be introduced in order to keep the lone pairs of electrons from flowing into the $\sigma^*$-orbital. As many linkages between the amino nitrogens and N=N bonds in **17** should be contained as possible.

**Acknowledgment.** The ab initio molecular orbital calculations were carried out on a HITAC-M200H computer, Institute for Molecular Science, with the IMSPAK program. The subsequent configuration analysis was carried out on a FACOM M-360 computer, Gifu University Computing Center. This work was partially supported by Saneyoshi Scholarship Foundation.

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# Electronic and Steric Factors Determining the Asymmetric Epoxidation of Allylic Alcohols by Titanium–Tartrate Complexes (The Sharpless Epoxidation)

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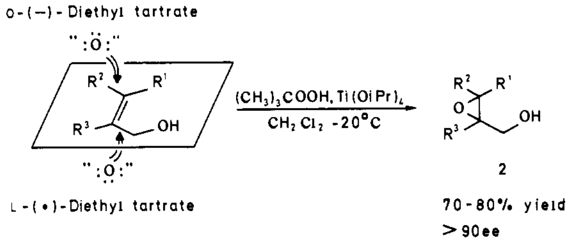
**Abstract:** The structure and epoxidation properties of titanium–tartrate asymmetric epoxidation catalysts have been studied by using the frontier orbital approach. It is suggested that an important factor determining the dimeric structure of these titanium–tartrate epoxidation catalysts is electronic, as one of the LUMOs, located at the titanium atom, is oriented so it facilitates nucleophilic trans coordination to the titanium of the carbonyl group in the tartrate. Coordination of a peroxide to titanium–tartrate is analyzed. From the frontier orbitals at the equatorial peroxygen, four possible orientations of the allylic alcohol are possible. Analysis of the preferred orientation of a hydroxyl and a methoxy group at the equatorial site at the titanium atom, and of an alkene around the peroxygen, led to a spiro orientation of the alkene part of the allylic alcohol at the peroxygen as the most probable. The preferred orientation of the allylic alcohol at the titanium atom is discussed in relation to electronic as well as steric interactions with the tartrate. The orientation and reactivity of the alkene part of the allylic alcohol can be traced to two two-electron interactions: one is the peroxygen lone pair electron interaction with the $\pi^*$ orbital of the alkene part of the allylic alcohol and the other is the interaction of the titanium–peroxygen antibonding orbital with the $\pi$ orbital of the alkene.

Epoxidation of alkenes, and especially asymmetric epoxidation, is a fundamental and important organic reaction type. The asymmetric epoxidation was pioneered by Herbst, who used chiral monoperoxycamphoric acid to produce chiral epoxides with an enantiomeric excess of 5% or less;[1] later Pirkle and Rinaldi were able to improve the enantiomeric excess to 9%.[2] Catalytic epoxidation with hydrogen peroxide and *tert*-butyl hydrogen peroxide catalyzed by chiral phase-transfer agents such as benzyl guinidinium salts was investigated by Hummelen and Wynberg, with moderate success.[3] The first transition metal catalyzed asymmetric epoxidation was reported independently by Sharpless et al.[4] and Yamada et al.,[5] the first with vanadium and the second molybdenum complexes. Further examples of molybdenum-catalyzed epoxidations were reported by Otsuka et al.,[6] who described the treatment of squalene with a mixture of *tert*-butyl hydroperoxide, chelated molybdenum oxide, and the chiral inducing agent (+)-diisopropyl tartrate. By this method it was possible to obtain (*S*)-2,3-squalene epoxide in 14% enantiomeric excess.

The real breakthrough in asymmetric epoxidation came when Sharpless et al. treated a mixture of commercially available titanium tetraisoproxide, *tert*-butyl hydroperoxide, and (+)- or (−)-diethyl tartrate with allylic alcohols.[7] With (−)-diethyl tartrate the oxidant approaches the allylic alcohol from the top side of the plane shown in **1**, whereas the bottom side is open for the (+)-diethyl tartrate reagent, giving rise to the corresponding optically active epoxy alcohols, **2**. This asymmetric epoxidation, now known as the Sharpless epoxidation, has already shown its power in the synthesis of natural products.[8]



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Recently the structures of a series of titanium–tartrate derivatives have been published,[7h,i,9] and two of these structures are

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[†] Aarhus University.

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(1) Herbst, H. B. In *Organic Reaction Mechanisms* (Special Publications No. 19); Chemical Society: London, 1965; p 83.

(2) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1977**, *42*, 2080.

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(7) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 464. (c) Katsuki, T.; Lee, A. M. W.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (d) Behrens, C. H.; Sharpless, K. B. *Aldrichim. Acta* **1983**, *16*, 67. (e) Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589. (f) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (g) Ko, S. Y.; Lee, A. W. M.; Masamume, S., Reed, L. A., III; Sharpless, K. B.; Walker, T. J. *Science* **1983**, *220*, 949. (h) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1986; Vol. 5, p 247. (i) Finn, M. G. Ph.D. Thesis, 1985, Massachusetts Institute of Technology.

