precipitate was filtered, washed with ether (3 × 10 mL), and dried in vacuo to afford 256 mg of $Et_3NH^+Br^-$ (98%). The combined ether solutions were evaporated, the resulting clear oil was dissolved in 8 mL of CH_2Cl_2, and the solvent was again removed; this was repeated once more to yield alcohol-free Ti(DIPT)($OiPr$)$_2$ (1.44 mmol) with no excess DIPT present.

The Ti-tartrate complex was taken up in CH_2Cl_2 and transferred to a dry 100-mL volumetric flask, to which was added 1.800 g of *i*PrOH (30.0 mmol). The flask was removed from the drybox and cooled to 0 °C under argon as before. The mixture of (*E*)-2-decen-1-ol and hexadecane (0.015 mL) was added, and the total volume of the solution after cooling was found to be 101 mL. After removal of the excess 1 mL of solution by cannula, the reaction and kinetic analysis were performed in the usual manner.

Entry 2. Generation of Ti(DIPT)($OiPr$)$_2$ was performed as above with the following reagents: [Ti(DIPT)($OiPr$)Br]$_4$ (733 mg, 1.75 mmol of Ti), Et_3N (206 mg, 2.0 mmol), and *i*PrOH (156 mg, 2.6 mmol). Filtration, evaporation, and two CH_2Cl_2/vacuum cycles were done as before to generate 1.75 mmol of Ti(DIPT)($OiPr$)$_2$, which was transferred to a dry 100-mL volumetric flask. To this solution was added (+)-DIPT (71 mg, 0.30 mmol), to provide an active Ti-tartrate concentration of 0.0145 M and a Ti to DIPT ratio of 1:1.17. After addition of *i*PrOH (1.766 g, 29.4 mmol), the flask was removed from the drybox and cooled to 0 °C, and substrate and standard were added as before. The reaction was then performed and analyzed in the usual way.

Table VII. Enantiomerically pure (*R*)-1-(1-cyclohexenyl)ethanol (entry 1), (*R*)-2-methylhept-1-en-3-ol (entry 2), and (*R*)(*E*)-1-cyclohexylbut-2-en-1-ol (entry 3) were prepared by kinetic resolution.[5] Pseudo-first-order kinetics were performed in the usual manner under conditions listed in Table D of the supplementary material.

Table VIII. Kinetic measurements in the presence of *n*-butyl alcohol as inhibitor were performed in the same way as the other pseudo-first-order reactions, with the use of Ti($OnBu$)$_4$ in place of Ti($OiPr$)$_4$, and *n*-butanol in place of isopropyl alcohol. Reactions in the presence of isopropyl alcohol-*d* as inhibitor were performed by adding the inhibitor alcohol to an alcohol-free sample of Ti(DIPT)($OiPr$)$_2$. Nondeuterated TBHP was used, so the molar ratio of OD to OH groups in the reaction was therefore [0.201 M (*i*PrOD)/0.0150 M (TBHP)] = 13.4. The corresponding reaction with *i*PrOH as inhibitor was performed in exactly the same way, with addition of isopropyl alcohol-*h* to alcohol-free Ti(DIPT)($OiPr$)$_2$. Aliquots were obtained, quenched, and analyzed in the usual manner. Details can be found in Table E of the supplementary material.

Table IX. Pseudo-first-order kinetics measurements were performed in the usual manner, with the ratios of titanium to ligand listed in Table F (supplementary material). The 2:1 catalysts were prepared by mixing Ti($OiPr$)$_4$ and the ligand in a 2:1 molar ratio. Unlike the 2:2 reactions, no "inactive" Ti complexes are assumed to be present, since the diol was not used in excess. Therefore, $[Ti]_{active}$ is the concentration of Ti($OiPr$)$_4$ used to prepare the 2:1 mixture. Experimental details are listed in Table F of the supplementary material.

Acknowledgment. We are grateful to the National Institutes of Health (GM28384) for financial support.

Supplementary Material Available: Details of the determination of hydroperoxide binding constants and kinetic rate parameters (8 pages). Ordering information is given on any current masthead page.

Mechanism of Asymmetric Epoxidation. 2. Catalyst Structure

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Abstract: The dominant species in equimolar mixtures of titanium tetraalkoxides and dialkyl tartrate esters is shown to be [Ti(tartrate)$(OR)_2]_2$, which is identified as the active catalyst for asymmetric epoxidation of allylic alcohols by tertiary alkyl hydroperoxides. The solution-phase structure of this species is consistent with the results of an X-ray structural determination of a titanium tartramide complex reported previously, as analyzed by IR and ^1H, ^{13}C, and ^{17}O NMR spectrometry. The first ^{17}O NMR spectra of titanium(IV) alkoxide and alkyl peroxide complexes are reported, as well as the results of a secondary deuterium isotope effect study on the asymmetric epoxidation reaction. General conclusions concerning the mechanism of asymmetric epoxidation are presented.

Here we present results concerning the solution-phase structure of the active titanium–tartrate catalyst in the asymmetric epoxidation reaction and thus provide the evidence underlying our assumptions concerning the mechanism of the process.[2] Single-crystal X-ray structure determinations have been performed on closely related complexes,[3] but usable crystals of a titanium–tartrate ester species have not been obtained. In any case, solid-phase structures are of limited utility in assigning the structures in solution of complexes that exchange ligands as readily as do titanium(IV) alkoxides. We also discuss some aspects of the mechanism that were not included in its initial presentation.[2] The preceding paper includes information concerning the kinetics of the asymmetric epoxidation reaction. Note the following abbreviations: DIPT, (*R,R*)-diisopropyl tartrate; DET, (*R,R*)-diethyl tartrate; DMT, (*R,R*)-dimethyl tartrate.

Results and Discussion

1. Molecular Weight. The molecular weight of [Ti(DIPT)($OiPr$)$_2]_2$ was first measured by vapor-phase osmometry as 752 and 796, compared to the calculated dimeric molecular weight of 797.[4] The Signer method,[5] a technique closely related to

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(2) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, Chapter 8.

(3) (a) Williams, I. D.; Pedersen, S. F.; Sharpless, K. B.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 6430–6431. (b) Pedersen, S. F.; Dewan, J. C.; Eckman, R. R.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 1279–1282.

(4) The first clue to the aggregation state of titanium tartrates in solution came not from a molecular weight measurement, but from diastereoselective epoxidations of secondary allylic alcohols in the presence of (*dl*)-tartrates. Kinetic resolutions of secondary allylic alcohols produce epoxy alcohol products highly enriched in the erythro diastereomer. Using (*dl*)-tartrates, we obtained diastereoselectivities that were independent of the extent of reaction and significantly lower than those found with homochiral tartrates.[13,14] In addition, the asymmetric epoxidation has been found to give a nonlinear response of product enantiomeric excess to changes in the enantiomeric purity of tartrate.[42] Neither observation is consistent with the action of monomeric Ti-tartrate catalysts. Furthermore, NMR spectra of the Ti-(*dl*)-tartrate system show distinct bands assignable to a (*dl*)-tartrate complex in addition to those found for the homochiral complex.[13] This would not be the case if Ti-tartrate were a 1:1 complex.

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Table I. Molecular Weight Determinations by the Signer Method

entry	sample[a]	solvent	concn[b]	MW_{obs}	N[c]	MW_{calcd}[d]
		Titanium Tetraalkoxides				
1	Bu_4Sn[e]	CH_2Cl_2	0.25	346	1.0	347
2	$Ti(OiPr)_4$	CH_2Cl_2	0.22	275	1.0	284
3	$Ti(OEt)_4$	CH_2Cl_2	0.23	623	2.7	684
4	$Ti(OEt)_4$	CH_2Cl_2	0.35	658	2.9	684
5	$Ti(OEt)_4$	CH_2Cl_2	0.50	844	3.7	684
6	$Ti(OBn)_4$	CH_2Cl_2	0.27	840	1.8	953
		1:1 Ti–Tartrate				
7	$Ti(DIPT)(OiPr)_2$	CH_2Cl_2	0.17	864	2.2	797
8	$Ti(DIPT)(OiPr)_2$	CH_2Cl_2	0.20	798	2.0	797
9	$Ti(DIPT)(OiPr)_2$	CH_2Cl_2	0.69	1119	2.8	797
10	$Ti(DET)(OEt)_2$	CH_2Cl_2	0.44	628	1.8	684
11	$Ti(DET)(OEt)_2$	CH_2Cl_2	0.28	703	2.1	684
12	$Ti(DET)(OiPr)_2$	CH_2Cl_2	0.42	620	1.7	740
13	$Ti(DET)(OiPr)_2$	CH_2Cl_2	0.25	700	1.9	740
14	$Ti(OC_{12})_2(DC_{12}T) + 2n\text{-}C_{12}H_{25}OH$	CH_2Cl_2	0.10	495	1.7	509[f]
15	$Ti(OC_{12})_2(DC_{12}T) + 2n\text{-}C_{12}H_{25}OH$	CH_2Cl_2	0.18	504	1.9	509[f]
16	$Ti(DIPT)(OiPr)_2$	pentane	0.36	1082	2.7	1194
17	$Ti(DIPT)(OiPr)_2$	pentane	0.51	1107	2.8	1194
18	$Ti(DIPT)(OiPr)_2$	pentane	0.32	1195	3.0	1194
19	$Ti(DIPT)(OtBu)_2$	pentane	0.34	919	2.2	853
20	$Ti(DIPT)(OtBu)_2$	pentane	0.38	868	2.0	853
21	$Ti(DET)(OiPr)_2$	pentane	0.38	1245	3.4	1111
22	$Ti(OC_{12})_2(DC_{12}T) + 2n\text{-}C_{12}H_{25}OH$	pentane	0.14	892	?	*f*
23	$Ti(OC_{12})_2(DC_{12}T) + 2n\text{-}C_{12}H_{25}OH$	pentane	0.09	893	?	*f*
24	$Ti(DIPT)(OiPr)_2$	ether	0.31	744	1.9	797
25	$Ti(DIPT)(OiPr)_2$	ether	0.24	787	2.0	797
		Ti–DNBnT, 2:1 Ti–DIPT				
26	1:1 $Ti(OiPr)_4$–DNBnT	CH_2Cl_2	0.29	1003	2.0	985
27	1:1 $Ti(OiPr)_4$–DNBnT	CH_2Cl_2	0.25	979	2.0	985
28	2:1 $Ti(OiPr)_4$–DNBnT	CH_2Cl_2	0.37	834	1.1	777
29	2:1 $Ti(OiPr)_4$–DNBnT	CH_2Cl_2	0.23	794	1.0	777
30	2:1 $Ti(OiPr)_4$–DIPT	CH_2Cl_2	0.52	657	1.0	683
31	2:1 $Ti(OiPr)_4$–DIPT	CH_2Cl_2	0.50	636	0.9	683

[a] Unless otherwise indicated (entries 14, 15, 22, and 23), samples were prepared by mixing the indicated molar equivalents of titanium tetraalkoxide and ligand and removing the liberated volatile alcohol in vacuo. Except for entry 1, the molecular weight standard was n-Bu_4Sn. [b] Concentration of titanium at equilibrium. [c] N, degree of association. [d] MW_{calcd}, molecular weight of oligomer nearest to the MW_{obs}. [e] Standard, azobenzene. [f] $DC_{12}T$, di-n-dodecyl tartrate; (OC_{12}) denotes the alkoxide of n-dodecyl alcohol. See Discussion.

vapor-phase osmometry, proved to be much more convenient. Table I lists the results for some titanium alkoxides, tartrates, and tartramides.

$Ti(OiPr)_4$ was found to be a monomer (entry 2), consistent with previously reported measurements.[6] The molecularity of $[Ti(OEt)_4]_n$ has been subject to some debate.[6,7] Our measurements (entries 3–5) indicate a trimeric aggregation state, with increasing amounts of higher oligmer(s) present at increasing concentrations.

In CH_2Cl_2, $[Ti(DIPT)(OiPr)_2]_n$ (entries 7 and 8), $[Ti(DET)(OEt)_2]_n$ (entries 10 and 11), and $[Ti(DET)(OiPr)_2]_n$ (entries 12 and 13) were found to be dimeric. In the time required for the experiment (7–10 days), $[Ti(DET)(OiPr)_2]_2$ was transesterified to a statistical mixture of complexes involving DET, DIPT, and the mixed diester. Entry 9 indicates that at high concentration (0.69 M Ti), larger oligomers or intermolecular interactions between dimers may be present.

Because the Signer method measures the total amount of solute in solution, most of these experiments were performed with alcohol-free samples. Two experiments included equimolar mixtures of (*R,R*)-di-*n*-dodecyl tartrate ($DC_{12}T$) and titanium tetra-*n*-dodecyl oxide (entries 14 and 15), with the 2 equiv of the nonvolatile dodecyl alcohol released per equivalent of tartrate remaining in solution. Thus, the solute comprised 2 equiv of alcohol (MW 186) plus the Ti–tartrate complex (MW 903 per monomeric unit); the observed molecular weight represents an average of these species. If 1.0 mmol each of tartrate and tetraalkoxide were used, the total amount of solute would be 3.0 mmol if the Ti–tartrate complex were a monomer, 2.5 mmol if it were a dimer, and 2.33 mmol if it were a trimer. The average molecular weights would then be 425 for monomeric Ti–tartrate, 510 for a dimer, and 547 for trimer. Entries 14 and 15 provide evidence that the Ti–tartrate complex is a dimer in the presence, as well as in the absence, of free alcohol. This conclusion is supported by the insensitivity of NMR and IR spectra to the presence of free alcohol (vide infra).

Because of the differences in kinetic behavior of asymmetric epoxidation in pentane and ether solvents compared to CH_2Cl_2,[8] the average molecular weights of several complexes were determined in these solvents. $[Ti(DIPT)(OiPr)_2]_n$ and $[Ti(DET)(OiPr)_2]_n$ are largely trimeric in pentane. The more sterically hindered $[Ti(DIPT)(OtBu)_2]_n$, on the other hand, is a dimer in pentane (entries 19 and 20).

Note also the results in pentane with $[Ti(DC_{12}T)(OnC_{12}H_{25})_2]_n$ in the presence of 2 equiv of *n*-dodecyl alcohol (entries 22 and 23). The largest possible observed molecular weight for this experiment (MW_{obs}) would be 638 (if N is very large), assuming that free alcohol and Ti–tartrate are independent, noninteracting molecules. The total number of moles of solute would then be the sum of the number of moles of alcohol and titanium complex. This assumption apparently breaks down in pentane since the observed molecular weight is 893, providing evidence for intermolecular associations among the polar solute molecules in the nonpolar solvent. The sterically shielded $[Ti(DIPT)(OtBu)_2]_2$ does not exhibit the same sort of aggregation.

