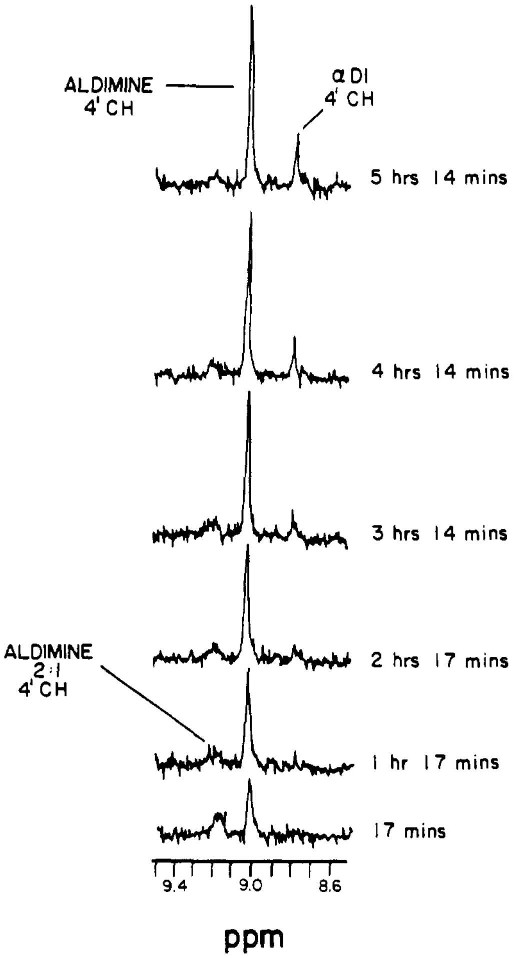

Figure 1. Growth of the 4′-CH proton resonances of αDI and the 1:1 and 1:2 Al(III):aldimine chelates in 0.1 M D_2O solution containing a 1:1:1 molar ratio of pyridoxal:alanine:Al(III) at pD 5.0 and 10.0 °C.

of the Al(III) aldimine complex.

Because the reverse transamination reaction is much more rapid, measurements of the reaction between pyridoxamine and pyruvate at about pD 5 in D_2O were made at 0 °C. Figure 2 shows the variation of integrated intensities of 4′-CH protons with time, indicating that formation of the same αDI Al(III) chelate occurs more rapidly initially than does formation of the aldimine. The concentration of the intermediate increases to its maximum value in about 2h and then decreases and levels off, while the concentration of the aldimine–Al(III) chelate continues to build.

In this transamination system (pyridoxal–alanine and pyridoxamine–pyruvic acid) the aldimine is much more stable than the ketimine, and the reaction system reaches an equilibrium consisting primarily of aldimine, regardless of which pair of compounds is used as the initial reactants. Thus it is seen that the changes of concentration of αDI in the course of achieving transamination, the relative rates of αDI and aldimine formation, and the fact that the same compound is formed in the forward and reverse reactions provide compelling evidence that αDI is the intermediate for both the forward (PL + ALA) and reverse (PM + PY) transamination reactions. The buildup of αDI concentration initially in advance of the increasing concentrations of aldimine, in the reaction between pyridoxamine and pyruvate, and the subsequent decrease in concentration to a lower value show it to be a mandatory intermediate for the transamination process leading from ketimine to aldimine.

A unique characteristic of the system described is the fact that the deprotonated intermediate is formed in concentrations that are high enough to be measured by NMR. This phenomenon is considered to be due mainly to the ability of the highly charged Al(III) ion to stabilize the adjacent negative charge of the carbanion intermediate. In the absence of metal ions, the proton coordinated to the azomethine nitrogen of the aldimine or the ketimine may serve a similar function. In such cases, however, the single positive charge of the proton would produce much less coulombic stabilization of the α-deprotonated form, with the result that it would be present at concentrations much lower than are detectable by proton NMR under the reaction conditions employed. The α- (or α′-) deprotonated species formed from either the aldimine (or the ketimine) is therefore suggested as the common intermediate for transamination, and for related reactions such as α- and α′-proton exchange, racemization, and elimination of electronegative substituents at the β position of the amino acid moiety. It has been pointed out that a carbanion[5] of the type represented by **4**, which is indicated here as being formed by α- and α′-proton dissociation, may also be formed by C–C bond dissociation, thus functioning as the intermediate in α-decarboxylation and dealdolation reactions.