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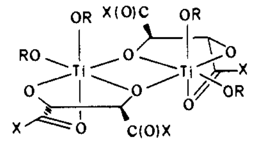
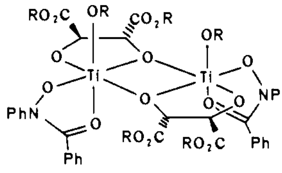
depicted below. The observed structures of titanium–tartrate



**3**: R = Pr$^i$
X = NHCH$_2$Ph



**4**: R = Et

complexes are all least dimeric.[7h,i,9] Since it is important in the sequel, let us describe briefly the structure of **3**: Each titanium atom is facially coordinated by a tartrateamide ligand through the two diolate oxygen atoms, and one of the carbonyl oxygen atoms. The two isopropoxide ligands are located trans to one of the diolate oxygens and to the carbonyl oxygen. The last titanium coordination site is occupied by a bridging diolate oxygen from the other tartrateamide moiety. This binds the two titanium atoms together, producing six-coordinate, pseudooctahedral coordination of both metal centers. With these structures of the titanium–tartrate complexes in hand, attempts have been made to explain the mechanism of the asymmetric epoxidation: It has been suggested that first the two alkoxide ligands are exchanged and the carbonyl oxygen dissociates (for **3**). This exposes a meridional set of coordination positions on each titanium atom for binding the allylic alkoxide and potentially bidentate *tert*-butyl peroxide.[7h,i,9,10]

A recent theoretical paper by Bach and Coddens[11] describes the mechanism for this type of asymmetric epoxidation using a very different approach from ours. Bach and Coddens used LiOOH as a model for the titanium–tartrate peroxo system and the analysis was performed with use of ab initio calculations.[11] On the basis of different approaches of the allylic alcohol around the peroxygens, they found no electronic origin for the high enantioselectivity found in the Sharpless epoxidation. Bach and Coddens then concluded that steric effects associated with the three-dimensional chiral nature of the catalyst are largely responsible for the transfer of oxygen to a specific enantioface of the alkene.[11]

Our approach here is quite different. We will build up a more detailed model of the titanium–tartrate complex, albeit by a more approximate computational method. Then on the basis of the electronic structure of that model we will try to see in detail if it is a steric and/or an electronic factor which underlies the asymmetric action. For these purposes we will mainly use the frontier orbital approach and extended Hückel calculations.[12] We know that the energy difference between the two transition states leading to the two different optically active epoxy alcohols is of the magnitude of just a few kcal·mol$^{-1}$. The extended Hückel method is not reliable at this level. Nevertheless we think that the approach presented here gives substantive clues about the mechanism of this type of asymmetric epoxidation and the structure of the catalysts.

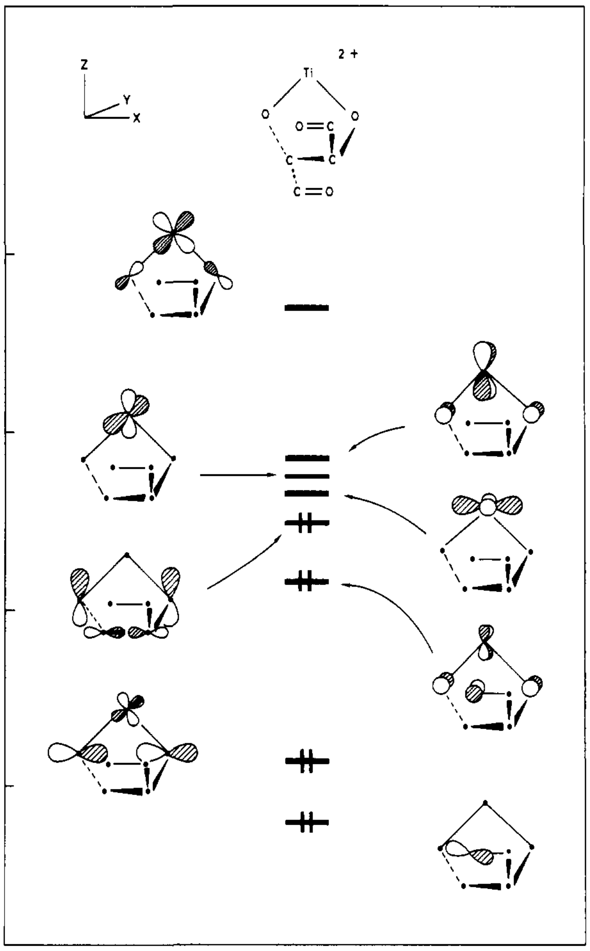
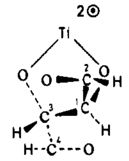


Figure 1. The frontier orbitals of the titanium–tartrate complex with $C_2$ symmetry. The hydrogens and the carbonyl group located below the $xz$ plane are omitted for clarity.

Let us start with a symmetric titanium ($R$,$R$)-tartrate system **5**. The frontier orbitals of **5** are shown in Figure 1. Only those



**5**

orbitals which are necessary for the analysis presented here are shown in Figure 1. The HOMO of the symmetric titanium–($R$,$R$)-tartrate complex, **5**, is mainly of $p_z$ and $p_x$ character on the two diolate oxygens and the two carbons in the tartrate ring, respectively. The second highest occupied MO (second HOMO) shown in Figure 1 is mainly located on the oxygens and is of $p_y$ symmetry; the part located on the diolate oxygens overlaps with $d_{yz}$ on titanium in a bonding way, whereas the part located on the carbonyl oxygen has lone pair character. The third HOMO is a bonding combination of titanium $d_{xz}$ and $p_x$ on the diolate oxygens, whereas the fourth HOMO is mainly located on the carbonyl oxygen and is a combination of $p_x$ and $p_y$. The LUMO of **5** is titanium $d_{x^2-y^2}$, the second LUMO is titanium $d_{z^2} - d_{xy}$, and third and fourth LUMOs are the antibonding counterparts of the second and third HOMOs discussed above.