Molecular weight measurements in ether show dimeric aggregation for $[Ti(DIPT)(OiPr)_2]_n$ (entries 24 and 25), consistent

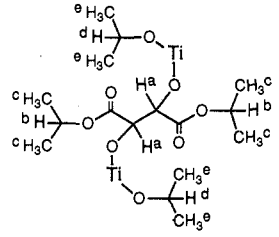
(5) (a) Clark, E. P. *Ind. Eng. Chem., Anal. Ed.* **1941**, *13*, 820–821. (b) Burger, B. J.; Bercaw, J. E. In *Experimental Organometallic Chemistry: A Practice in Synthesis and Characterization*; Wayada, A. L., Darensbourg, M.Y., Eds.; ACS Symposium Series 357; American Chemical Society: Washington, DC, 1987; Chapter 4, pp 94–96.

(6) Bradley, D. C.; Mehrotra, R. C.; Gaur, D. P. *Metal Alkoxides*; Academic Press: New York, 1978; Chapter 4.

(7) Russo, W. R.; Nelson, W. H. *J. Am. Chem. Soc.* **1970**, *92*, 1521–1526.

(8) Woodard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.*, preceding paper in this issue.

Table II. NMR Assignments for $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ and Components in $CDCl_3$ at Room Temperature (ppm Downfield from TMS)



sample	nucleus	H^a	H^b	Me^c	H^d	Me^e	C=O
$[Ti(DIPT)(O\textit{i}Pr)_2]_2$	^1H	5.08	5.02	1.2	4.69	1.2	
	^{13}C	85.7	70.3, 68.8	21.6	78.8	25.2	175.7, 172.4
$Ti(O\textit{i}Pr)_4$	^1H				4.50	1.21	
	^{13}C				76.1	26.4	
DIPT	^1H	4.32	5.01	1.20			
	^{13}C	72.1	70.1	21.5			171.0

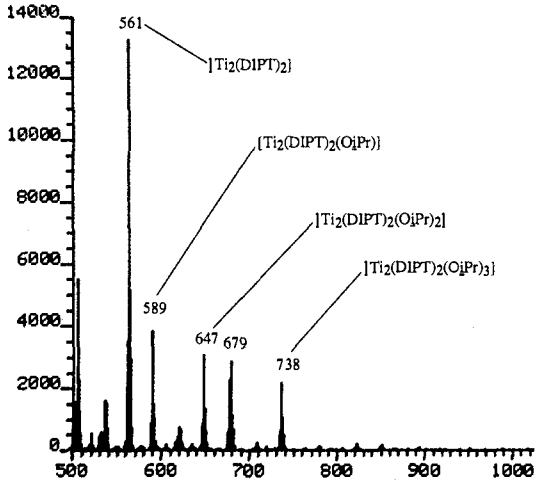


Figure 1. Electron impact mass spectrum of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$.

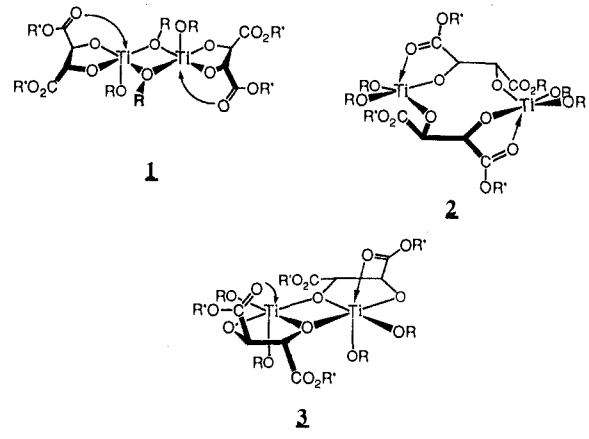


Figure 2. Three possible structures of $[Ti(tartrate)(OR)_2]_2$.

with the idea that a more polar solvent (e.g., Et_2O or CH_2Cl_2) reduces association among solute molecules.

Signer measurements were also performed in CH_2Cl_2 for complexes of $Ti(O\textit{i}Pr)_4$ and (2*R*,3*R*)-*N*,*N*′-dibenzyltartramide (D*N*BnT, vide infra). The 1:1 complex was found to be a dimer in solution (entries 26 and 27) and the 2:1 complex a monomer (two Ti atoms and one ligand per complex) (entries 28 and 29). The 2:1 Ti–DIPT complex also has an average of two Ti atoms and one ligand per molecule (entries 30 and 31).

2. Mass Spectrometry. The assignment of titanium tartrates as dimeric species was supported by low-resolution electron impact mass spectra. Parent ions were never observed; the highest molecular weight ion was usually parent minus coordinated alkoxide. Figure 1 shows the mass spectrum of an alcohol-free preparation of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ in CH_2Cl_2 solution. Similar results were obtained for $Ti(O\textit{t}Bu)_4$ + DIPT, $Ti(O\textit{t}Bu)_4$ + DET, $Ti(O\textit{i}Pr)_4$ + DIPT, and $Ti(O\textit{i}Pr)_4$ + DET.[9]

3. Solid-State Structures. Three general types of structures for $[Ti(tartrate)(OR)_2]_2$ (each in accord with the basic NMR and IR evidence discussed below) can be considered. The possibilities depicted in Figure 2, include an alkoxide-bridged, tartrate-capped dimer, **1**, a 10-membered-ring form, **2**, and the tartrate-bridged structure, **3**. One characteristic that sets **3** apart from the others is the presence of both bridging and terminal (nonbridging) tartrate oxygen atoms. Bridging alkoxides are a ubiquitous feature of Ti(IV) chemistry. This bonding mode allows the Lewis acidic Ti(IV) center in tetraalkoxide complexes to exist in five-, and six-coordinate configurations, except when steric congestion blocks the formation of bridging alkoxide units.

We have changed our initial[10] proposal for the Ti–tartrate structure (conformation **2**, with five-coordinate Ti atoms) to that depicted in **3** as a result of X-ray structural determinations of five related complexes.[3] Each features six-coordinate metal centers and bridging tartrate ligands; that is, the titanium centers are invariably linked by bridging tartrate alkoxide oxygen atoms and not by bridging isopropoxides or ethoxides. While none of these crystal structures are of the "parent" asymmetric epoxidation system, the most important[3a] is of the titanium complex of (2*R*,3*R*)-*N*,*N*′-dibenzyltartramide $[Ti(D\textit{N}BnT)(O\textit{i}Pr)_2]_2$ (**4**), which is a moderately effective template for asymmetric epoxidation.[11] Another significant solid-state structure[3] includes diethyl tartrate and chelating *N*-phenyl hydroxamate groups in the same molecule: $\{Ti(DET)(ON(Ph)O][OEt]\}_2$ (**5**). The structure that we propose for the active catalyst of asymmetric epoxidation, **3**, is directly analogous to that of **4**, and is similar to **5**.

Two features of the crystal structures of **4** and **5** that have been incorporated in the proposed structure **3** should be noted. The

(9) Peaks in the mass spectrum of molecular weight greater than that of the dimer were observed only for the mixture of $Ti(O\textit{i}Pr)_4$ and DIPT when the sample holder was heated to about 150 °C. Corresponding roughly to a trimeric molecular weights, these peaks were weak in intensity and disappeared when free isopropyl alcohol was removed from the mixture before analysis. For all samples, the pattern bands corresponded to cleavage of alkoxide ligands and methyl, isopropyl, and *tert*-butyl groups. The spectrum of $Ti(O\textit{i}Pr)_4$ + DET was complicated by transesterification of the tartrate ester. The spectrum of the monomeric and relatively stable complex $Ti(O\textit{t}Bu)_4$ also lacked a parent ion peak. An intense band due to loss of a methyl group was the signal found at highest molecular weight. $[Ti(OEt)_4]_n$ showed only peaks between monomer and dimer values, in spite of its trimeric or tetrameric nature in solution.

(10) Sharpless, K. B.; Woodard, S. S.; Finn, M. G. *Pure Appl. Chem.* **1983**, *55*, 1823–1836.

(11) For example, asymmetric epoxidation of (*E*)-α-phenylcinnamyl alcohol with the "standard" 1:1.2 Ti–ligand ratio proceeds in 98% enantiomeric excess with the same absolute configuration as the reaction using tartrate esters (compared to >99% for DIPT). Use of a 2:1 Ti–ligand ratio, however, provides the *enantiomeric* epoxy alcohol in 80% ee.[39]

Table III. Coalescence Temperature Measurements for the Fluxional Equilibration of Ti-Tartrates in $CDCl_3$

complex	peak, ppm	assgnmt[a]	$\delta\nu_{k=0}$, Hz	T_c, K	k_c,[b] s^{-1}	$\Delta G^{\ddagger}_{eq}$,[b] kcal/mol
$[Ti(DMT)(OiBu)_2]_2$	1.31	Ti-OiBu	2.5	271	5.6	14.9
	5.11	H^a, H^b	91	314	202	15.1
	4.97, 5.34	H^a, H^b	1.6	265	3.6	14.8
$[Ti(DET)(OiBu)_2]_2$	1.29	Ti-OiBu	5.6	283	12.4	15.1
	5.13	H^a, H^b	65	310	144	15.1
	5.00, 5.26	H^a, H^b	3.1	279	6.9	15.2
$[Ti(DET)(OEt)_2]_2$	5.22	H^a, H^b	28.5	250	63.3	12.8

[a] H^a, H^b are the tartrate methine protons: RO_2C-C*H*(OTi)-C*H*(OTi)-CO_2R. [b] $k_c = \pi(\delta\nu_{k=0})/(2)^{1/2}$, $\Delta G^{\ddagger}_{eq} = (1.987 \times 10^{-3})(T)[23.76 + \ln(T/k_c)]$.

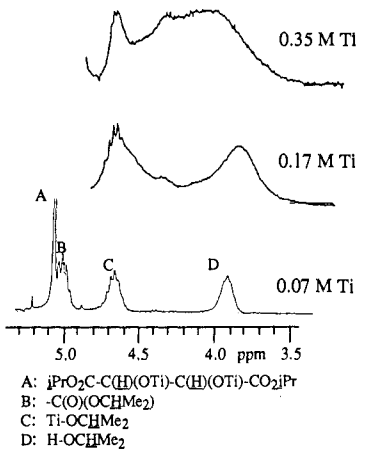


Figure 3. ^1H NMR of Ti(DIPT)($OiPr)_2$ + 2*i*PrOH in $CDCl_3$.

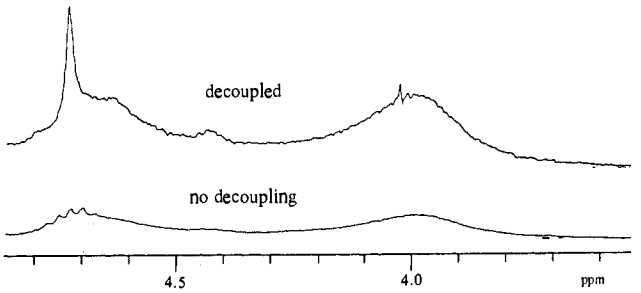


Figure 4. Methine proton resonances of isopropoxides and isopropyl alcohol in the ^1H NMR spectrum of Ti(DIPT)($OiPr)_2$ + 2*i*PrOH in $CDCl_3$ (0.18 M). Top: isopropyl methyl resonances decoupled.

Table IV. Results of Dynamic NMR Band-Shape Analysis

complex	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	T,[a] K
$[Ti(DIPT)(OiBu)_2]_2$	15.0 ± 0.2	0 ± 2	255–297
$[Ti(DET)(OiBu)_2]_2$	15.0 ± 0.1	0 ± 2	271–323
$[Ti(DMT)(OiBu)_2]_2$	15.4 ± 0.2	0 ± 2	253–323
$[Ti(DIPT)(OiPr)_2]_2$	14.5 ± 0.3	0 ± 2	260–284
$[Ti(DET)(OEt)_2]_2$	5.1 ± 0.5	−31 ± 4	246–295

[a] Temperature range spanned by the useful exchange-broadened spectra.

Ti–O–C bond angles of the ethoxide and isopropoxide ligands are 150–160°, indicating overlap of oxygen lone pairs with empty d orbitals on titanium. This is a common feature of d^0 metal alkoxide systems,[3,12] and we assume that allylic alkoxide ligands adopt the same Ti–O–C bond angles in the ground state. In addition, the central Ti_2O_2 core is planar and the bridging tartrate alkoxide oxygens are sp^2-like in that the carbon atom to which each is attached also lies very close to the Ti_2O_2 plane.

4. ^1H and ^{13}C NMR in $CDCl_3$. A. Concentration Effects: Alcohol–Alkoxide Exchange. The ^1H and ^{13}C NMR spectra of $[Ti(DIPT)(OiPr)_2]_2$, from which free isopropyl alcohol has been removed show a single set of resonances for tartrate and bound isopropoxide. Table II lists the peak assignments for these complexes and the uncomplexed ligands. Note the downfield shifts that accompany binding to the Lewis acidic metal. One carbonyl resonance (172.4 ppm) in the ^{13}C NMR close to that of DIPT alone is assigned to a free (uncoordinated) ester group. The other carbonyl is shifted downfield and is therefore assigned to an ester group bound to titanium through the carbonyl oxygen atom.

The ability of Ti(IV) to exchange bound isopropoxide for alcohol in solution is essential to the successful operation of the asymmetric epoxidation catalyst.[8] Every band in the NMR spectrum is affected by such ligand exchange.

An example is presented in Figure 3, showing a portion of the ^1H NMR spectrum of an equimolar mixture of $Ti(OiPr)_4$ and DIPT at 0.35, 0.17, and 0.07 M Ti. Under more dilute conditions (not shown), free isopropyl alcohol (3.98 ppm) and bound isopropoxide (4.70 ppm) are sharp heptet signals of equal intensity. At 0.07 M, these signals begin to broaden, and at 0.17 M an intermediate resonance appears. At 0.35 M, the distinct isopropyl alcohol methine resonance has been replaced by a broad band stretching from 4.8 to 3.9 ppm. However, there remains a narrower resonance at 4.7 ppm superimposed on the more broadened signal, which is due to one of the two isopropoxide ligands. The nonequivalence of isopropoxides is also demonstrated when the upfield methyl resonances (1.3–1.1 ppm) are irradiated (Figure 4). This decoupling reveals a sharpened isopropoxide methine resonance superimposed on a broader one. The free *i*PrOH signal at 3.98 ppm is also not sharpened very much. The 4.8–3.9 ppm feature, then, is the product of exchange of 2 equiv of isopropyl alcohol with bound isopropoxide, one isopropoxide undergoing exchange with isopropyl alcohol at a faster rate than the other. The two chemically different isopropoxide ligands undergo exchange with each other in the absence of free alcohol (vide infra).