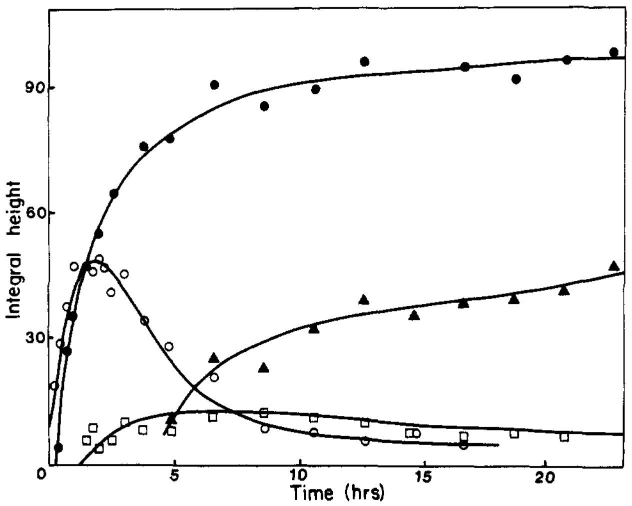

Figure 2. Integral height of 4-CH proton NMR resonances of a 1:1:1 molar ratio of pyridoxamine:pyruvate:Al(III) vs. time (t = 0 °C, pD 5.0, 0.10 M components): (●) 1:1 aldimine complex; (▲) 2:1 aldimine complex; (○) 1:1 αDI complex; (□) 2:1 αDI complex.

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Role of Peroxo vs. Alkylperoxo Titanium Porphyrin Complexes in the Epoxidation of Olefins

Sir:

We have recently reported on the stereoelective epoxidation of olefins with alkyl hydroperoxides catalyzed by molybdenum porphyrins[1] and proposed that the active species is a *cis*-hydroxy(alkylperoxo)(porphyrinato)molybdenum(IV) complex,[2] reminiscent of the intermediate suggested by Sheldon[3-5]

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(1) Ledon, H. J.; Durbut, P.; Varescon, F. *J. Am. Chem. Soc.* **1981**, *103*, 3601-3603.

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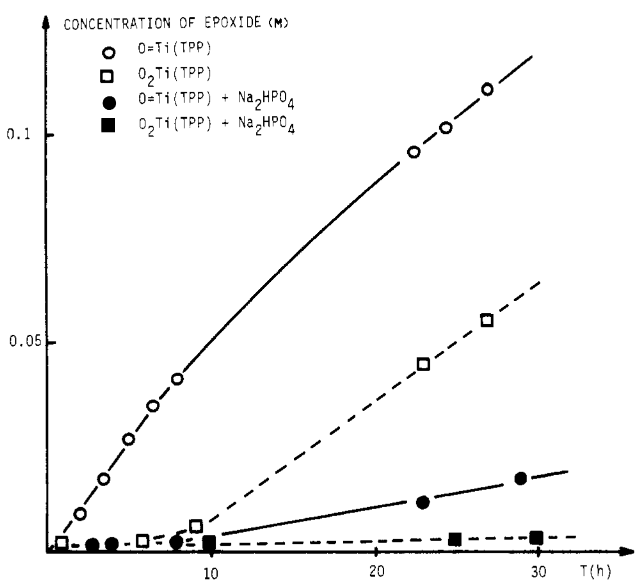