From the shape of the frontier orbitals depicted in Figure 1 no preference for the approach of a nucleophile in the $xz$ plane seems obvious. But the fragment is highly coordinatively unsaturated or electron deficient. An intramolecular interaction to relieve partially this unsaturation becomes possible. The LUMO $d_{x^2-y^2}$ on titanium points in a direction which favors an interaction

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(8) See, e.g.,: (a) Wood, R. D.; Ganem, B. *Tetrahedron Lett.* **1982**, *23*, 707. (b) McWhorter, W. W., Jr.; Kang, S. H.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3693. (c) White, J. D.; Avery, M. A.; Choudhry, S. C.; Dhingra, O. P.; Whittle, A. J. *J. Am. Chem. Soc.* **1983**, *105*, 6517. (d) Helbig, W. *Liebigs. Ann. Chem.* **1984**, 1165. (e) Takono, S.; Morinoto, N.; Ogasawara, K. *Synthesis* **1984**, 834. (f) Adams, C. E.; Walker, F. J.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 421. (g) Trost, B. M. *Science* **1983**, *219*, 245. (h) Mosher, H. S.; Morrison, J. D. *Ibid.* **1983**, *221*, 1013. (i) Masamune, S.; Choy, W.; Petersen, J. D.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. (j) Rossitier, B. E. In *Asymmetric Synthesis*; Morrison, J. D.; Academic Press: New York, 1986; Vol. 5, Chapter 7.

(9) Williams, I. D.; Pedersen, S. F.; Sharpless, K. B.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 6430.

(10) Mimoun, H.; Chaumette, P.; Mignard, M.; Saussine, L.; Fischer, J.; Weiss, R. *Nouv. J. Chim.* **1983**, *3*, 467.

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(12) (a) Hoffmann, R. *J. Chem. Phys.* **1963**, 39, 1397. (b) Hoffmann, R.; Lipscomb, W. N. *Ibid.* **1962**, *36*, 2179; **1962**, *37*, 177, 2872.

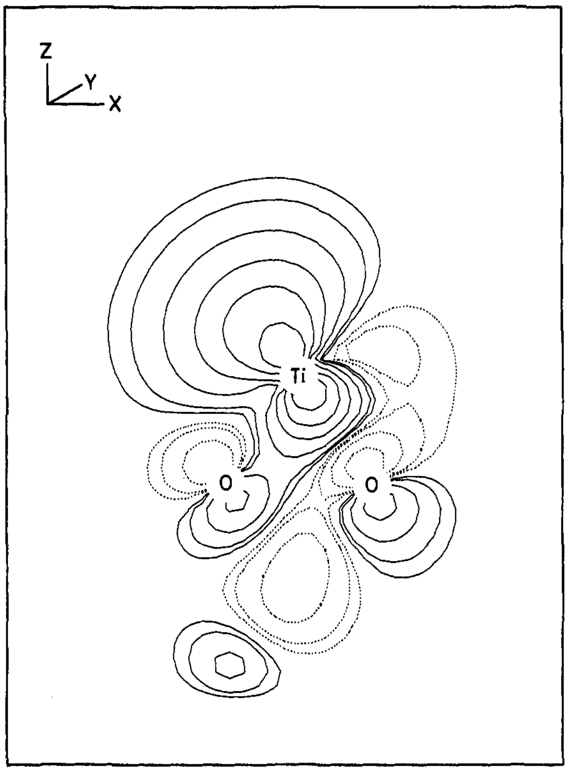
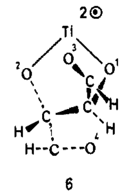


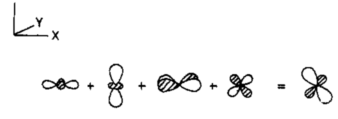
**Figure 2.** Contour plot of one of the LUMOs of the unsymmetric titanium–tartrate **6**. The contour levels of $\psi$ are 0.2, 0.1, 0.055, 0.025, 0.01, and 0.005. The plane is $xz$.

with the lone pair electrons located on the oxygen in the carbonyl function. This interaction can be achieved by a rotation around the $C^1$–$C^2$ bond or the $C^3$–$C^4$ bond in **5**, leading to an unsymmetric titanium–(*R*,*R*)-tartrate complex, **6**.