^{13}C NMR spectra of $[Ti(DIPT)(OiPr)_2]_2$ + *i*PrOH exhibit similar concentration-dependent exchange behavior.[13]

B. Variable-Temperature ^1H NMR. The ^{13}C NMR spectra of $[Ti(DIPT)(OiPr)_2]_2$ in the absence of alcohol show two resonances each for the carbonyl and carbinol centers of tartrate (Table II), yet the ^1H NMR spectrum displays only a single set of tartrate signals. A fluxional exchange process that renders the two halves of unsymmetrically bound tartrate equivalent on the ^1H NMR time scale at room temperature is therefore indicated. Variable-temperature ^1H NMR of Ti–tartrates reveals the nonequivalent nature of the ester groups and carbinol centers of bound tartrate.[14] We have determined the kinetic parameters for the fluxional exchange process by coalescence temperature measurements and band-shape analysis.

The results of coalescence temperature (T_c) measurements are listed in Table III. In order to calculate[15] a free energy barrier

(12) (a) Fanwick, P. E.; Ogilvy, A. E.; Rothwell, I. P. *Organometallics* **1987**, *6*, 73–80. (b) LaPointe, R. E.; Wolczanski, P. T.; Mitchell, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 6382–6389. (c) Lubben, T. V.; Wolczanski, P. T.; Van Duyne, G. D. *Organometallics* **1984**, *3*, 977–983. (d) Coffindaffer, T. W.; Rothwell, I. P.; Huffman, J. C. *Inorg. Chem.* **1983**, *22*, 2906–2910. (e) Chisholm, M. H.; Eichhorn, B. W.; Folting, K.; Huffman, J. C.; Tatz, R. J. *Organometallics* **1986**, *5*, 1599–1606. (f) Bryndza, H. E.; Calabrese, J. C.; Marsi, M.; Roe, D. C.; Tam, W.; Bercaw, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 4805–4813. (g) Rees, W. M.; Churchill, M. R.; Fettinger, J. C.; Atwood, J. D. *Organometallics* **1985**, *4*, 2179–2185.

(13) Finn, M. G. Ph.D. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 1986.

(14) Woodard, S. S. Ph.D. Dissertation, Stanford University, Stanford CA, 1981.

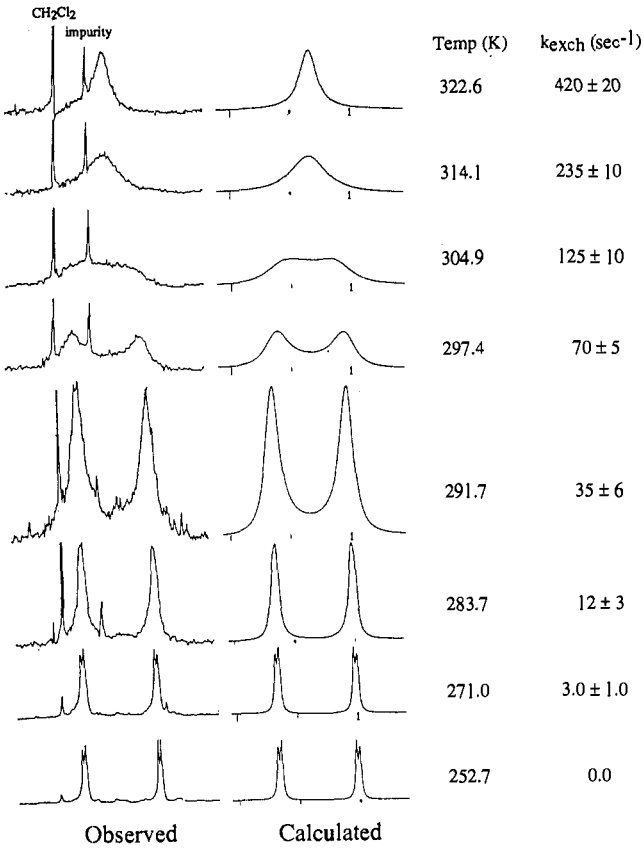


Figure 5. Dynamic NMR band-shape analysis of Ti(DET)(O*t*Bu)$_2$ in $CDCl_3$ (5.5–4.7 ppm region displayed).

to equilibration ($\Delta G^{\ddagger}_{eq}$), the separation of peak positions at the slow-exchange limit ($\delta\nu_{k=0}$) was obtained by cooling the samples to 230–235 K.

Band-shape analyses of ^{1}H NMR spectra were performed to obtain more precise activation parameters for the fluxional exchange process. An example of observed and calculated spectra are shown in Figure 5 for the tartrate methine resonances of [Ti(DET)(O*t*Bu)$_2$]$_2$. Table IV lists the activation parameters for fluxional exchange in five titanium–tartrate complexes. Details can be found in the Experimental Section.

For three of the five complexes, the exchange broadening of more than one resonance was evaluated and in each case the resulting thermochemical parameters were identical within the error of measurement. A single fluxional process is therefore responsible for the NMR exchange behavior.

For complexes with *tert*-butoxide and isopropoxide ligands, the observed free energy of activation for fluxional equilibration was invariant with temperature ($\Delta S^{\ddagger} \approx 0$ eu), indicative of a unimolecular exchange process. Only [Ti(DET)(OEt)$_2$]$_2$ showed activation parameters characteristic of a bimolecular reaction at the concentration studied (approximately 0.25 M). This does not reflect a difference in structure but rather a difference in accessible exchange mechanisms. Exchange of alkoxide ligands among Ti(IV) centers in the absence of free alcohol is probably an associative reaction. It is therefore likely that NMR line broadening in [Ti(DET)(OEt)$_2$]$_2$ is the result of a facile bimolecular exchange of ethoxide ligands with concomitant skeletal rearrangement of the tartrates. When the complex bears the larger isopropoxide or *tert*-butoxide ligand, an associative ligand exchange is blocked, and a unimolecular reaction of higher enthalpy of activation is unmasked. The putative unimolecular fluctional exchange process is depicted in Figure 6.

This degenerate skeletal rearrangement exchanges bridging and terminal oxygens (marked with asterisks in Figure 6), axial and

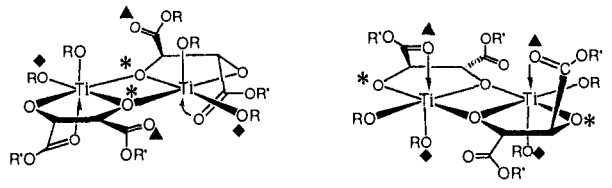


Figure 6. Proposed fluxional exchange of Ti–tartrates in solution.

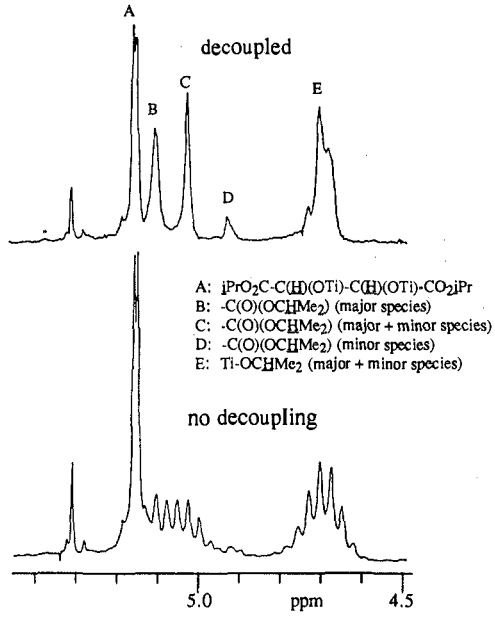


Figure 7. Downfield region of ^{1}H NMR of [Ti(**DIPT**)(O*i*Pr)$_2$]$_2$ in $CDCl_3$ at 267 K. Top: isopropyl methyl resonances decoupled.

equatorial monodentate alkoxides (diamonds), and bound and free ester groups (triangles). A 10-membered-ring structure, analogous to **2** in Figure 2, is a possible, but unobserved, intermediate.

C. Additional Components in Solution. The ^{1}H NMR of a sample of [Ti(DIPT)(O*i*Pr)$_2$]$_2$ in $CDCl_3$ cooled to −6 °C (Figure 7) reveals an additional set of resonances due to a minor Ti–tartrate structure, which undergoes exchange with the major species in solution and thus does not appear at higher temperature. NMR band-shape analysis showed that the major species undergoes fluxional equilibration as described above, and that this unimolecular rate is larger (by approximately a factor of 30) than the rates at which the minor species exchanges with the major one and at which the minor species undergoes its own fluxional equilibration. Precise activation parameters for the exchange processes involving the minor compound were not obtained.

Resonances that correspond to a minor Ti–tartrate component also appear in ^{13}C NMR spectra of other complexes such as [Ti(DIPT)(O*t*Bu)$_2$]$_2$ and [Ti(DMT)(O*t*Bu)$_2$]$_2$. In contrast to the ^{1}H NMR, the ^{13}C NMR spectrum of [Ti(DIPT)(O*i*Pr)$_2$]$_2$ does not show resonances due to a minor component in solution. Similarly, ^{1}H NMR spectra of [Ti(DIPT)(O*t*Bu)$_2$]$_2$ and [Ti(DMT)(O*t*Bu)$_2$]$_2$ show only a single species at low temperature. Variations in peak positions and exchange rates among various complexes account for the fact that species other than the Ti–tartrate dimer, which are always present in 1:1 Ti–tartrate mixtures, are visible in the NMR in $CDCl_3$ only in particular instances. Other solvents provide better resolution.

In Figure 8 is shown the downfield region of the ^{1}H NMR spectrum at room temperature of an equimolar mixture of [Ti(DIPT)]$_2$ and Ti(O*i*Pr)$_4$ in CD_2Cl_2, at 0.07 and 1.0 M total Ti concentrations. Two Ti–tartrates are clearly visible, particularly when methyl groups are decoupled to resolve the Ti–O*i*Pr methine resonances. Note the presence of a larger amount of the minor component at the higher concentration. The relative intensities of major and minor bands in the NMR were found to be sensitive to overall concentration for several different Ti–tartrates in different solvents ($CDCl_3$, CD_2Cl_2, C_6D_6, toluene-d_8, and cyclo-

(15) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press: London, 1982.

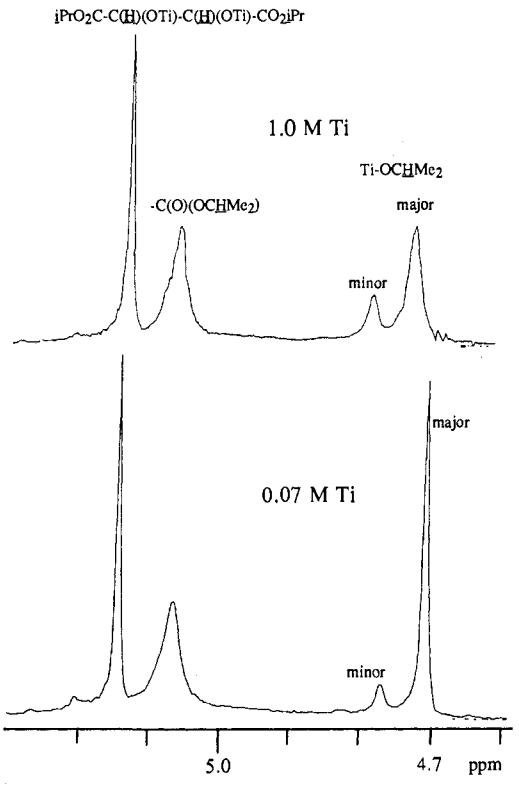


Figure 8. Downfield region of ^1H NMR of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ in CD_2Cl_2 at ambient temperture (isopropyl methyl resonances decoupled).

hexane-d^{12}), suggesting an equilibrium among species of different molecularity.

Variation of the amount of DIPT relative to $Ti(O\textit{i}Pr)_4$ allowed us to assign the minor species as a 2:1 Ti–DIPT complex, $Ti_2(DIPT)(O\textit{i}Pr)_6$. The intensity of the minor resonance at 4.77 ppm was found to diminish as the Ti to DIPT ratio was incrementally decreased from 2.00:1.95 to 2.00:2.20, completely disappearing in the ^1H NMR spectrum of the latter mixture. Formation of the minor complex is therefore suppressed with added tartrate, consistent with its formulation as $Ti_2(DIPT)(O\textit{i}Pr)_6$. Kinetic measurements show that a 2:1 Ti–tartrate complex is responsible for the loss of enantioselectivity and rate in asymmetric epoxidation using exactly a 2:2 mixture.[8]

A 2:1 mixture of $Ti(O\textit{i}Pr)_4$ and DIPT from which free isopropyl alcohol has been removed (Figure 9) shows a strong isopropoxide methine resonance at 4.77 ppm in CD_2Cl_2 and $CDCl_3$, matching the minor resonance of a 1:1 mixture in these solvents. $Ti_2(DIPT)(O\textit{i}Pr)_6$ itself undergoes disproportionation to some extent, giving two products visible in the ^1H and ^{13}H NMR: $Ti(O\textit{i}Pr)_4$ and $[Ti(DIPT)(O\textit{i}Pr)_2]_2$. In contrast, only one of the disproportionation products of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ could be observed in the NMR; no distinct resonances for complexes such as $[Ti_2(DIPT)_3(OR)_2]_n$ or $[Ti_2(DIPT)_4]_n$ were found.[16]

^1H and ^{13}C NMR spectra of 2:2 Ti–tartrate mixtures in benzene-d_6, toluene-d_8, cyclohexane-d^{12}, CD_3CN, and THF-d_8 have also been examined.[13] While the first three solvents provide remarkable increases in resolution (to the extent that each nonequivalent methyl group of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ is resolved at room temperature), and all of these solvents enhance the resolution of the minor Ti–tartrate species, the results of these studies are essentially the same as those presented above for $CDCl_3$ and CD_2Cl_2.

Thus, the NMR spectra establish the presence of minor amounts (approximately 5–15%, depending on solvent and concentration) of $Ti_2(tartrate)(OR)_6$ and, by implication, complexes having more

(16) ^1H NMR spectra of 1:2 mixtures of $Ti(OR)_4$–tartrate (and other ratios having greater tartrate than Ti) are poorly resolved, with many broad bands. Such complexes present in small amounts are likely to be missed in spectra of 2:2 Ti–tartrate species, with which they can chemically exchange.

