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A NEW PARADIGM FOR ALKENE EPOXIDATION

ACTIVATION OF HYDROGEN PEROXIDE BY ORGANOPHOSPHORUS ELECTROPHILES

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Abstract: Diphenylphosphinic anhydride and certain other organophosphorus electrophiles mediate the high-yield conversion of alkenes to epoxides by hydrogen peroxide in buffered aqueous tetrahydrofuran.

The direct epoxidation of simple alkenes by hydrogen peroxide requires that the latter be "activated". Such activation by acylation produces the well-known peracids; similar activation by isocyanates,[1] orthoesters,[2] carbonyldiimidazole[3] or hexafluoroacetone[4] have been described. To our knowledge, activation of H_2O_2 into a generally useful epoxidizing agent by organophosphorus reagents has not been reported.[5]

We now describe the in situ activation of 50% H_2O_2 in buffered aqueous tetrahydrofuran (final solvent ratio ca. 3 : 1 THF/H_2O) by stoichiometric amounts of organophosphorus anhydrides and halides, leading to the efficient epoxidation of a variety of alkenes. For example, diphenylphosphinic anhydride (**1**), readly prepared on a large scale from methyl diphenylphosphonate and α,α-dichlorotoluene,[6] smoothly mediates the conversion by H_2O_2 of the alkenes listed in Table 1 to the indicated epoxides in good to excellent yields; a representative procedure is given in the footnote.[7] Except for the less reactive terminal alkene of entry 9, these conversions are complete in 12 to 20 hours at -5° C using 1 equiv. of H_2O_2 and 1.5 equiv. of anhydride **1** in THF containing 3 equiv. of K_2CO_3. The identities of all isolated epoxide products were confirmed by comparison of reported NMR data or by independent synthesis.

The stereochemical comparison represented by entries 2 and 3 indicates that these reactions are syn stereoselective and presumably concerted. It thus differs from the radical mechanism proposed for the wholly nonstereoselective, low-yield epoxidations of the trans and cis-stilbenes by superoxide ion and $Ph_2P(O)Cl$ reported by Kim.[8] Entry 7 in Table 1 indicates a high degree of cis-stereoselection with respect to the allylic hydroxyl, possibly by Henbest-type[9] hydrogen bonding of the putative hydroperoxyphosphinic acid intermediate to the neighboring OH group, as depicted in the following scheme:

Scheme : cis selective epoxidation

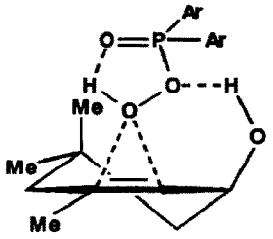
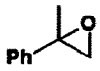
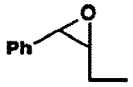
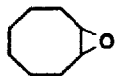
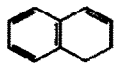
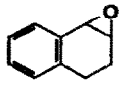
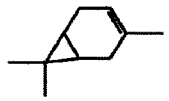
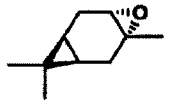
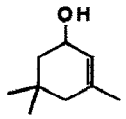
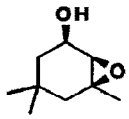
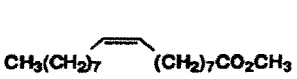
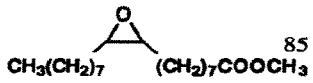
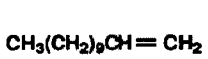


Table 1 : $Ph_2P(O)O(O)PPh_2$ (**1**) + Alkene $\xrightarrow{H_2O_2}$ Epoxide

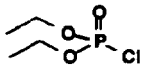
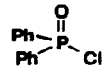
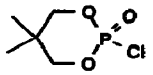
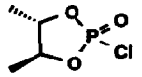
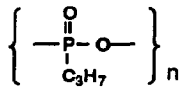
Entry	Alkene	product	Yield (%) [a]
1			87
2			93
3			90
4			88
5			100
6			80
7			81
8			85
9			60[b]

a) Purifed product (Kugelrohr or silica gel purification)

b) Based on NMR analysis of the crude material, after 48 h of reaction

We find that certain cyclic and acyclic phosphoryl halides, as well as propanephosphonic anhydride,[10] may also be used to mediate these epoxidations (Table 2). On the other hand, $Ph_2P(O)Cl$ and $PhP(O)Cl_2$ were unsuitable under these conditions; control experiments showed that H_2O_2 alone or in the presence of $Ph_2P(O)OH$ were likewise ineffective.

Table 2 : Epoxidations reactions of 1,2-dihydronaphthalene in the presence of RR'P(O)X, 50% aq. H_2O_2, K_2CO_3, THF.

Entry	RR'P(O)X[a]	(eq)	H_2O_2 (eq)	T °C	Time (h)	% of conversion[b]
1		(3)	(1.1)	-10	20	93
2		(1.5)	(1)	-10	20	25
3		(1.5)	(1)	-5	20	100
4		(1.5)	(3)	-5	2	94
5	 (racemic)	(1.5)	(1.5)	-35	4	91
6		(3)	(3)	-5	20	88

a) The phosphorus compounds of entries 4 and 5 were prepared according to known procedures.[11]

b) Determined by GC analysis.

Although details of mechanism and transition state structure are not yet established, we suggest that initial formation of a hydroperoxyphosphorus species may occur in these reactions, followed by a highly-ordered, concerted transition state for syn-addition of the terminal oxygen to the alkene π-bond.

This hypothesis leads to the intriguing possibility that use of such activators chiral at the phosphorus atom may permit the enantioselective delivery of the peroxide oxygen to an isolated alkene substrate. Experiments with chiral phosphorus activators are in progress to test this concept.[12]

References and Notes

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7. A typical procedure follows : To 1.5 ml of tetrahydrofuran are successively added with stirring 1,2-dihydronaphthalene (78 mg, 0.60 mmol.), diphenylphosphinic anhydride (376 mg, 0.90 mmol), anhydrous K_2CO_3 powder (248 mg, 1.79 mmol.). The stirred mixture is cooled at -5° C and 0.41 ml (0.61 mmol.) of a 50 % aqueous solution of hydrogen peroxide is added.The reaction mixture is stirred 20 hours at -5° C, then diluted with 40 ml of ether, the solution washed three times with saturated $NaHCO_3$, with distilled water then brine. The organic layer is dried over anhydrous $MgSO_4$, the solvent evaporated at reduced pressure, and the residue purified by Kugelrohr distillation at 1 mm to give 87.5 mg (99.7 %) of pure epoxide .

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