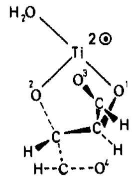
6

The structure of **6** has been modified so it is very similar to the titanium–tartrate moiety in **3**. Within the extended Hückel framework the total energy of **6** has been calculated to be several eV's lower than **5**. The stabilization of **6** relative to **5** comes mainly from bonding interaction between titanium and the oxygen in the carbonyl group (see Appendix II for a cautionary note). The overlap population between Ti and $O^3$ in **6** is 0.356 (compared with ~0 in **5**), indicating a relatively strong coordination of oxygen. For comparison the overlap population between titanium and the diolate oxygens, $O^1$ and $O^2$ in **6**, is 0.527 and 0.556, respectively, but these are also located 0.27 Å nearer the titanium atom. There is much orbital mixing as a consequence of this deformation. A significant asymmetry is introduced into one of the LUMOs located at −8.60 eV. Through a mixing of $d_{x^2-y^2}$, $d_{z^2}$, $d_{xy}$, and $d_{xz}$ shown below in **7**, this d orbital becomes asymmetric, concentrated in the $xz$ plane. A contour plot of this orbital is shown in Figure 2.

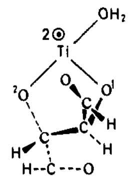


7

Given the asymmetry of the unoccupied orbital shown in Figure 2, a trans approach of $H_2O$ (a model for the bridging diolate oxygen from the other tartrate moiety) leading to **8a** should thus be expected to give the most stable titanium–tartrate–water complex. Calculation of the total energy for **8a** and the corresponding cis water complex, **8b**, verify this, as the former complex has a total energy that is 0.47 eV lower than the latter (see Appendix II).



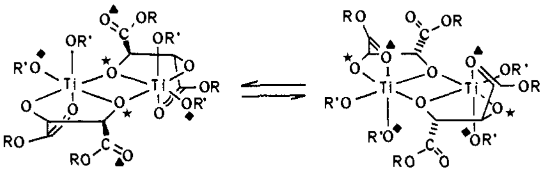
8a



8b

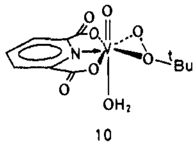
In an attempt to get a more realistic model for the titanium–tartrate system we have added another titanium atom bound to $O^1$ or $O^2$ in both **8a** and **8b** (bearing in mind that tartrate never binds to a single titanium center without bridging to another one), which leads to four new titanium–tartrate systems. Calculation of the total energy for these four systems gives the most stable systems as the two in which the titanium atom is bridging between the water and tartrate oxygen, bound to $O^2$ and the water oxygen in **8a** and to $O^1$ and the water oxygen in **8b**, with the former as the most stable. We thus have the analogy with the dimeric titanium–tartrate structures (as, e.g., **3**). In the following analysis we will then use **8a** as a model for the titanium–tartrate complex.

Thus it appears that by intramolecular binding of the carbonyl oxygen to the titanium atom an asymmetry has been introduced in the titanium–tartrate system. The bridging diolate oxygen from the other tartrate moiety prefers to bind trans (as in **8a**) rather than cis (**8b**) to the carbonyl group. This helps to explain the observed structure of the titanium–tartrate derivatives.[7h,i,9] Binding $O^4$ instead of $O^3$ to the titanium atom in **8a** would then lead to coordination of the bridged diolate oxygen at the other side of the titanium. NMR spectra at room temperature indicate a fluxional equilibrium process that interconverts the structures shown below in **9**:[7h,i]



9

With the internal carbonyl oxygen axially coordinated and the water molecule equatorially bound to the titanium atom, two vacant sites, one axial and the other equatorial, located trans to $O^2$ and $O^3$ in **8a**, remain available for nucleophilic coordination. These coordination sites are occupied by the isopropoxide ligands in the crystal structure (see **3**).[7h,i,9] We will assume, as a starting point for the following analysis, that these two isopropoxide ligands are replaced by a bidentate *tert*-butyl peroxide. Recently Mimoun et al. have found such a bidentate *tert*-butyl peroxide in a (dipic)VO(OO-*t*-Bu)$H_2O$ (**10**) complex.[10]



10

Binding of $HOO^-$, as a model for $t$-$BuOO^-$, to **8a** can take place in two ways. In one, hydrogen is bound to the axial peroxygen **11a**, and in the second it is bound to the equatorial peroxygen **11b**.

The interaction of a peroxo moiety with the d-block of a transition metal leading to a transition metal–peroxo system has recently been described[13] and will not be repeated here.

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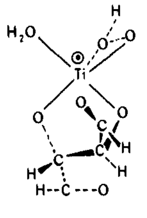
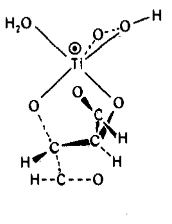
(13) (a) Jørgensen, K. A.; Hoffmann, R. *Acta Chem. Scand.* **1986**, *B40*, 411. (b) Jørgensen, K. A.; Hoffmann, R. *J. Am. Chem. Soc.* **1986**, *108*, 1867.



11a



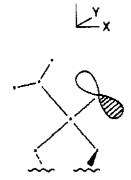
11b

Calculation of the total one-electron energy for the two different binding sites of the hydrogen to the peroxygen, either to the axial peroxygen (**11a**) or to the equatorial peroxygen (**11b**), gives the first as the most stable by 0.43 eV.

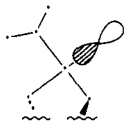
It should be noted that the calculations are performed with the carbonyl bound to axial coordination site and that it is not possible to trace the preferred binding of the hydrogen to the axial peroxygen to some specific orbital. The system no longer possesses any symmetry, which leads to a rather complex orbital picture.