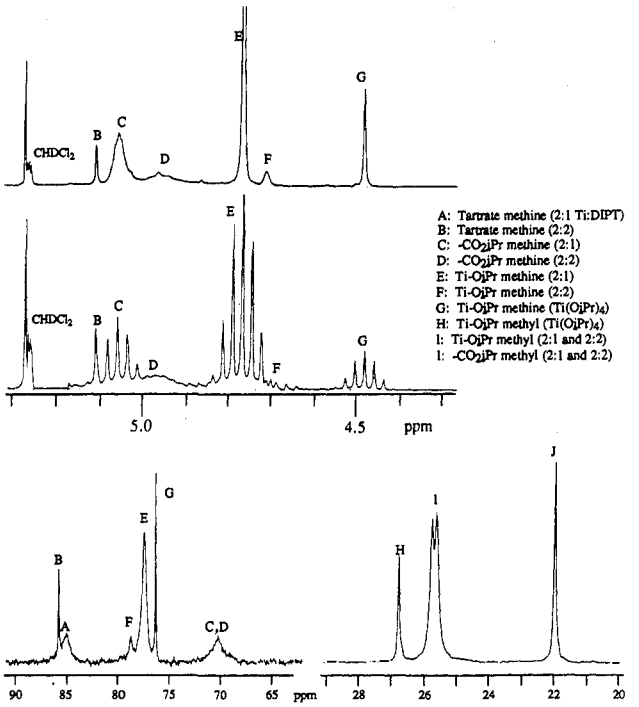


Figure 9. ^1H and ^{13}C (bottom) NMR of $Ti_2(DIPT)(O\textit{i}Pr)_6$ in CD_2Cl_2 at ambient temperature. Top: isopropyl methyl resonances decoupled. Bottom: broad-band proton decoupled.

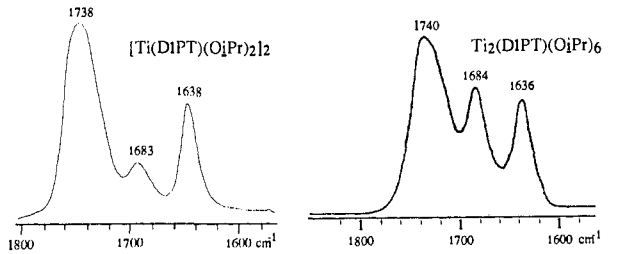


Figure 10. IR spectra of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ and $Ti_2(DIPT)(O\textit{i}Pr)_6$ in CH_2Cl_2 in the CO-stretching region.

tartrate than titanium, in a 2.0:2.0 mixture of $Ti(OR)_4$–tartrate. We have evaluated the kinetic contributions of each of these species to the epoxidation reaction and have concluded that the major species, $[Ti(tartrate)(OR)_2]_2$, is the dominant catalyst in the reaction mixture.[8]

5. Infrared Spectroscopy. The infrared spectra of titanium tartrates in CH_2Cl_2 also indicate the presence of at least two species in solution. The spectrum of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ in CH_2Cl_2 (Figure 10) shows carbonyl stretching bands at 1738, 1683, and 1638 cm^{-1}. The first is due to an uncoordinated ester unit, the second and third to ester groups bound to titanium through the carbonyl oxygen. The band at 1683 cm^{-1} is smaller than the other two when the Ti to tartrate ratio is 2:2. When the Ti to tartrate ratio is either greater or less than unity, the intensity of the 1638-cm^{-1} band is diminished relative to that of the 1683-cm^{-1} resonance. This pattern is the same in the absence and presence of an excess of free isopropyl alcohol.[13] Thus, the less intense band at 1683 cm^{-1} is due to the bound carbonyl groups of the disproportionation products of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$. The IR spectrum of $Ti_2(DIPT)(O\textit{i}Pr)_6$ (Figure 10) is consistent with such an assignment, showing increased intensity at 1684 cm^{-1} (the 2:1 Ti–DIPT complex itself) and diminished intensity at 1636 cm^{-1} (the 2:2 disproportionation product).

The presence of two chemically different tartrate ester groups in $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ is therefore indicated by both the IR and NMR spectra, and the major IR bands at 1738 and 1638 cm^{-1} can be assigned to free and bound carbonyls of structure **3**. The strong resonance near 1640 cm^{-1} appears to be an exclusive property of 2:2 Ti–tartrates among complexes of titanium (IV)

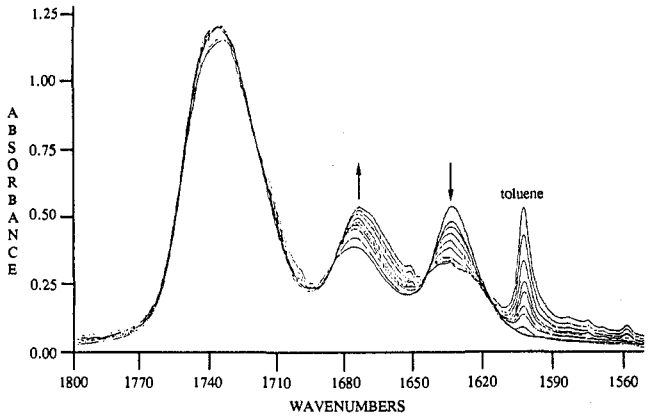


Figure 11. Sequential addition of TBHP to $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ in CH_2Cl_2 at ambient temperature.

alkoxides with α-hydroxy esters. We have found no complex of a titanium tetraalkoxide and a monobasic α-hydroxy ester[17] in any Ti–ligand ratio that shows a band near 1640 cm^{-1}. When the metal center of the 2:2 Ti–tartrate system is made more electron deficient by replacement of the alkoxide ligands with chloride or electron-withdrawing alkoxides such as pentafluorophenoxide or hexafluoroisopropoxide, the 1640-cm^{-1} resonance is replaced by bands near 1660 cm^{-1}, and an epoxidation system of "inverse" enantioselection is produced.[18,39]

We speculate that the 1640-cm^{-1} band may be characteristic of a structural feature necessary for the effective operation of the parent asymmetric epoxidation catalyst. The facial arrangement adopted by the bound carbonyl oxygen and the terminal and bridging tartrate alkoxide oxygen atoms in structure **3** could be such a structural unit that is exclusive to $[Ti(tartrate)(OR)_2]_2$. The advantage to the catalyst that may be afforded by this facial arrangement of chelating atoms is discussed below.

It is interesting to note that changes in the pattern of the carbonyl bands of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ with changes in solvent correlate with magnitudes of asymmetric induction,[8] pseudo-first-order kinetic behavior,[8] and molecular weight measurements in different solvents. In particular, the pattern of C=O stretching bands is similar for the two solvents that give high enantiomeric excess, the "normal" kinetic rate law, and dimeric species in solution—CH_2Cl_2 and ether. The C=O region in pentane is different, with the 1638-cm^{-1} band diminished with respect to the 1680-cm^{-1} absorbance. Recall that Signer molecular weight measurements indicated the presence of significant amounts of trimeric material even at lower concentrations. These spectra were reproducible for the same sample cycled between different solvents several times by evaporation and solvation under inert atmosphere.

Addition of TBHP in toluene to a dilute CH_2Cl_2 solution of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ produced the isosbestic changes in the C=O stretching region of the IR spectrum shown in Figure 11. The band at 1635 cm^{-1} diminished and a new C=O band appeared at 1673 cm^{-1}, slightly different from that present before hydroperoxide addition (1676 cm^{-1}). Similar results were observed for triphenylmethyl (trityl) hydroperoxide.

Complexation of hydroperoxide has a profound effect on the infrared spectrum by changing either the structure of the complex or the strength of the carbonyl–titanium interaction within the same overall structure. NMR spectra of Ti–tartrate + hydroperoxide are uninformative, with broadened resonances for both ^{13}C and ^{1}H nuclei. We would not expect simple monodentate coordination of hydroperoxide to produce such changes in the IR and NMR spectra, so it is possible that bidentate interaction of bound alkyl peroxide with titanium is indicated.[19] Due to their

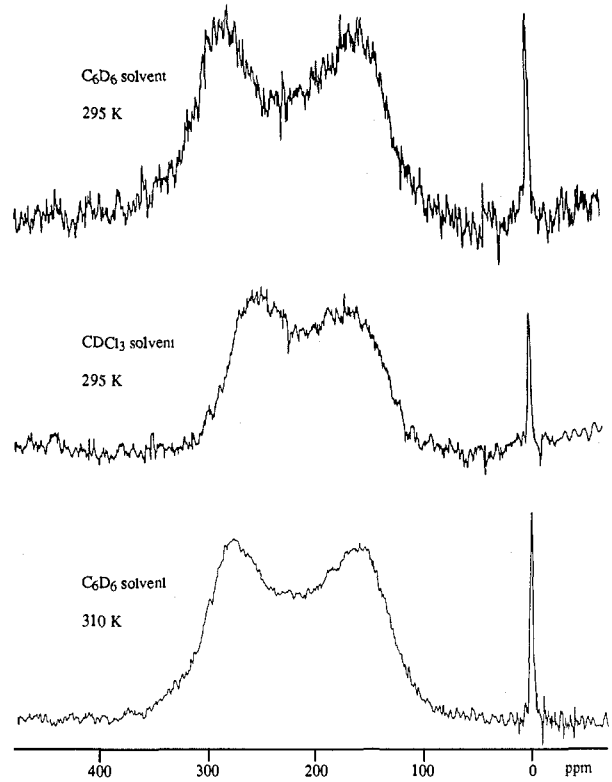


Figure 12. ^{17}O NMR of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$; external Et_2O, 0.0 ppm.

thermal instability, we have not isolated a pure alkyl peroxide complex of Ti–tartrate, and so we have no other information regarding the structure of this species. From the IR it appears that one ester carbonyl per tartrate remains bound to the metal, since the intensity of the free C=O stretch changes very little with added hydroperoxide.

6. ^{17}O NMR. In an effort to resolve bridging from terminal modes of alkoxide binding, tartrate esters enriched in ^{17}O at the alcohol position were prepared and their ^{17}O NMR[20] spectra studied. In addition, natural-abundance ^{17}O NMR spectra were obtained for a series of group IV metal alkoxides and for complexes of ^{17}O-enriched benzyl alcohol and (*R*)-ethyl lactate. Some of these results are compiled in Table 5, which contains the first ^{17}O NMR data reported for d^0 transition metal alkoxide and alkylperoxide complexes.

Transformation of an alcohol to a metal alkoxide is accompanied by a strong downfield shift of the ^{17}O resonance, consistent with a withdrawal of electron density from the oxygen atom. It proved impossible to estimate the difference in chemical shift between a bridging and terminally bound alkoxide ligand, since contributions from inductive and resonance effects[20b-i] are difficult to

(17) The α-hydroxy esters examined were ethyl and isopropyl 2-hydroxypropionate (lactates), ethyl 2-hydroxy-2-phenylacetate (ethyl mandelate), and ethyl 2-hydroxy-2-cyclohexylacetate.[13]

(18) Ellman, J.; Burns, D. B.; Finn, M. G.; Sharpless, K. B.; unpublished results.

(19) That much remains to be explored concerning the mode of binding of hydroperoxides to Ti-tartrate is indicated by the following observation: use of electron-deficient hydroperoxides such as 2-cyanopropyl 2-hydroperoxide or tris(*p*-nitrophenyl)methyl hydroperoxide with a 2:1 Ti–DET mixture produces epoxy alcohol products of enantioselectivity opposite to those obtained with TBHP. Burns, D. B. M.Sc. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 1985.

(20) (a) Kitzinger, J.-P. In *NMR of Newly Accessible Nuclei*; Laszlo, P., Ed; Academic Press: New York, 1983; Vol. 2, Chapter 4. (b) Boykin, D. W.; Baumstark, A. L. *Tetrahedron* **1989**, *45*, 3613–3651. (c) Baumstark, A. L.; Balarishnan, P.; Dotrong, M.; McCloskey, C. J.; Oakley, M. G.; Boykin, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 1059–1062. (d) Monti, D.; Orsini, F.; Ricca, G. S. *Spectrosc. Lett.* **1986**, *19*, 91–99. (e) Chesnut, D. B.; Johnson, W. P. *J. Magn. Reson.* **1985**, *65*, 110–121. (f) Balakrishnan, P.; Baumstark, A. L.; Boykin, D. W. *Org. Magn. Reson.* **1984**, *22*, 753–756. *Tetrahedron Lett.* **1984**, *25*, 169–172. (g) Nguyen, T. T.-T.; Delseth, C.; Kintzinger, J.-P.; Carrupt, P.-A.; Vogel, P. *Tetrahedron* **1980**, *36*, 2793–2797. (h) Crandall, J. K.; Centeno, M. A. *J. Org. Chem.* **1979**, *44*, 1183–1184. (i) Eliel, E. L.; Pietrusiewicz, K. M.; Jewell, L. M. *Tetrahedron Lett.* **1979**, 3649–3652. (j) Miller, K. F.; Wentworth, R. A. D. *Inorg. Chem.* **1979**, *18*, 984–988. (k) Harrison, A. T.; Howarth, O. W. *J. Chem. Soc., Dalton Trans.* **1985**, 1173–1177. (l) Gerothanassis, I. P.; Momenteau, M. *J. Am. Chem. Soc.* **1987**, *109*, 6944–6947.