Figure 1. Rate of cyclohexene epoxidation by *t*-BuOOH in the presence of titanium tetraphenylporphyrins. [O=Ti(TPP)] or [O_2Ti(TPP)] = 1.83 mM; [*t*-BuOOH] = 0.28 M and [cyclohexene] = 2.46 M in benzene at 70 °C.

and Sharpless.[6] Without any direct evidence for such a compound, it seemed nevertheless reasonable to predict that if the mechanism we have proposed was correct, any oxometalloporphyrin complex should be an epoxidation catalyst, provided that the metal is a rather good Lewis acid and not too strong an oxidant.[4] Here we present the use of the well-characterized oxo(tetraphenylporphyrinato)titanium(IV), O=Ti(TPP) (**1**),[7] as catalyst for the epoxidation of olefins with alkyl hydroperoxides.

A solution of cyclohexene (30 mmol) in anhydrous oxygen-free benzene (8 mL) was heated at 70 °C under argon, in the presence of *tert*-butyl hydroperoxide (3.3 mmol) and O=Ti(TPP) (22 μmol). The concentration of cyclohexene oxide was monitored by GC using *n*-decane as internal standard. As shown in Figure 1, the formation of epoxide exhibits no induction period. After 27 h of reaction, a selectivity of 80% to cyclohexene oxide was obtained for 45% conversion of the hydroperoxide, determined by iodometric titration.[8] No decomposition of the porphyrin complex was observed under these conditions, and the fact that much lower selectivities to epoxide have been reported with either Ti(OBu)$_4$ or O=Ti(acac)$_2$ as catalysts[3] rules out the possibility that a free titanium species is the actual catalyst in our system. On the other hand, the high selectivity that is obtained with use of SiO_2-supported titanium derivatives[3,9] has been attributed to the stabilization of monomeric titanyl (Ti=O) species, conversely to the homogeneous complexes, which tend to polymerize.[5] The peroxo complex O_2Ti(TPP) (**2**)[10] was formed during the epoxidation, isolated from the reaction mixture, and

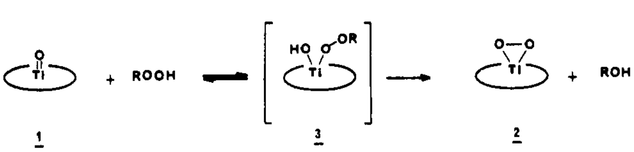
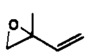
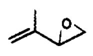


Figure 2.

Table I. Epoxidation of Isoprene Catalyzed by O=Ti(TPP) in CH_2Cl_2 at 70 °C in a Glass-Lined Autoclave

ROOH	RELATIVE RATIO 		
t-BuOOH	0.8 (0.7)[a]	:	1
cumylOOH	2.2 (2.8)[a]	:	1

[a] Data in parentheses are the ratios for O=Mo(TPP)OMe catalysis.

characterized by IR, NMR, and UV-visible spectroscopy. In fact, when O=Ti(TPP) (**1**) in benzene solution is treated with 150 equiv of *tert*-butyl hydroperoxide, O_2Ti(TPP) (**2**) is obtained in 30% yield after chromatography over silica gel. The *cis*-hydroxo(alkylperoxo) complex **3** is most likely involved in the reaction of O=Ti(TPP) (**1**) with alkyl hydroperoxides (Figure 2). However, O_2Ti(TPP) is not able to oxidize olefins under stoichiometric conditions. No reaction was observed when a solution of O_2Ti(TPP) (**2**, 100 μmol) and cyclohexene (5 mmol) in benzene (9.5 mL) was degassed by three freeze, pump, and thaw cycles and heated at 70 °C for 3 days in the dark.[11] On the other hand, **2** was observed to be an active catalyst (Figure 1), but in this case, an induction period of about 5 h was obtained, and then the rate of reaction increased to reach a value comparable to that exhibited by O=Ti(TPP) (**1**) as catalyst.