If we accept a structure of the titanium–tartrate peroxo complex as shown in **11a**, the equatorial peroxygen should thus be expected to be the oxygen that epoxidizes the alkene. Calculation of the overlap population between titanium and the axial and equatorial peroxygen gives 0.40 and 0.31, respectively. The bond to the equatorial O is already weakened, facilitating its migration from the complex to an acceptor.

The interaction of the peroxo group with the titanium–tartrate complex generates the following combinations of the equatorial peroxygen orbitals. One, with an energy at −13,1 eV, is a combination of $-p_x$ and $p_z$, schematically shown in **12a**. The other, located at −14.2 eV, is a combation of $p_x$ and $p_z$, **12b**.



12a



12b

Contour plots of these two orbitals are shown in Figure 3.

The overlap population between titanium and oxygen in the water molecule is in **8a** 0.411 and in **11a** 0.383, indicating that this bonding is only slightly weakened by the coordination of the peroxide to titanium. The relatively small change in overlap population suggests that the water, which is a model for the bridging diolate oxygen, remains bound to the titanium at this stage of the reaction.

A model for the titanium–tartrate peroxo complex has now been constructed on the basis of the frontier orbitals of the system. This model is in substantive accord with the structure suggested by Sharpless and co-workers.[7h,i,9]

To proceed further we turn to a frontier orbital analysis which anyway has guided us this far, and which we have found useful in discussing other oxidation reactions.[13] In such an analysis one focuses primarily on important two-electron bonding interactions. In the case of one reagent being an olefin the natural focus becomes the acceptor function of the olefin, its $\pi^*$ orbital.

It appears from **12a**, **12b**, and Figure 3 that the equatorial peroxygen is set up for two symmetry allowed interactions with a $\pi^*$ orbital of an alkene. In one the alkene is perpendicular to the titanium peroxygen bond, leading to a spiro transition state, which corresponds to an interaction between the $\pi^*$ of the alkene and the orbital shown in **12a** and Figure 3a. The other possibility is that the alkene is oriented parallel to the titanium–peroxygen bond, resulting in an interaction between the $\pi^*$ of the alkene and the orbital shown in **12b** and Figure 3b. In principle these orientations then lead to four possible epoxy isomers, two for each of the orientations because of the two enantio faces of the alkene. Please observe that we have not taken the allylic alcohol and its binding to the titanium atom into account. This will be considered later. The four different possibilities are depicted below. These four approach geometries, **13a–d**, correspond more or less to those suggested by Finn and Sharpless.[7h,i]

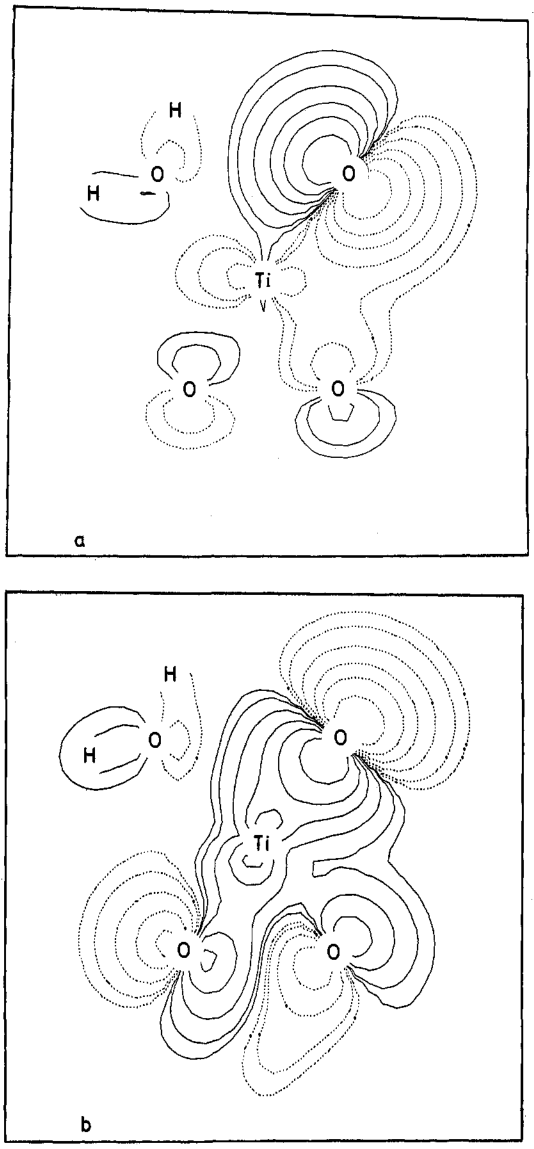
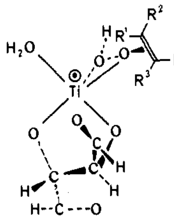
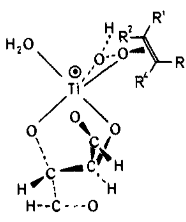


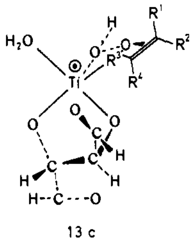
**Figure 3.** Contour plots of the HOMOs located at the equatorial peroxygen: (a) **12a**, (b) **12b**. The contour levels and plane are as in Figure 2.