Table V. ^{17}O NMR ($CDCl_3$ Solution Unless Otherwise Indicated)

entry	sample	chem shift[a]	$W_{1/2}$[b]	notes
1	D_2O	0.0	2	
2	Et_2O	15.5	5	
3	*i*PrOH	37.2	11	
4	2-phenyl-2-propanol-^{17}O	60.0	5	
5	Bn-*OH[c]	8.7	5	
6	*DIPT[d]	−5.1	19	hydroxyl
7	di-L-menthyl (2*R*,3*R*)-tartrate-^{17}O	−3.2	25	hydroxyl
8	di-L-menthyl (2*S*,3*S*)-tartrate-^{17}O	−2.6	24	hydroxyl
9	ethyl lactate-^{17}O	8.4	15	hydroxyl
10	$Ti(OtBu)_4$	303.5	8	
11	$Ti(OiPr)_4$	295	6	
12	$[Ti(OEt)_4]_n$	268	31	weak signal
13	$[Ti(OnBu)_4]_n$	261	40	weak signal
14	$[Ti(*OBn)_4]_n$[c]	251	98	benzyl oxide[g]
15	$Ti(OtBu)_3(*OBn)$[c]	236.5	13	benzyl oxide[h]
16	$Ti(OtBu)_2(*OBn)_2$[c]	238.5	23	benzyl oxide[h]
17	$Ti[OCH(CF_3)_2]_4$	227.5	18	
18	$Zr(OtBu)_4$	224.5	19	
19	$[Ti(*DIPT)(OiPr)_2]_2$[d]	268, 180		
		293, 177		C_6D_6
20	$[Ti(*DIPT)(OtBu)_2]_2$[d]	245, 181		325 K
21	$Ti_2(*DIPT)(OtBu)_6$[d]	247, 180		318 K
22	$[Ti(*DMnT)(OiPr)_2]_2$[e]	301, 156		
23	$[Ti(*DMnT)(OEt)_2]_2$[e]	320, 170		CD_2Cl_2
24	$[Ti(DIPT)(*OBn)_2]_2$[c]	294	40	benzyl oxide
		145	50	C(O)(*OBn)[i]
25	$[Ti_2(lactate)_3(OtBu)(*OBn)_4]_n$	292	35	benzyl oxide
		145	50	C(O)(*OBn)[i]
26	$(Me)_2(Ph)C*O*OH$[f]	258, 216	20, 15	
27	$(Me)_2(Ph)C*O*OMe$[f]	299, 223	15, 12	peroxide
28	$(Me)_2(Ph)C*O*OH$[f] + $Zr(OtBu)_4$ (1:1)	187	25	Zr−*O*OR
29	$(Me)_2(Ph)C*O*OH$[f] + $Ti(OtBu)_4$ (1:1.2)	284	25	Ti−*O*OR
30	$(Me)_2(Ph)C*O*OH$[f] + $Ti(OiPr)_4$ (1:1)	294	40	Ti−*O*OR
		65	10	$Me_2PhC*O*OH$
		552	5	Ti−*O−Ti
		537, 499	20, 20	Ti−*OCMe_2Ph ?
31	$(Me)_2(Ph)C*O*OH$[f] + $[Ti(DIPT)(OtBu)_2]_2$	260, 216	25, 25	hydroperoxide

[a] ppm downfield from D_2O. [b] Peak width at half-height, ppm. [c] *OBn, alkoxide of ^{17}O-enriched benzyl alcohol. [d] *DIPT, (+)-DIPT enriched in ^{17}O at the hydroxyl positions. [e] *DMnT, di-L-menthyl (2*R*,3*R*)-tartrate enriched in ^{17}O at the hydroxyl positions. [f] Hydroperoxide oxygen atoms enriched in ^{17}O. [g] Molecularity is 1.75 ± 0.3 by Signer molecular weight determination. [h] Monomeric by Signer molecular weight determination. [i] Product of transesterification to produce the labeled benzyl ester.

separate from structural (bridging vs terminal) factors.[21]

It is significant, however, that the ^{17}O NMR spectra of 2:2 complexes of $Ti(OR)_4$ with ^{17}O-enriched tartrates (Figure 12) show two peaks of equal intensity. Samples of $[Ti(*DIPT)(OiPr)_2]_2$ (*DIPT = ^{17}O-enriched DIPT) in $CDCl_3$ and C_6D_6 display two bands separated by approximately 100 ppm (Table V, entry 19). It is unlikely that terminally bound tartrate oxygen atoms in different coordination sites would have such different chemical shifts. With this assumption, we assign these bands to the bridging and terminal tartrate alkoxide oxygen centers in structure **3**. We believe that the nonequivalent tartrate alkoxide oxygens of a possible 10-membered-ring structure such as **2** are likely to be indistinguishable in the ^{17}O NMR.

The spectra of $[Ti(*DIPT)(OtBu)_2]_2$ display an interesting temperature dependence. At ambient temperature in $CDCl_3$, one broad band at 206 ppm ($W_{1/2}$ = 100 ppm) is observed. At approximately 315 K, two bands are seen (245 and 181 ppm), but at 330 K, the peaks coalesce again. Similar temperature-dependent behavior has been reported previously for (HMPA)-$CrO(^{17}O_2)_2$.[22b] Increased resolution at higher temperature is attributed to the decrease in spin–lattice relaxation rate that accompanies a decrease in solution viscosity.

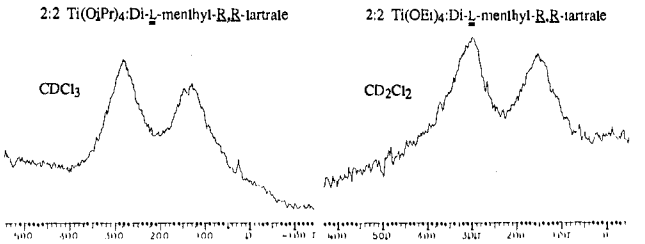


Figure 13. ^{17}O NMR of dimethyl tartrate complexes; external Et_2O, 0.0 ppm.

It is likely that coalescence at higher temperature in the ^{17}O NMR of $[Ti(*DIPT)(OtBu)_2]_2$ reflects fluxional exchange between terminal and bridging sites. Below 0 °C, signals for all the labeled tartrate complexes disappeared entirely. The ^{17}O signals of Ti–tartrates are much broader than those of tetraalkoxide complexes due to an increased sensitivity to quadrupole relaxation, since the oxygen atoms are in an asymmetric environment.[20]

^{17}O NMR spectra of the 2:2 complexes of $Ti(OiPr)_4$ and $Ti(OEt)_4$ with ^{17}O-enriched (2*R*,3*R*)-di-L-menthyl tartrate (*DMnT) also show two well-resolved peaks (Figure 13). The latter is significant because secondary alkoxides form less stable bridging bonds than primary alkoxides, as demonstrated by the molecularities of $Ti(OiPr)_4$ (monomer) and $[Ti(OEt)_4]_3$ (oligomer). It might be argued that the use of isopropoxide or *tert*-butoxide as monodentate ligands could force the complex to adopt a tartrate-bridged configuration by making the alkoxide-bridged

(21) For example, while α-hydroxy esters such as tartrate and lactate display hydroxyl resonances that are *upfield* from alkyl-substituted alcohols (Table V; entries 6–9 vs 3 and 5), the benzyl oxide resonance of titanium complexes bearing tartrate and lactate are considerably *downfield* from those complexes bearing unfunctionalized alkoxides (entries 14–16 vs 24 and 25). Possible contributions of inductive, resonance, and structural effects make an explanation difficult.

(22) (a) Postel, M.; Brevard, C.; Arzoumanian, H.; Reiss, J. G. *J. Am. Chem. Soc.* **1983**, *105*, 4922–4926. (b) Curci, R.; Fusco, G.; Sciacovelli, O.; Triosi, L. *J. Mol. Catal.* **1985**, *32*, 251–257. (c) Zimin, Y. S.; Stepanov, A. G.; Nekipelov, V. M. *React. Kinet. Catal. Lett.* **1985**, *28*, 145–152; *Chem. Abstr.* **1985**, *103*, 188455z. (d) Harrison, A. T.; Howarth, O. W. *J. Chem. Soc., Dalton Trans.* **1985**, 1173–1177.

structure inaccessible. The similar ^{17}O and ^{1}H (not shown) NMR spectra of the two DMnT complexes suggests that they adopt the same structure. Dimenthyl tartrate is an effective chiral auxiliary in the asymmetric epoxidation reaction.[2]

Note also that $[Ti(DIPT)(*OCH_2Ph)_2]_2$, made from ^{17}O-enriched benzyl alcohol, shows only one band for coordinated benzyl oxide (Table V, entry 24). Two would be expected if the dimer were bridged by benzyl oxide ligands, giving rise to terminal and bridging labeled oxygens. The single observed ^{17}O band is consistent with structure **3**, in which axial and equatorial benzyl oxides are not resolved.

Therefore, ^{17}O NMR of labeled tartrate ester complexes are consistent with the proposed tartrate-bridged dimeric structure **3** and not consistent with alkoxide-bridged structures or with an open-ring configuration as in **2**.

Covalent mononuclear d^0 metal oxo–peroxo complexes have been examined by ^{17}O NMR spectrometry.[22] Signals for *tert*-butyl hydroperoxide[22] and 2-phenyl-2-propyl (cumene) hydroperoxide[22c] have been observed, but ^{17}O NMR spectra for complexes of alkyl hydroperoxides with d^0 transition metals have not been reported.

^{17}O NMR spectra of enriched cumene hydroperoxide and cumyl methyl peroxide show well-resolved signals for the different oxygen atoms (entries 27 and 28). Addition of 1 equiv of the hydroperoxide to $Zr(OtBu)_4$ or $Ti(OtBu)_4$ shows little free hydroperoxide in solution and a single peak corresponding to the alkyl peroxide products $[M(OtBu)_3(OOCMe_2Ph)]_n$ (M = Ti, Zr) (entries 29 and 30). Note that the zirconium alkyl peroxide has a chemical shift approximately 100 ppm upfield of its Ti counterpart, similar to the 79 ppm difference between titanium and zirconium tetra-*tert*-butoxides (entries 11 and 19). A single alkyl peroxide peak is similarly observed for mixtures of cumene hydroperoxide and $Ti(OiPr)_4$, but this resonance quickly disappears due to a facile oxidation of isopropyl alcohol to acetone, with the production of labeled metal–oxo moieties (Ti–*O–Ti) and free and bound 2-phenyl-2-propanol-^{17}O (entry 30).

Since the equilibrium constant for replacement of alkoxide on $[Ti(tartrate)(OR)_2]_2$ complexes with tertiary hydroperoxides is small,[8] no bound Ti–$OOCMe_2Ph$ unit is visible in the ^{17}O NMR spectrum of a mixture of $[Ti(DIPT)(OtBu)_2]_2$ and ^{17}O-enriched cumene hydroperoxide (entry 31). Addition of an allylic alcohol produced an immediate appearance in the ^{17}O NMR of labeled epoxy alcohol and 2-phenyl-2-propanol. No intermediate resonances were observed at room temperature.

7. Infrared Spectroscopy of Deuterium-Labeled Alkoxides. In another attempt to distinguish between bridging and terminal modes of alkoxide binding, we have explored the changes in C–H vibrational modes accompanying substitution of deuterium for hydrogen on the carbinol carbon of secondary alkoxides. It was anticipated that the H–D difference spectra for terminal alkoxides would be different from those of bridging alkoxides in characteristic ways. An "H-D" or "difference" spectrum is the subtraction of the IR spectrum of the deuterium-substituted complex (labeled at only one site, such as the methine proton of isopropyl alcohol) from that of the same molecule under the same conditions but containing unlabeled (protio) alkoxide. In such a difference spectrum, only vibrations that involve the labeled bond show nonzero absorbance.

4-Heptanol-*4-d* was prepared by reduction of 4-heptanone with $LiAlD_4$. Deuterium substitution was indicated in the IR by a C–D stretching band centered at 2120 cm^{-1}. Titanium tetra-4-heptoxide, $Ti[OCH(C_3H_7)]_4$, and its deuterium-labeled analogue were prepared by the quantitative reaction of the alcohols with $Ti(NMe_2)_4$. The Ti–tartrate complexes of 4-heptoxide were then prepared by reaction of the tetraalkoxides with $Ti(DIPT)_2$.

Superimposing the H–D difference spectrum for $Ti[OCX(C_3H_7)]_4$ over that of $\{Ti(DIPT)[OCX(C_3H_7)_2]_2\}_2$ (X = H, D) shows them to be nearly identical (Figure 14), even though the metal is bound by tartrate in one case and only by 4-heptoxide ligands in the other. Since $Ti[OCH(C_3H_7)]_4$ is a monomer in solution, the difference FTIR spectra suggest that 4-heptoxide occupies a terminal position in the solution-phase structure of $\{Ti(DIPT)[OCH(C_3H_7)_2]_2\}_2$.

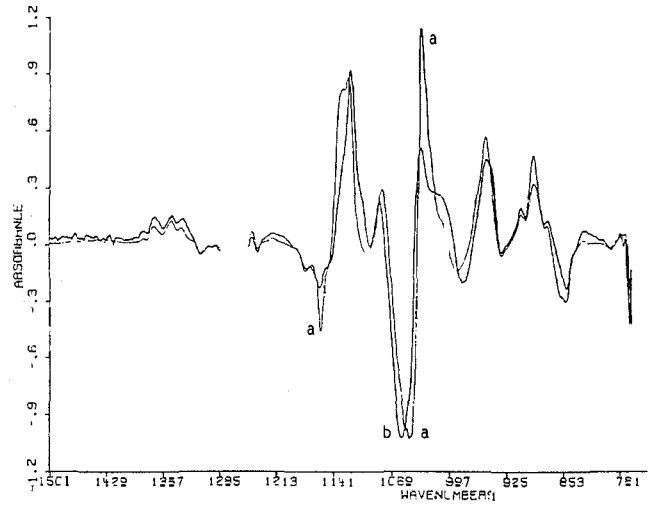


Figure 14. H–D difference IR spectra for $Ti(4\text{-heptoxide})_4$ (a) and $[Ti(DIPT)(4\text{-heptoxide})_2]_2$ (b).

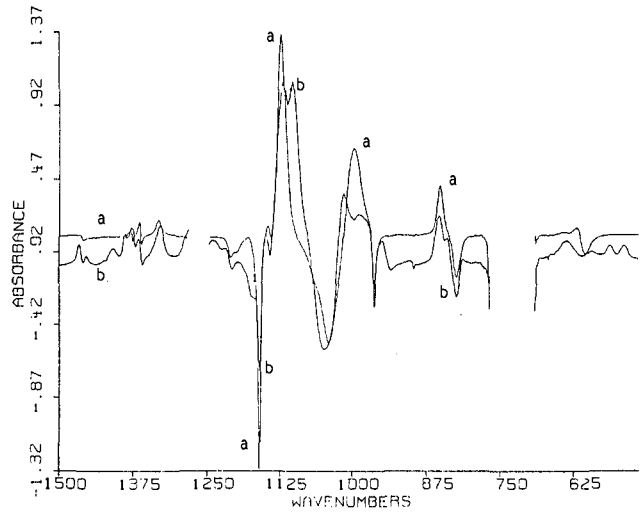


Figure 15. H–D difference IR spectra for $Ti(OiPr)_4$ (a) and $[Ti(DIPT)(OiPr)_2]_2$ (b).

$Ti(OiPr)_4$ is also largely monomeric, so an identical experiment was performed with commercially available isopropyl-*2-d* alcohol. The overlay of H–D difference spectra for $Ti(OiPr)_4$ and $[Ti(DIPT)(OiPr)_2]_2$ is displayed in Figure 15, again showing a good match, though not as close as the 4-heptoxide case [perhaps because of the small amount of oligomeric material present in $Ti(OiPr)_4$].[23]

8. Structure of the Active Catalyst. For the following reasons, the asymmetric epoxidation catalyst is believed to be a dimer:

A. The average molecularity of $[Ti(tartrate)(OR)_2]_x$ in solution is 2.

B. NMR measurements in different solvents show that a single structure comprises at least 80% of the total mixture in solution. Therefore, this major structure must be a dimer.

C. NMR spectra also identify at least one of the minor species in solution as the 2:1 Ti–tartrate complex. This material has been shown to be a much more sluggish epoxidation catalyst than the 2:2 complex.[8] Species containing more tartrate than titanium have also been shown to be poor catalysts for epoxidation of allylic alcohols.