As also shown in Figure 1, the addition of Na_2HPO_4 (40 equiv/equiv of Ti) reduced the rate of cyclohexene epoxidation catalyzed by O=Ti(TPP) by 1 order of magnitude whereas the same amount of Na_2HPO_4 completely inhibited the reaction catalyzed by O_2Ti(TPP) (less than 1% of epoxide after 27 h).

Epoxidation of isoprene catalyzed by O=Ti(TPP) (**1**) exhibits a large variation in regioselectivity according to the nature of the hydroperoxide that is used (Table I). This demonstrates the presence of the entire alkyl peroxide moiety in the active complex. Almost identical effects observed with either titanium or molybdenum porphyrins[2] suggest that both active species are closely related.

These results accommodate well with our assumption that the *cis*-hydroxo(alkylperoxo) complex **3** (R = alkyl, Figure 2) is involved in the catalytic cycle. Attempts to identify such an intermediate (R = *t*-Bu) during the reaction of O=Ti(TPP) (**1**) with an excess of anhydrous *tert*-butyl hydroperoxide, using either NMR or UV-visible spectroscopy, failed, probably owing to its low concentration in the medium. Only the slow formation of O_2Ti(TPP) (**2**) was observed. However, very strong evidence supports the existence of the analogous *cis*-hydroxo(hydroperoxo) complex **3** (R = H) as an intermediate in the reaction of O=Ti(TPP) (**1**) with H_2O_2. In fact, with use of titanyl porphyrins bearing substituents on only on side of the macrocycle, it has been demonstrated that the formation of the peroxo complex from the related oxo complex in the presence of hydrogen peroxide proceeds with retention of configuration at the metal center and, moreover, labeling

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experiments indicate that the O–O bond of H_2O_2 remains intact during the ligand exchange.[12]

Very recently, it has been reported that the rate of oxo–peroxo exchange for titanyl tetra-4-pyridylporphyrin in the presence of H_2O_2 exhibits a first-order dependence on the proton concentration.[13] Thus, if the formation of the proposed intermediate **3** is proton assisted, the effects of the addition of Na_2HPO_4 on the rate of the epoxidation could be very simply explained by the lowering of the acidity of the reaction mixture. Quite similarly, the rate of the epoxidation of cyclohexene by *tert*-butyl hydroperoxide catalyzed by molybdenum porphyrins was found to be very sensitive to the addition of acidic (CH_3COOH/CH_3COONa) or basic ($NaHCO_3$) compounds to the reaction mixture and, likewise, the slowest rate was observed in the presence of Na_2HPO_4. Finally, the inhibition of the epoxidation catalyzed by $O_2Ti(TPP)$ (**2**) in the presence of Na_2HPO_4 indicates the requirement of protons to form an active species from **2**. The well-documented proton-assisted opening of the peroxo ring of group 8 transition-metal complexes[15] could provide a reasonable pathway for such an activation:

$$O_2Ti(TPP) + H^+ \rightarrow HOO\text{–}Ti(TPP)^+$$

In conclusion, the absence of an induction period, the effect of Na_2HPO_4 on the rate of epoxidation, the formation of the peroxo complex **2** as a side product during the reaction, and the variations of regioselectivity with the nature of the alkyl hydroperoxide used are in full agreement with the involvement of the cis-hydroxo(alkylperoxo) complex **3** as the most likely active species. To the best of our knowledge, this study provides the first example where a peroxo transition-metal complex is strictly inactive in oxidation, whereas several experimental results tend to propose a related alkylperoxo derivative as a mild epoxidizing reagent under catalytic conditions. We can conclude that the epoxidation of olefins with peroxo transition-metal complexes can occur only if a vacant site is available on the metal center. This requirement would simply explain the rather puzzling inertness of the peroxo iron(III) porphyrin complex $O_2Fe(TPP)^-$.[16] On the other hand, coordination of the olefin is not required in transition-metal-mediated epoxidation of olefins with hydroperoxides.

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Registry No. **1**, 58384-89-7; cyclohexene, 110-83-8; isoprene, 78-79-5.

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