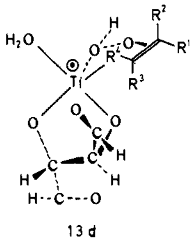
13a



13b



13c



13d

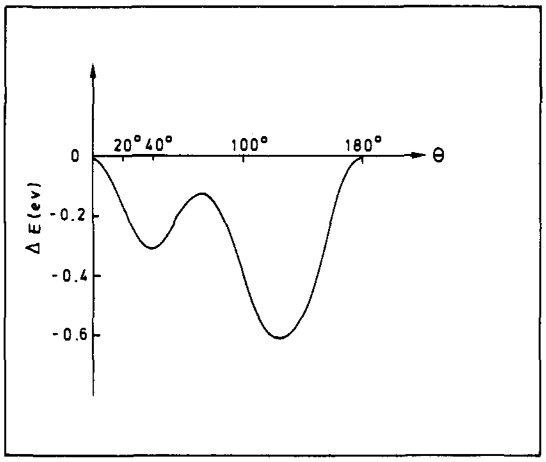
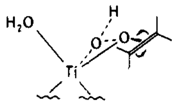


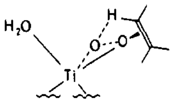
**Figure 4.** The change in total energy for the titanium–tartrate peroxo–alkene system as a function of rotation of the alkene as shown in **14**.

As a starting point for the epoxidation step let us investigate if there is a preferred orientation of an alkene at the peroxygen. Figure 4 shows the change in energy for the titanium–tartrate peroxo–alkene system, **14**, as a function of a rotation of the alkene around the equatorial peroxygen.[14]



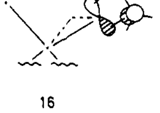
14

It appears from Figure 4 that the most stable conformation of this type of titanium–tartrate peroxo–alkene system is one in which the alkene is rotated about 110° relative to the titanium equatorial peroxygen bond. This stable conformation is shown in **15**. The computed stabilization of the spiro orientation of the alkene, relative to the parallel orientation, is 0.62 eV.



15

The preferred orientation of the alkene can be traced to the frontier orbitals: the lone pair electrons, located at the equatorial peroxygen and antisymmetric with respect to the titanium–peroxygen bond interact with the $\pi^*$ orbital of the alkene, **16**. There is an analogous interaction in the parallel geometry, but the two



16

are differentiated by the energy of oxygen lone pairs. **12a**, the lone pair perpendicular to the Ti–$O^2$ bond, is ~0.9 eV higher in energy (therefore a better donor to the olefin) than the other lone pair, **12b**.

We here want to point out that we have not been able to distinguish between a planar or spiro transition state in the epoxidation of alkenes by group VI transition metal $\eta^2$-peroxo complexes[13a] and that the preferred orientation of the alkene in the titanium–tartrate peroxo complex probably is due to the tartrate moiety.

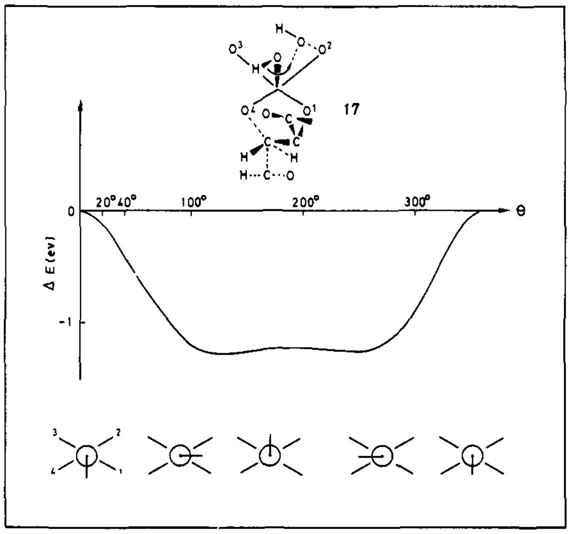
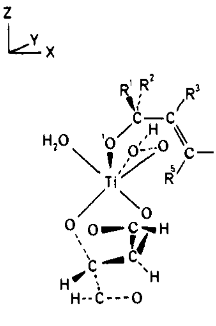


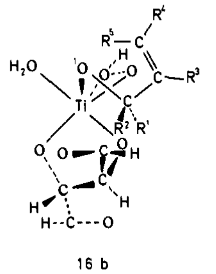
**Figure 5.** The change in total energy for **17** for the rotation of the hydroxyl group. 0° corresponds to hydrogen between the two diolate oxygens.

In the analysis performed by Bach and Coddens in order to elucidate the mechanism of the Sharpless epoxidation reaction, LiOOH and allylic alcohols were used.[11] On the basis of a quantitative analysis of the net charge in the frontier orbitals they suggested that a planar orientation of the peroxo moiety with respect to the alkene is only about 1 kcal·mol⁻¹ lower in energy than a spiro transition state.[11] In our more realistic model for the catalyst (but perhaps using a less reliable computational method) we find that the spiro orientation of the alkene is substantially favored.