D. The pseudo-first-order rate of epoxidation varies linearly with Ti–tartrate concentration over a 10-fold range,[8] suggesting that the active catalyst does not participate in a bimolecular

(23) The difference IR spectra of titanium tetraisopropoxide and titanium tetra-4-heptoxide are not the same. Since the experiment measures differences in C–H and C–D bending modes, which are affected by adjacent substituents, isopropoxide and 4-heptoxide would not be expected to give the same pattern.

equilibrium reaction with a species of different aggregation state. That is, the dominant dimeric species does not give rise to a trace amount of active reagent by dissociation to two monomers or by association to higher aggregates. The only way for a nondimeric species to be the epoxidation catalyst is for it to be present in trace amounts and for it to be inert to association–dissociation equilibria. The existence of such a substitutionally moribund Ti–tartrate complex is unlikely, and in any case, a catalytically active complex must undergo facile ligand exchange.

For the following reasons, the catalyst structure in solution is thought to correspond to **3**:

A. ^1H and ^{13}C NMR and IR spectra are consistent with such a structure.

B. ^{17}O NMR spectra show resonances of two different tartrate alkoxide oxygens and only one type of monodentate alkoxide, consistent with the tartrate-bridged dimer structure and inconsistent with the 10-membered-ring structure **2** (Figure 2), which has only terminal tartrate alkoxide bonds.

C. Difference FTIR spectra of deuterium-labeled alkoxide complexes show the presence of only terminal isopropoxides in $[Ti(DIPT)(O\textit{i}Pr)_2]_2$, ruling out an isopropoxide-bridged structure analogous to **1** (Figure 2).

9. Comments on the Proposed Mechanism of the Asymmetric Epoxidation Reaction. A detailed discussion of our mechanistic proposal has appeared elsewhere.[2] Here we present additional data to support some of the assumptions underlying that proposal, and additional points concerning the relationship between reactivity and structure of the putative Ti–tartrate catalyst are discussed.

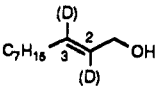
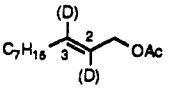
As previously described,[8] titanium tetraalkoxides are more active as epoxidation catalysts in the presence of tartrate than in its absence. This important example of ligand-accelerated catalysis[24] is a consequence of the fact that one of the tartrate-bearing titanium complexes (in this case, the major complex present) is the most reactive catalyst in the equilibrium mixture.

For the asymmetric epoxidation reaction, good kinetic reactivity must include both rapid ligand exchange (to bring the allylic alcohol and hydroperoxide into juxtaposition on the metal center) and efficient and selective oxygen transfer. We propose that structure **3** contains unique structural elements that facilitate this activity.

The bridging tartrate oxygen structure provides a relatively rigid framework in which the bound ester carbonyl groups can dissociate and reassociate rapidly without gross changes in the structure of the complex. Alkoxide ligand exchange on Ti(IV) is likely to proceed by an associative mechanism with respect to the incoming and departing alcohol molecules. In structure **3**, such a mechanism can be facilitated by the dissociation of an ester carbonyl oxygen, providing an open coordination site. Thus, it is observed that exchange of isopropyl alcohol with isopropoxide in $[Ti(tartrate)(O\textit{i}Pr_2)_2]_2$ causes a coalescence of signals at room temperature at a concentration of 0.35 M in Ti (0.7 M in *i*PrOH; Figure 3), whereas a similar mixture of *i*PrOH and $Ti(O\textit{i}Pr)_4$ shows well-resolved alcohol and alkoxide signals. Ligand exchange is therefore more rapid on the Ti–tartrate complex.

The ability to open a coordination site by carbonyl dissociation, bind an incoming alcohol, and then expel the product alcohol with reassociation of the carbonyl is thought to be an important factor in the overall activity of the Ti–tartrate catalyst. By the same token, the ability of the carbonyl group to dissociate in order to accommodate bidentate coordination of the alkyl peroxide, which activates it toward oxygen transfer,[25] also aids the epoxidation step. Furthermore, the coordinated carbonyl group may serve to stabilize the dimer structure and prevent higher oligomers from being thermodynamically favored. These issues have been tested by the preparation of linked bistartrate ligands, as reported elsewhere.[26a]

Table VI. Secondary Deuterium Isotope Effects in Epoxidation Reactions

substrate	oxidant	D position	k_H/k_D
	Ti-DIPT-TBHP	C2	0.990 ± 0.023
		C3	0.958 ± 0.028
	$Ti(O\textit{i}Pr)_4$-TBHP	C2	0.971 ± 0.025
		C3	0.950 ± 0.025
	*m*CPBA	C2	0.928 ± 0.025
		C3	0.927 ± 0.030
	*m*CPBA	C2	0.950 ± 0.025
		C3	0.967 ± 0.025

Structure **3** also has features that are important for the oxygen-transfer step between the coordinated alkyl peroxide and the coordinated allylic alkoxide. First, each Ti center in the structure is equivalent by virtue of its C_2 symmetry. It is important to establish whether each metal atom is equally active as a template for reaction, whether they must act in concert (for example, one binding the substrate and the other the alkyl peroxide), or whether both mechanisms occur. Unfortunately, experimental results currently available do not permit a resolution of this question.[27]

It is least probable that epoxidation occurs by both the single metal-centered mechanism and the binuclear metal-centered mechanism at competitive rates. The exquisite enantioselectivity and substrate tolerance of the reaction is unlikely to be the product of both of these processes, which would have very different transition-state environments. If **3** is indeed the structure of the active catalyst, then it is difficult to rationalize the enantioselectivity in a binuclear metal-centered arrangement. Examples of a single metal-centered epoxidation of an allylic alcohol[29] and an oxidation of a metal–alkyl to an alkoxide[30] are known for d^0 transition-metal alkyl peroxides. For the reasons given above and in the absence of definitive results to the contrary, we assume that asymmetric epoxidation occurs on a single titanium center of dimeric structure **3**.

The tartrate skeleton imposes a dissymmetric environment of pseudo-C_2 symmetry on each metal center of **3**.[2] In order for the epoxidation reaction to proceed, the olefin and peroxide moieties must be oriented in a particular fashion with respect to one another.[2] It is the superposition of the stereoelectronic requirements of the epoxidation transition state and the steric environment of the reaction template that provides high enantioselectivity.

Of particular interest are the observations that triphenylmethyl hydroperoxide and TBHP provide much better enantioselectivity than *n*-butyl hydroperoxide.[8] For steric reasons, the equatorial alkoxide position of **3** appears to be the most likely site for coordination of the alkylperoxide.[2] That Ph_3COOH gives very good and *n*-BuOOH gives relatively poor asymmetric induction indicates

(24) For another example of ligand-accelerated catalysis, see: (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. SOc.* **1988**, *110*, 1968–1970. (b) Jacobsen, E. N.; Markó, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 737–739. (c) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 1123–1125.

(25) (a) Bach, R. D.; Wolber, G. J.; Coddens, B. A. *J. Am. Chem. Soc.* **1984**, *106*, 6090–6099. (b) Bach, R. D.; Wolber, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1410–1415. (c) Lang, T. J.; Wolber, G. J.; Bach, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 3275–3282. (d) Bach, R. D.; Willis, C. L.; Domagala, J. M. In *Progress in Theoretical Organic Chemistry*; Csizmadia, I. G., Ed.; Elsevier: Amsterdam, 1977; Vol. 11, pp 221–229.

(26) (a) Carlier, P. A.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 4016–4018. (b) Burns, C. J.; Martin, C. A.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 2826–2834. (c) Kalantar, T. H. Ph.D. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 1989.

(27) We note, however, that epoxidation of cyclohexen-3-ols proceeds with poor enantiomeric discrimination with Ti–tartrate, but provides exclusively syn epoxy alcohol stereochemistry.[28] If the allylic alcohol and TBHP were bound to different metal atoms of structure **3**, oxygen transfer would be expected to afford the anti epoxy alcohol. What is required is a diolate ligand L that binds in a stable fashion to one of the Ti atoms of $[Ti(tartrate)(OR)_2]_2$ without disrupting the structure of the complex. The kinetic activity of such a $Ti_2(tartrate)_2(L)(OR)_2$ species could then potentially be related to the ability of the metal atoms in $[Ti(tartrate)(OR)_2]_2$ to act independently or together in the asymmetric epoxidation reaction. A variation of this approach has been taken in our laboratories.[26]

(28) Martin, V. S.; Sharpless, K. B., unpublished results.

(29) Lubben, T. V.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1985**, *107*, 701–703.

(30) Van Asselt, A.; Trimmer, M. S.; Henling, L. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 8254–8255.

that the latter allows the reaction to proceed by additional pathways that are inaccessible to the former. In particular, the alkyl peroxide bound in a η^2 fashion may be restricted to one ligand site and transition-state alignment when the alkyl group is large. If the alkyl peroxide is too small, the reactants can achieve the required orientation for oxygen transfer from more than one orientation about the metal center, with a concomitant loss in enantioselectivity.[31]

To gain detailed information about the orientation of the olefin relative to the peroxide, a secondary deuterium isotope effect study was performed for the epoxidation of (*E*)-2-decen-1-ol by {[Ti(DIPT)(O*i*Pr)$_2$]$_2$ + TBHP}, {Ti(O*i*Pr)$_4$ + TBHP}, and *m*-chloroperbenzoic acid (*m*CPBA), as well as the epoxidation of (*E*)-2-decenyl acetate by *m*CPBA. It has been suggested from similar studies that the transition state for epoxidation of styrene by peracid involves formation of one C–O bond of the developing epoxide more than the other.[32a,b]

The results, summarized in Table VI and described in detail in the Experimental Section, show a slightly greater isotope effect at C3 and therefore perhaps a small preference for bond formation to C3 in the titanium-mediated reactions.[33] However, the difference in isotope effect at C2 and C3 is not large enough to conclude that bond formation is significantly skewed, so the peroxide oxygen atom is aligned with the center of the C=C bond in our transition-state models.[2]

Conclusions

The data reported here allow us to draw the following general conclusions about the mechanism of the asymmetric epoxidation reaction.

(1) The Ti–tartrate catalyst can be regarded as a reactivity and stability spike in a complicated mixture of equilibrating complexes. The concentration of each complex in the mixture is dictated by thermodynamic considerations alone, so that conventional ideas about "control" of catalyst structure are irrelevant. The discovery of this catalyst system was serendipitous in that it was impossible to anticipate that a single species would dominate the Ti–tartrate equilibrium mixture and that this species would be so kinetically active. We have since found by tests of approximately 50 tartrate analogues[2,26] and other compatible transition-metal alkoxides that tartrate and titanium are perfectly matched. Slight deviations in ligand structure and/or a change in the metal alkoxide severely reduces the effectiveness of the reaction.

(2) While perhaps not essential, ligand acceleration of the reaction of interest is extremely beneficial. It ensures that the enantioselective version of the reaction (the one in which a chiral auxiliary ligand is present) will be the most viable kinetic pathway. In the absence of ligand-accelerated catalysis, extreme care must be taken to ensure that the chiral auxiliary is always, and in a consistent manner, associated with the transition state.

(3) Titanium–tartrate affords consistent enantioselectivity for widely different substrate structures by virtue of a combination of stereoelectronic and steric factors. The molecular orbital requirements of the epoxidation reaction itself serve to restrict the reactive orientations of the participants; we have made the following stereoelectronic assumptions in considering the mechanism of asymmetric epoxidation:[2] (a) The alkyl peroxide is activated by bidentate coordination to the Ti(IV) center; (b) the olefinic moiety is constrained to attack the coordinated peroxide along the O–O bond axis; and (c) the epoxide C–O bonds are formed simultaneously.

The steric environment about the metal center is then able to favor one of the possible configurations or disfavor all but one.[34] An examination of structure **3** provides the following steric proposals:[2] (a) The bulky alkyl peroxide is forced to adopt a single orientation when bound in a bidentate fashion. (b) The allylic alkoxide is thereby restricted to reaction at a single coordination site on the metal center; consideration of the resulting steric interactions with the catalyst framework provides a rationale for observed kinetic resolution patterns.[2] (c) Efficient catalytic turnover is provided by a labile coordinated ester functionality that allows for rapid alcohol–alkoxide exchange.

(4) While we have been able to make a reasoned proposal of the favored arrangements of tartrate and reactants on the metal at the transition state, the relative importance of the factors that contribute to enantioselection has not been established.[2]

We have previously suggested several possibilities having to do with geometrical aspects of allylic alkoxide and alkyl peroxide orientation and with the stereoelectronic consequences of allylic alkoxide conformations on the reactivity of the olefin.[2] In addition, Jorgensen and co-workers have published the results of a frontier molecular orbital study of the asymmetric epoxidation system,[34] identifying electronic factors that favor the formation of structure **3** and proposing an oxygen-transfer mechanism that is substantially the same as ours.[2,34] Bach and co-workers have been active contributors to the theoretical examination of the reaction[25] and have put forward a cogent picture of the transition state based on ab initio methods.[25a] As yet, evidence supporting a single hypothesis to the exclusion of the others has not been obtained. It must be noted, however, that a recent proposal by Corey featuring an ion-pair transition state is inconsistent with the observed kinetic rate expression.[35]

The ability of the asymmetric epoxidation reaction to tolerate wide variations in substrate structure signals the operation of a directing interaction that is independent of substituents on the allylic alcohol skeleton. Although the ultimate asymmetric determinant(s) have not yet been conclusively identified, the picture that has emerged of the asymmetric epoxidation mechanism provides useful lessons for the design of new enantioselective catalytic systems.

Experimental Section

Spectroscopy, chromatography, and solvent purification were conducted as described.[8] Synthesis and handling of metal alkoxide complexes were performed under a dry nitrogen atmosphere in a recirculating inert-atmosphere glovebox (Vacuum Atmospheres). ^{17}O-Enriched water (23% ^{17}O, 61.5% ^{18}O) was purchased from Monsanto Research Corp., Mound Facility. Elemental analyses were performed by the Robertson Laboratory Inc., Florham Park, NJ.

Molecular Weight Determinations. Molecular weights were measured in solution by the Signer method.[5] Tetra-*n*-butyltin, purified by distillation, was used as the molecular weight standard. Measurements in CH_2Cl_2 and ether required 7–10 days to reach equilibrium, in pentane 5–6 days. Each sample was allowed to stand for at least an additional 4 days. Samples were routinely analyzed by NMR after molecular weight determination and were invariably found to be pure and without decomposition.

For each new sample, after equilibrium had been achieved, solvent was distilled from the unknown to the standard solution (by cooling the standard solution with liquid nitrogen), and the system was allowed to

(31) Jorgensen and co-workers have proposed that electronic factors control the placement of alkyl peroxide in the titanium coordination sphere for asymmetric epoxidation.[34] The dependence of enantioselectivity on hydroperoxide size is evidently not predicted by their model.

