl-4-(2-methoxiranyl)oxabicyclo[4.1.0]heptane (**14c**) [96-08-2] was also isolated. An inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 85% yield using procedure B. A 2% yield of bis-epoxide **14c** was also isolated. Using procedure C an inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 39% yield. Using procedure D an inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 49% yield. A 15% yield of bis-epoxide **14c** was also isolated. Using procedure E an inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 85% yield. A 1% yield of bis-epoxide **14c** was also isolated. Using procedure F an inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 75% yield. An 11% yield of bis-epoxide **14c** was also isolated. Using procedure G an inseparable mixture (1:1) of epoxides **14a** and **14b** was obtained in 70% yield. A 16% yield of bis-epoxide **14c** was also isolated.

Epoxidation of 1,3-Cyclooctadiene (15). 1,3-Cyclooctadiene (100 mg, 0.92 mmol) was converted to 9-oxabicyclo[6.1.0]non-2-ene (**15a**) [6690-12-6] in 39% yield and 3,10-dioxatricyclo[7.1.0.0^{2,4}]decane-(1 α , 2 α , 4 α , 9 α) (**15b**) [97373-34-7] in 24% yield. 1,3-Cyclooctadiene gave only epoxide **15a** in 65% yield using procedure B. In contrast, procedure C produced a 45% yield of epoxide **15a** and a 14% yield of **15b**. Using procedure D, diene **15** produced a 18% yield of monoepoxide **15a** and a 17% yield of bis-epoxide **15b**. 1,3-Cyclooctadiene gave only epoxide **15a** in 12% yield using procedure E and in 80% yield using procedure F. Using procedure G, diene **15** produced a 46% yield of monoepoxide **15a** and a 13% yield of bis-epoxide **15b**.

(c) Large-Scale Epoxidations: Epoxidation of Cyclooctene with Procedure A. Solid NaHCO_3 (30.00 g, 0.36 mol) was suspended in a solution of cyclooctene (20.00 g, 0.18 mol) and DCC (73.00 g, 0.36 mol) in 420 mL of methanol. Hydrogen peroxide (150 mL of a 30% solution, 1.32 mol) was added dropwise over a 1-h period. An ice–water bath was used to keep the reaction temperature below 25 °C. The mixture was stirred at room temperature for an additional 48 h. The solids were removed by filtration, and the filtrate was partitioned between ether and water. Standard ethereal workup, followed by distillation (bp 54–56°/5 mm), gave 13.1 g (58%) of cyclooctene oxide (9-oxabicyclo[6.1.0]nonane) [286-62-4].

Epoxidation of Prop-2-enylbenzene with Procedure A. Solid Na_2CO_3 (36.00 g, 0.34 mol) was suspended in a solution of prop-2-enylbenzene (20.00 g, 0.17 mol), and DCC (70.00 g, 0.34 mole) in 500 mL of ethanol. Hydrogen peroxide (160 mL of a 30% solution, 1.40 mol) was added dropwise over a 1-h period. An ice–water bath was used to keep the reaction temperature below 25 °C. The mixture was stirred at room temperature for an additional 48 h. The solids were removed by filtration, and the filtrate was partitioned between ether and water. Standard ethereal workup, followed by vacuum distillation (58–65 °C/1 mm), gave 14.2 g (61%) of epoxide [4436-24-1].

Epoxidation of Cyclohexene with Procedure B. Solid KHCO_3 (19.40 g, 194 mmol) was suspended in a solution of cyclohexene (65.60 g, 0.79 mol) and DIC (20.00 g, 159 mmol) in 400 mL of ethanol. Hydrogen peroxide (100 mL of a 30% solution, 0.88 mol) was added dropwise over a 3-h period. An ice–water bath was used to keep the reaction temperature below 25 °C. The mixture was stirred at room temperature for an additional 18 h. Approximately two-thirds of the solvent was carefully removed at room temperature in vacuo. Solids were removed by filtration, and the filtrate was partitioned between ether and water. Standard ethereal workup, followed by vacuum distillation, gave 8.90 g (57%) of cyclooctene oxide.

Epoxidation of (–)- β -Pinene with Procedure B. Solid KHCO_3 (19.4 g, 194 mmol) was suspended in a solution of (–)-

β -pinene (66.10 g, 480 mmol) and DCC (20.00 g, 96.9 mmol) in 300 mL of ethanol. Hydrogen peroxide (100 mL of a 30% solution, 0.88 mol) was added dropwise over a 6-h period. An ice-water bath was used to keep the reaction temperature below 25 °C. The mixture was stirred at room temperature for an additional 18 h. Approximately two-thirds of the solvent was carefully removed at room temperature on a rotary evaporator. Solids were removed by filtration, and the filtrate was partitioned between ether and water. Standard ethereal

workup, followed by vacuum distillation (bp 98–100°/27 mm), gave 8.85 g (60%) of (–)- β -pinene oxide.

Supporting Information Available: Experimental details (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO972026N