The preferred perpendicular orientation of the alkene relative to the titanium–equatorial peroxygen bond reduces the four possible isomers, **13a–d**, to two, as we can exclude for the moment **13c,d**, which have the alkene parallel with the titanium–equatorial peroxygen bond. The two likely transition states for the epoxidation are represented in **16a,b**. Now we have added the fact that it is not a free alkene that we have, but an alkoxide derived from the allylic alcohol and bound to the Ti through its oxygen end as shown.



16 a



16 b

In the view of **16a** the dihedral angle is oriented about 160° relative to the symmetry line in the titanium–tartrate moiety (the $-z$ direction in the coordinate system), whereas in **16b** the angle is about 80°. The geometrical distortions necessary for transforming **16a** to **16b** are rotation about the Ti–$O^1$ bond from about 160° to about 80° followed by a 180° rotation of the $O^1$–$CR^1R^2$ bond.

The next step in the analysis of the reaction mechanism will be to study if there is a preferred orientation of a hydroxyl group placed in the axial position of the titanium–tartrate system, **17**. The reason for choosing the hydroxyl group is to minimize the steric interaction with the tartrate carbonyl group. Figure 5 shows the variation in energy as a function of the dihedral angle for the hydroxyl group (0° corresponds to hydrogen oriented in the $-z$ direction). Figure 5 shows a valley and in its bottom two small minima: one at about 140° and the other at about 260°. The stabilization of the hydroxyl group at these two positions appears to be due to interaction of the lone pair electrons located on the

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[14] The calculations have been performed with a titanium–tartrate moiety with $C_2$ symmetry to avoid steric repulsion between the carbonyl oxygen and alkene hydrogens.

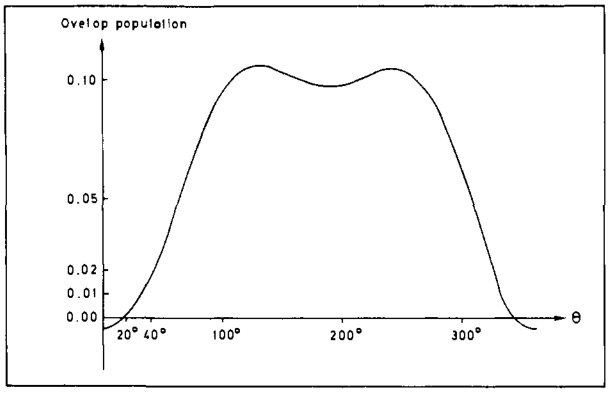
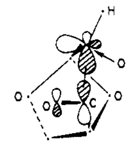


**Figure 6.** The change in overlap population between oxygen in the hydroxyl group and carbon in the carbonyl group as a function of rotation of the hydroxyl group.

hydroxyl oxygen and the unoccupied orbital at the carbonyl group. This orbital is of $\pi^*$ character, localized at carbon in the tartrate group, **18** (the peroxo, the carbonyl group under the plane, and the hydrogens in the tartrate are omitted for clarity). Figure 6 shows a plot of the overlap population between the hydroxyl oxygen and the carbon in the carbonyl group as a function of the dihedral angle, $\theta$, for the hydroxyl group (0° corresponds to hydrogen oriented in the $-z$ direction). The overlap population shows maxima at the same dihedral angle as the total energy curve in Figure 5 shows minima, supporting the lone pair – $\pi^*$ interaction as the reason for the stabilization. The magnitude of the overlap populations is also from our experience indicative of real bonding and thus has a stabilizing role.



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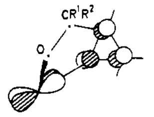
The minimum in the total energy and the maximum in overlap population found at a dihedral angle of about 140° correspond to an orientation of the hydroxyl group which is very similar to the dihedral angle in **16a**. The other minimum, at about 260°, does not allow interaction between the alkene part of the allylic alcohol and the equatorial peroxygen. The alkene part in this alternative is oriented more or less above the oxygen in the water molecule, so that no peroxygen is available for migration. The energy difference between the two orientations of the hydroxyl group leading to the two different transition states, **16a** and **16b**, is about 8 kcal·mol$^{-1}$. Exchanging the tartrate moiety in **17** (Figure 5) with a 1,2-ethanediol and calculating the total energy for this system as a function of the dihedral angle for rotation of the hydroxyl group give a flat curve with no stabilization. This shows that the carbonyl (or ester/amide) function in the tartrate is essential, of utmost importance for the orientation of the hydroxyl group. One might then, on basis of the above, expect that epoxidation of allylic alcohol in the presence of 1,2-ethanediol instead of tartrate should not facilitate epoxidation of a specific enantioface of the alkene.

The overlap population between titanium and oxygen in the water molecule remains constant at 0.36 as the hydroxyl group rotates. The titanium–oxygen bond is thus only slightly weakened by the coordination of the hydroxyl group in the axial position. The relatively small change in overlap population suggests to us that the active epoxidation reagent maintains its dimeric form during the reaction.

Exchanging the hydroxyl group in **17** with a methoxy group (in an attempt to get a more realistic model for the binding of the allylic alcohol at the titanium atom) gives an energy curve roughly similar to that in Figure 5 as a function of the rotation of the methoxy group. There are two main differences in the energy curves of the rotation of the hydroxyl and methoxy groups around the titanium atom: The biggest and most important is the depth of the valley. The stabilization of the methoxy group is several eVs larger than that in the hydroxyl case. The increased stability of the methoxy group, relative to the hydroxy group, is mainly due to steric repulsion between the hydrogens on the methyl group and the carbonyl group on the tartrate moiety, when the methoxy group is oriented toward the carbonyl group (which corresponds to a dihedral angle of 0° in Figure 5). The other difference between the two curves is that the angular range of the bottom of the valley is reduced size in the methoxy case. It ranges here from about 150° to 220°.