(32) (a) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231–5233. (b) Choi, H.-S.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 901–902. For other studies of secondary isotope effects in related reactions, see: (c) Hanzlik, R. P.; Shearer, G. O. *Biochem. Pharmacol.* **1978**, *27*, 1441–1444. (d) Havel, J. J.; Hunt, C. J. *J. Phys. Chem.* **1976**, *80*, 779–782. (e) Hanzlik, R. P.; Westkaemper, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 2464–2467.

(33) Note that epoxidation of the allylic acetate by *m*CPBA apparently occurs with a slight preference for bond formation to C2 in the transition state, in contrast to epoxidation of the allylic alcohol. This may reflect a change in mechanism (directed for the alcohol and not directed for the acetate) or the fact that acetate is more electron withdrawing than the alcohol group.

(34) The recognition of *attractive* stabilization of transition-state structures has been devoted almost exclusively to enzymes and the synthetic systems designed to mimic them. The asymmetric epoxidation reaction has some important characteristics in common with enzymatic reactivity.[41] While we have focused on the steric blocking properties of the Ti–tartrate framework, Jorgensen and co-workers have identified a possible attractive interaction between the allylic alkoxide and the tartrate ester moiety that may have a role in directing the conformation of the transition state: Jorgensen, K. A.; Wheeler, R.; Hoffmann, R. *J. Am. Chem. Soc.* **1987**, *109*, 3240–3246.

(35) Corey, E. J. *J. Org. Chem.* **1990**, *55*, 1693–1694. The putative ion-pair transition state contains 4 equiv of spectator alcohol in addition to the substrate and oxidant. Such a mechanism would not be expected to show the inverse squared dependence of rate on inhibitor alcohol concentration that is observed under pseudo-first-order conditions.[8]

reach equilibrium. In every case, the equilibrium volumes were the same as the first determination. Experimental error is approximately ±10%.

Mass Spectrometry of Titanium-Tartrates. Low-resolution electron impact mass spectrometry was performed on a Varian MAT-44 instrument at 22.3 eV. Solutions of approximately 0.4 M in titanium were prepared in CH_2Cl_2, transferred to dry capillary tubes, and sealed with vacuum grease in the drybox. Each sample tube was placed in the probe holder, the seal was broken, and the probe was quickly placed in the instrument and evacuated, exposing the solution to air for several seconds. After the solvent was removed, the probe was heated slowly to volatilize the sample.

NMR and IR Analyses of Titanium-Tartrates. NMR spectra were measured with Bruker 250- or 270-MHz spectrometers, or with a Varian 300-MHz instrument. Fourier transform IR spectra were obtained on Nicolet 7199 or 60-SX instruments.

$CHCl_3$ was usually dried by distillation onto activated 4-Å molecular sieve beads. In several cases, $CDCl_3$ was satisfactorily dried with two successive treatments of activated 4-Å sieves without distillation. Other NMR solvents were passed through neutral alumina (activity I) before use.

Ti-tartrate complexes were usually prepared by mixing the appropriate molar equivalents of titanium tetraalkoxide and tartrate diester in CH_2Cl_2 at room temperature in the drybox. For alcohol-free samples, three repeated cycles of dissolution in CH_2Cl_2 followed by evaporation in vacuo were performed before the sample was dissolved in the NMR solvent of choice. NMR spectra were found to be insensitive to concentration, except as noted in the text. For band-shape analysis, the samples were approximately 0.25 M in titanium.

It should be noted that complexes prepared from commercially available DIPT and DET and titanium tetraalkoxides (both purified by distillation) were pale yellow. When tartrates were synthesized by other means (by esterification of tartaric acid, or as for the ^{17}O-labeled samples), no yellow color was observed in the titanium complexes. The yellow impurity led to no differences in the NMR and IR spectra or in enantioselectivity of epoxidation. It was later found that silica gel chromatography of the commercial DIPT is sufficient to eliminate the yellow color observed upon formation of its complex with $Ti(O\textit{i}Pr)_4$.

Alcohol-free samples were also prepared by mixing appropriate amounts of $[Ti(tartrate)_2]_n$ and $Ti(OR)_4$. The bistartrate complexes were prepared by mixing 2 equiv of tartrate with the tetraalkoxide of the same alkoxide group [for example, DIPT with $Ti(O\textit{i}Pr)_4$] and removing the liberated alcohol by repeated solvation/vacuum cycles until free alcohol could not be detected by IR or NMR. $Ti(DIPT)_2$ and $Ti(DET)_2$ are viscous oils at room temperature and brittle solids below 0 °C. $Ti(DMT)_2$ is a free-flowing powder at room temperature.

NMR Band-Shape Analysis. NMR band-shape analysis was performed with the DNMR4 program of Bushweller et al. (Quantum Chemistry Program Exchange No. 466).

In order to avoid transesterification of the tartrate esters, combinations in which transesterification is very slow [with $Ti(O\textit{t}Bu)_4$] or degenerate were used. Alcohol-free samples of $[Ti(DIPT)(O\textit{i}Pr)_2]_2$ and $[Ti(DET)(OEt)_2]_2$ were employed to avoid the contribution of alcohol-alkoxide exchange to the line broadening of the NMR spectra. Since these measurements require cleanly resolved signals, only the *tert*-butoxide and isopropoxide methine protons of the Ti-OR resonances were employed. Of the tartrate ester groups, only the isopropyl methine protons of DIPT were used. Every resonance of every Ti-tartrate sample, however, exhibited exchange broadening with changes in temperature.

Each sample was brought to a temperature within 5 °C of that of the NMR probe and then quickly transferred to the instrument. Spectra were obtained after an additional 10–15 min to allow for complete temperature equilibration. The NMR probe temperature was measured with a sample of ethylene glycol or methanol,[36] handled in the same manner as just described, both before and after Ti-tartrate spectra were obtained.

Exchange rates were obtained by varying the rate parameter in the DNMR4 program until the calculated spectra matched the observed, as judged by visual inspection. The reported error limits represent twice the variation in calculated exchange rate necessary for a noticeable difference to emerge between calculated and observed signals. The "relaxation rate" parameter (T_2) in the DNMR4 program for each analysis was varied until the peak width at half-height of a nonexchanging singlet in the spectrum (typically residual CH_2Cl_2) was reproduced in the calculated spectrum. This value was then used in the simulation of the exchanging resonances of interest. (The results were found to be quite insensitive to this value: changing the input value of T_2 by a factor of 2 did not change the value of the exchange rate constant by more than a few percent.)

Data for band-shape analysis appears in Tables VII and VIII.

(36) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 303.

Table VII. Slow-Exchange Parameters for Band-Shape Analysis

complex	resonance	peak positions at $k_{exch} = 0^a$
$[Ti(DET)(O\textit{t}Bu)_2]_2$	DET methine[b]	1296.4, 1231.7 (J = 3.0 Hz)
	Ti-O-*t*Bu	324.2, 318.7
$[Ti(DIPT)(O\textit{t}Bu)_2]_2$	DIPT methine[b]	1284.7, 1245.8 (J = 4.7 Hz)
	*i*Pr ester methine[c]	1272.0, 1262.2
$[Ti(DMT)(O\textit{t}Bu)_2]_2$	DMT methine[b]	1310.6, 1224.4 (J = 1.8 Hz)
	Ti-O-*t*Bu	318.6, 316.1
$[Ti(DIPT)(O\textit{i}Pr)_2]_2$	DIPT methine[b]	1286.0, 1279.3 (J = 7.0 Hz)
	*i*Pr ester methine[c,d]	1275.9 (0.43), 1257.5 (0.50), 1234.8 (0.07)
	Ti-O-*i*Pr methine[d,e]	1191.0 (0.07), 1184.7 (0.50), 1178.1 (0.43)
$[Ti(DET)(OEt)_2]_2$	DET methine[b]	1322.2, 1297.4

[a] In hertz at 250 Hz/ppm. [b] Tartrate methines refer to the italicized atoms: RO_2C-C*H*(OTi)-C*H*(OTi)-CO_2R. [c] *i*Pr ester methine: $Me_2\textit{H}CO_2C$-CH(OTi)-CH(OTi)-$CO_2C\textit{H}Me_2$. Peak positions reported for singlets resulting from decoupling of methyl resonances. [d] Numbers in parentheses refer to relative integral intensities. [e] Ti-O-*i*Pr methine: Ti-O-C*H*Me_2.

Oxygen-17 NMR. General Procedures. ^{17}O NMR spectra were recorded in 10-mm tubes at 33.89 MHz on a Bruker spectrometer or in 5-mm tubes at 40.67 MHz on a Varian instrument, with the following parameters.

Bruker: 50° pulse; sweep width, 42 000 Hz; acquisition delay, 0.16 μs; pulse delay, 0.02 s; acquisition time, 0.098 s; 4K data points; no zero filling; exponential multiplication factor, 50–100.

Varian: 45° pulse; sweep width, 40 000 Hz; acquisition delay, 0.20 μs; pulse delay, 0.02 s; acquisition time, 0.375 s; 30K data points; no zero filling; exponential multiplication factor, 50–100.

Signal strength was found to be insensitive to acquisition delay. However, pulse breakthrough was a problem that could only be addressed by increasing the receiver delay at the expense of signal strength. If too short a receiver delay was used, the baseline signal became erratic to the point of completely masking real signals. A compromise value was chosen so that weak resonances requiring long acquisitions still had some instability to the baseline. Proton decoupling was not performed.

Chemical shifts were referenced to external diethyl ether, $Ti(O\textit{t}Bu)_4$, or $Ti(O\textit{i}Pr)_4$. At least one and usually two of these standards were run at the beginning of every session and the peak positions were found to be very reproducible. For peaks of less than 40 ppm line width, an error of ±2 ppm was found; for wider bands, an error of ±5 ppm was observed. Chemical shifts are reported relative to D_2O.

Spectra of natural-abundance samples were obtained at high concentration (approximately 1–2 M). ^{17}O-enriched samples were examined at 0.1–0.3 M. No variations with concentration were observed.

Preparation of ^{17}O-Labeled Cumene Hydroperoxide. α,α-Dimethylbenzyl hydroperoxide (cumene hydroperoxide) was prepared by autoxidation using $^{17}O_2$ gas (20% ^{17}O), purchased from Cambridge Isotope Laboratories, as follows.

A 100-mL round-bottomed flask was charged with 24.0 g of cumene (0.20 mol), which had been freed of trace phenols by passage through a column of silica gel (240 mesh, 20 cm × 1 cm diameter), capped with a reflux condenser, and placed on a volumetric gas buret apparatus. After evacuation the apparatus was charged with $^{17}O_2$ at 1 atm pressure. The reaction flask was heated to 80–88 °C with vigorous stirring. After a 15-h induction period, $^{17}O_2$ uptake began and slowly accelerated. After 77 h, a total of approximately 0.87 L of O_2 was consumed.

The reaction mixture was flash chromatographed in 1:9 EtOAc-hexane (20 × 5 cm), and the product was taken up in 30 mL of CH_2Cl_2 and transferred to a brown bottle containing activated 3-Å sieve beads. After standing for 3 h at room temperature, the solution was filtered, the sieves were washed with dry CH_2Cl_2 (3 × 10 mL), and the combined solution was stored over a second batch of sieves. The solution was again filtered, the remaining sieves were washed with dry CH_2Cl_2 (3 × 10 mL), and the solvent was removed to afford 4.05 g (69% based on O_2) of neat cumene hydroperoxide as a clear oil: ^1H NMR ($CDCl_3$) δ 7.63 (s, 1 H, OOH), 7.45–7.20 (m, 5 H), 1.55 (s, 6 H); IR (film) 3410 (br, O-H), 812 (O-O) cm^{-1}.

Preparation of ^{17}O-Labeled (Hydroxyl) Tartrate. ^{17}O-enriched tartrates were prepared by catalytic dihydroxylation of di-L-menthyl fumarate by the following procedures.

A solution of 21.56 g of L-menthol (0.138 mol) in 250 mL of toluene was treated with 29 g of polyvinylpyridine (approximately 0.27 mol of active amine) under dry nitrogen. To this stirred mixture was added a solution of fumaryl chloride (9.59 g, 0.0627 mol) in 5 mL of toluene; the reaction mixture turned light pink. After 48 h at reflux, the reaction mixture was cooled and filtered to afford a light brown solution. Evap-

Table VIII. NMR Band-Shape Analysis Data

complex	resonance	T, K	T_2, s	k_{exch}[a]	$\Delta G^{\ddagger}$, kcal/mol
$[Ti(DET)(OtBu)_2]_2$	DET methine	271.0	0.16	3.0 ± 1.0	15.2 ± 0.3
		283.7	0.22	12 ± 2	15.2 ± 0.2
		291.7	0.20	35 ± 5	15.0 ± 0.1
		297.2	0.23	62 ± 3	15.0 ± 0.1
		297.4	0.39	70 ± 5	14.9 ± 0.1
		304.9	0.24	125 ± 10	14.9 ± 0.1
		314.1	0.25	235 ± 10	15.0 ± 0.1
		322.6	0.39	420 ± 20	15.1 ± 0.1
	Ti–O–*t*Bu	271.0	0.33	6.0 ± 2.0	14.8 ± 0.3
		283.7	0.25	14 ± 2	15.1 ± 0.1
		291.7	0.29	30 ± 5	15.1 ± 0.1
		297.2	0.23	50 ± 10	15.1 ± 0.2
		297.4	0.35	75 ± 15	14.9 ± 0.2
		304.9	0.35	130 ± 15	14.9 ± 0.1
$[Ti(DIPT)(OtBu)_2]_2$	DIPT methine	255.4	0.13	0.75 ± 0.25	15.0 ± 0.2
		267.3	0.14	2.0 ± 1.0	15.2 ± 0.3
		271.0	0.21	6.5 ± 0.5	14.8 ± 0.1
		274.4	0.23	6.0 ± 1.0	15.0 ± 0.1
		238.7	0.25	18 ± 2	14.9 ± 0.1
	*i*Pr ester methine	255.4	0.09	0.2 ± 0.15	15.7 ± 0.5
		267.3	0.21	4.0 ± 1.5	14.9 ± 0.2
		274.4	0.20	6.0 ± 1.0	15.0 ± 0.1
		283.7	0.23	18 ± 1	14.9 ± 0.1
		297.4	0.21	66 ± 3	14.9 ± 0.1
$[Ti(DMT)(OtBu)_2]_2$	DMT methine	271.0	0.31	2.5 ± 0.5	15.3 ± 0.1
		274.4	0.25	3.0 ± 0.5	15.4 ± 0.1
		283.7	0.33	6.5 ± 1.0	15.5 ± 0.1
		297.2	0.20	25 ± 5	15.5 ± 0.2
		297.4	0.27	30 ± 5	15.4 ± 0.1
		304.9	0.27	82 ± 6	15.2 ± 0.1
		309.5	0.34	115 ± 10	15.2 ± 0.1
		314.1	0.36	140 ± 10	15.3 ± 0.1
		322.6	0.36	210 ± 10	15.5 ± 0.1
$[Ti(DIPT)(OiPr)_2]_2$	*i*Pr ester methine	260.0	0.15	2 ± 1	14.8 ± 0.3
		267.3	0.32	7 ± 1	14.6 ± 0.1
		274.4	0.20	14 ± 3	14.6 ± 0.2
		283.7	0.20	25 ± 6	14.8 ± 0.2
	DIPT methine	267.3	0.32	11.5 ± 0.5	14.3 ± 0.1
$[Ti(DET)(OEt)_2]_2$	DET methine	246.0	0.25	29 ± 2	12.7 ± 0.1
		252.7	0.19	32 ± 3	13.0 ± 0.1
		262.0	0.14	43 ± 3	13.3 ± 0.1
		271.0	0.17	70 ± 3	13.5 ± 0.1
		283.7	0.21	110 ± 5	13.9 ± 0.1
		295.1	0.22	160 ± 10	14.3 ± 0.1

oration of solvent and flash chromatography (5:95 EtOAc–hexane) afforded 16.39 g of di-L-menthyl fumarate as a yellow oil; $[\alpha]^{25}_D$ −84.7° (*c* 6.03, 95:5 EtOH–H_2O); ^1H NMR ($CDCl_3$) δ 6.83 (s, 2 H), 4.78 (dt, J_1 = 10.4 Hz, J_2 = 4.4 Hz, 2 H), 2.04 (dm, J_1 = 10 Hz, 2 H), 1.88 (doublet of quintets, J_1 = 7.4 Hz, J_2 = 2 Hz, 2 H), 1.71 (br d, 4 H), 1.59–1.35 (m, 4 H), 1.27 (t, J = 7.4 Hz, 2 H), 1.07 (m, 6 H), 0.92 (dd, J_1 = 6.8 Hz, J_2 = 3 Hz, 12 H), 0.77 (d, J = 6.8 Hz, 6 H); IR ($CHCl_3$) 1712 ($\nu_{C=O}$), 1640 ($\nu_{C=C}$) cm^{-1}.

It was found that the quinuclidine adduct of OsO_4 undergoes exchange with $^{17}OH_2$ readily in THF or *tert*-butanol. The following procedure for OsO_4-catalyzed dihydroxylation of dimenthyl fumarate is based on that of Van Rheenen and co-workers.[37]

A 100-mL round-bottomed flask was charged with *N*-methylmorpholine *N*-oxide monohydrate (3.70 g, 0.0274 mol). The solid was heated in a 90–95 °C bath with stirring under vacuum (0.15 Torr) overnight, after which some of the material had sublimed to the upper part of the flask. After cooling to room temperature, dry *tert*-butanol was introduced (7 mL), followed by $^{17}OH_2$ (1.00 g, 0.0514 mol) and OsO_4 (0.63 mL of a 0.1 g/mL solution in hexane, 2.4 × 10^{-4} mol). The reaction vessel was heated to 35–40 °C with stirring while a solution of 4.80 g of di-L-menthyl fumarate (0.0122 mol) in 3 mL of *tert*-butanol was added to the reaction flask over 12 h with a syringe pump. TLC (1:9 EtOAc–hexane) showed the olefin to be oxidized very rapidly upon addition, such that no unreacted olefin accumulated during the addition. This slow-addition procedure was designed to maximize ^{17}O incorporation.

(37) Van Rheenen, V. I.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973–1976.

Following complete addition of the substrate, the reaction mixture was degassed by two freeze/pump/thaw cycles and the solvent was removed by bulb-to-bulb distillation under vacuum to recover unused $^{17}OH_2$. The resulting brown sticky solid was taken up in CH_2Cl_2 and ether (1:2, 300 mL) and washed with aqueous $NaHSO_3$ (1.8 M) until the disappearance of the brown color. The aqueous phase was extracted with CH_2Cl_2 (60 mL), and the combined organic phases were washed with saturated NaCl, dried ($MgSO_4$), and concentrated to afford 5.19 g of crude product as a yellow oil. The diastereomeric diols have R_f values of 0.75 and 0.71 on TLC (silica) in 1:9 EtOAc–hexane. Flash chromatography twice (5:95 EtOAc–hexane) afforded 1.87 g of the less polar diastereomer, (2*R*,3*R*)-di-L-menthyl tartrate (**6**), 0.45 g of the more polar diastereomer, (2*S*,3*S*)-di-L-menthyl tartrate (**7**), and 2.02 g of a mixture of diols (total 4.34 g, 82%). These colorless diol diesters are viscous oils that foam under vacuum. The absolute configuration assignments are derived from the optical rotations of DIPT generated by transesterification of these menthyl esters. The ^{17}O enrichment was estimated at 22%.

For **6**: ^1H NMR ($CDCl_3$) δ 4.84 (dt, J_1 = 13.3 Hz, J_2 = 5.0 Hz, 2 H), 4.35 (d, J = 8.4 Hz, 2 H), 3.11 (d, J = 8.4 Hz, 2 H, OH), 2.07 (br d, 2 H), 1.96 (m, 2 H), 1.72 (br d, 4 H), 1.6–1.4 (m, 4 H), 1.07 (m, 4 H), 0.92 (t, 14 H), 0.77 (d, J = 6.2 Hz, 6 H); ^{13}C NMR (CD_2Cl_2) δ 171.7, 77.0, 72.4, 47.4, 41.0, 34.5, 31.8, 26.7, 23.7, 22.1, 20.9, 16.3; IR (CH_2Cl_2) 1740 ($\nu_{C=O}$). Anal. Calcd for $C_{24}H_{42}O_6$: C, 67.57; H, 9.92. Found: C, 67.23; H, 9.68.

For **7**: ^1H NMR ($CDCl_3$) δ 4.88 (dt, J_1 = 13.3 Hz, J_2 = 4.7 Hz, 2 H), 4.49 (d, J = 7.3 Hz, 2 H), 4.14 (d, J = 7.3 Hz, 2 H, OH), 2.05 (br d, 2 H), 1.88 (m, 2 H), 1.72 (br d, 6 H), 1.6–1.4 (m, 4 H), 1.08 (m, 4 H), 0.92 (d, 14 H), 0.79 (d, J = 7 Hz, 6 H); ^{13}C NMR (CD_2Cl_2) δ 171.7, 77.2, 72.6, 47.4, 41.1, 34.5, 31.8, 26.3, 23.4, 22.1, 20.9, 16.0; IR (CH_2Cl_2)

same as for **6**. Anal. Calcd for $C_{24}H_{42}O_6$: C, 67.57; H, 9.92. Found: C, 67.42; H, 9.89.

Transesterification of the dimenthyl esters was somewhat difficult. Of several acid-catalyzed methods tried, reaction with $Ti(OiPr)_4$ in isopropyl alcohol proved to be the best. Thus, samples of **6** or **7** in 35 mL of dry isopropyl alcohol were treated with approximately 0.5 equiv of $Ti(OiPr)_4$, and refluxed for 12 h. Quenching with a mixture of 20% aqueous tartaric acid and ether (50 mL), extraction with ether and CH_2Cl_2, drying ($MgSO_4$), and removal of solvent afforded mixtures of L-menthol, DIPT, and partially transesterified material (menthyl isopropyl tartrate). Flash chromatography (2:3 EtOAc–hexane) afforded 50–70% yields of ^{17}O-enriched DIPT. The less polar dimenthyl tartrate, **6**, afforded (+)-DIPT: $[\alpha]^{25}_D$ +13.00° (*c* 6.2, CCl_4). The more polar dimenthyl tartrate, **7**, afforded (−)-DIPT: $[\alpha]^{25}_D$ −13.06° (*c* 10.25, CCl_4). Commercially available (+)-DIPT shows $[\alpha]^{25}_D$ +13.08° (*c* 5.85, CCl_4). ^1H and ^{13}C NMR spectra of the labeled DIPT were identical with those of authentic samples. Infrared spectroscopy in CH_2Cl_2 showed an O–H stretching frequency of 3521 cm^{-1} for the labeled tartrate, compared to 3528 cm^{-1} for unlabeled tartrate. Anal. Calcd for (+)-DIPT from **6**, $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.09; H, 7.73.

It was later discovered that base-catalyzed transesterification of DIPT to DET (EtOH solvent, catalytic NaOMe, room temperature, 12 h) resulted in negligible epimerization of the tartrate (about 1%) by optical rotation. This method, then, may be superior to titanium-catalyzed transesterification for the production of DET from dimenthyl tartrate.

Preparation of ^{17}O-Labeled Benzyl Alcohol. A solution of benzaldehyde (2.00 g, 0.0187 mol) in THF (50 mL) was treated with approximately 20 mg of *p*-toluenesulfonic acid and 1.00 g (0.0516 mmol) of $^{17}OH_2$ under a nitrogen atmosphere. After 2 h at room temperature, the reaction mixture was cooled to −20 °C and a suspension of 2.7 g of $LiAlH_4$ (0.071 mol) in diethyl ether (100 mL) cooled to −20 °C was added portionwise by cannula. After stirring for 2 h while warming to room temperature, workup afforded 1.96 g of benzyl alcohol-^{17}O as a colorless oil. Distillation at ambient pressure (bp 204 °C) afforded 1.85 g (91%) of dry benzyl alcohol of an estimated 17% ^{17}O enrichment. Anal. Calcd for C_7H_8O: C, 77.75; H, 7.46. Found: C, 77.49; H, 7.53.

Secondary Deuterium Isotope Effects in Epoxidations of 2-Decen-1-ol Substrates. Preparation of Substrates. (*E*)-2-Decen-1-ol (**8**) was prepared by reduction of 2-decyn-1-ol by $LiAlH_4$–NaOMe in the manner of Corey and co-workers.[38]

(*E*)-3-Deuterio-2-decen-1-ol (**9**) was prepared by a similar reduction, followed by quenching with iodine in THF to yield (*E*)-3-iodo-2-decen-1-ol. The iodo alcohol was treated with 2 equiv of *t*BuLi and quenched with D_2O in THF to provide a 4:1 mixture (by NMR) of **9** and the protio allylic alcohol, respectively. Mass spectra indicated the deuterium content to be 83.7%. This product was used as obtained and the competition experiment adjusted for an 84% deuterium content. GC analysis showed no (*Z*)-allylic alcohol to be present for each of the (*E*)-allylic alcohols prepared.

For **9**: ^1H NMR ($CDCl_3$) δ 5.69 (m, 0.2 H), 5.64 (m, sharpens to br s upon irradiation at 4.09 ppm, 1 H), 4.09 (d, *J* = 5.7 Hz, 2 H), 2.05 (t, *J* = 7.3 Hz, 2 H), 1.25–1.38 (m, 9 H), 0.90 (t, *J* = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 133.26 (d, small), 128.7 (d), 63.5, 32.1, 31.8, 29.1, 22.6, 14.0. Anal. Calcd for $C_{10}H_{19}OD$: C, 76.87; H, 12.90. Found: C, 76.78; H, 12.62.

Reduction of 2-decyn-1-ol with $LiAlD_4$ (approximately 98 atom % D) and NaOMe followed by treatment with I_2 provided (*E*)-3-iodo-2-deuterio-2-decen-1-ol. Lithiation and hydrolysis with H_2O provided (*E*)-2-deuterio-2-decen-1-ol (**10**) of 98.5 atom % deuterium, as determined by mass spectrometry.

For **10**: ^1H NMR ($CDCl_3$) δ 5.69 (br t, collapses to br s on irradiation at 4.09 ppm, 1 H), 4.09 (d, *J* = 6.0 Hz, 2 H), 2.05 (q, *J* = 6.7 Hz, 2 H), 1.28 (m, 9 H), 0.89 (t, *J* = 6.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 132.9, 128.5 (t), 63.2, 32.1, 31.7, 29.0, 22.5, 14.9. Anal. Calcd for $C_{10}H_{19}OD$: C, 76.87; H, 12.90. Found: C, 76.67; H, 13.08.

The *tert*-butyldimethylsilyl ethers of the allylic alcohols were found to give reproducible quantitative mass spectra, using the $[M - 57]^+$ (M − *t*-Bu) peak. These derivatives were made by the following general method: to a solution of 1 equiv of allylic alcohol and 3 equiv of triethylamine was added 2 equiv of *tert*-butyldimethylsilyl trifluoromethanesulfonate at 0 °C. After 10 min, 1 mL of water was added, followed by 5 mL of 0.5 N HCl. The organic phase was dried (Na_2SO_4) and the solvent removed to give a colorless oil. Flash chromatography (1:5 EtOAc–hexane) yielded the pure silyl ethers.

Low-resolution electron impact mass spectra were performed on a Finnigan MAT 8200 spectrometer at 70 eV. The precision was improved by limiting the scanning region to *m/e* values of 208–218 and by averaging 95–100 spectra taken in succession at a period of steady overall ion abundance; standard deviations for the intensities of the peaks of interest were ±2% (relative). The observed isotope ratios at 213, 214, 215, and 216 amu matched the calculated ratios within 5%. The ratio of peak intensities at 213 and 214 amu were more accurate (2%) and were used to determine the ratio of deuterio- to protio-substituted allylic alcohols, as in the following example.

For **9**, the C3-*d* allylic alcohol, the mass spectrum confirmed the presence of approximately 20% of the diprotio allylic alcohol indicated by the NMR spectrum. The relative intensities of peaks at 213 and 214 amu were 19.31 and 100, respectively. In the following discussion, let $[A]^+$ stand for the $[M - t\text{-Bu}]^+$ ion. For $C_{12}H_{25}OSi$, the relative intensities should be $[A]^+ = 100$ and $[A + 1]^+ = 18.34$. Assuming that the [213] peak was entirely due to the $[A]^+$ of the diprotio substrate, its contribution to the [214] peak must be (19.31)(18.34%) = 3.54. Therefore, the contribution of the deuterated substrate to the [214] peak was 100 − 3.54 = 96.46, and the H to D ratio (the ratio of the $[A]^+$ ions of each molecule) was 19.31/96.46 = 1.00/5.00; the diprotio allylic alcohol therefore comprised 16.7% of the total. Further details of the secondary deuterium isotope effect experiments can be found in the supplementary material.

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Supplementary Material Available: Experimental details for the determination of secondary deuterium isotope effects (5 pages). Ordering information is given on any current masthead page.

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