We conclude then that transition state **16a** is the most probable. Migration of the equatorial peroxygen to this specific face of the alkene (the peroxygen comes toward the alkene part of the allylic alcohol from the bottom of the plane) leads to an allylic epoxide whose stereochemistry is in accordance with the experimental observations.[7,8] Our model is also consistent with the reactivity of allylic alcohols of varying substituent patterns, as summarized by Sharpless et al.[7,15]

Let us continue with the epoxidation step: It has been observed that electron-withdrawing groups on the olefin, such as nitro, decrease the reaction rate of epoxidation, while electron-donating groups increase the rate.[7h,i] As mentioned earlier, the preferred spiro orientation of the alkene at the peroxygen was due to favorable interaction between the $\pi^*$ orbital of the alkene and the lone pair electrons at the peroxygen perpendicular to the titanium–peroxygen bond. One of the LUMOs in the titanium–tartrate peroxo complex is the antibonding titanium d-peroxygen p combination; the alkene $\pi$ orbital can then interact with this antibonding orbital as depicted in **19** leading to a weakening of the titanium–peroxo bond. Electron-donating groups attached to the alkene part of the allylic alcohol push up the $\pi$ orbital in energy, which makes its interaction with the peroxygen more favorable leading to an increased reaction rate, whereas the opposite is observed for electron-withdrawing groups. This donation of electrons from the $\pi$ orbital of allylic alcohol into the titanium–peroxygen antibonding $\pi$ type of orbital then explains the observed reactivity.[7h,i]



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The orientation of the alkene part of the allylic alcohol around the equatorial peroxygen and the reactivity of the allylic alcohol with the titanium–tartrate peroxo complex thus appears to be determined by two two-electron interactions: One is the interaction of the $\pi^*$ orbital of the allylic alcohol with the lone pair electrons at the equatorial peroxygen, leading to a spiro orientation of the alkene part of the allylic alcohol relative to the titanium equatorial peroxygen bond. The other interaction is between the $\pi$ orbital of the allylic alcohol with the antibonding titanium equatorial peroxygen bond. We are led to consider this second interaction by the electronic effect of substituents on the olefin. The reaction mechanism outlined here is in good agreement with the one suggested by Sharpless and co-workers.

## Summary

We have here tried to explain the structures of the titanium–tartrate asymmetric epoxidation catalysts and their asymmetric epoxidation properties using the frontier orbital approach. Starting with a symmetric titanium-($R$,$R$)-tartrate unit we have shown first that interaction between an unoccupied d-orbital on the titanium atom and one of the lone pair electrons at the carbonyl oxygen stabilizes the system. By this interaction an asymmetry in one of the LUMOs located at the titanium atom is created; this asymmetric causes a preference for coordination of a water molecule trans to the titanium-coordinated carbonyl group. This preferred orientation of water is chosen as a model for the bridging

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(15) Schweiter, M. J.; Sharpless, K. B. *Tetrahedron Lett.* **1985**, *26*, 2543.

**Table I.** Parameters Used in Extended Hückel Calculations

| | | | exponents | |
|---|---|---|---|---|
| | orbital | $H_{ii}$ (eV) | $\zeta_1$[a] | $\zeta^2$ |
| H | 1s | −13.6 | 1.3 | |
| C | 2s | −21.4 | 1.55 | |
| | 2p | −11.4 | 1.325 | |
| O | 2s | −32.3 | 2.20 | |
| | 2p | −14.8 | 1.975 | |
| Ti | 4s | −8.97 | 1.6 | |
| | 4p | −5.44 | 1.6 | |
| | 3d | −10.81 | 4.321 (0.46805)[a] | 1.673 (0.68608) |

[a] Coefficients and exponents in a double-$\zeta$ expansion.

diolate oxygen found in the dimeric titanium–tartrate structures. The observed trans location of the other tartrate group found in these dimeric systems is thus explained. An axial position, trans to the titanium coordinated carbonyl group, and an equatorial position, cis to the water molecule, are then vacant, ready for interaction with nucleophiles. It is assumed that the peroxide coordinates at these two sites in a bidentate way. Calculations show that the most stable complex is obtained when hydrogen is bound to the axial peroxygen, leaving the equatorial peroxygen vacant for migration. The lone pair orbitals at the equatorial peroxygen are set up for two types of interaction with the $\pi^*$ orbital of an alkene. These may be called "spiro" and "parallel" to the titanium peroxygen bond, leading to four possible conformations. Calculations show that the a spiro type of orientation is most favorable, as a perturbation theoretical analysis would indicate.

Assuming that the oxygen in the allylic alcohol replaces the carbonyl group axially coordinated to the titanium atom, we investigated next the preferred orientation of a hydroxyl and methoxy group. These models for the allylic alcohol give a preferred geometry in which the hydrogen or the methyl are roughly trans to the tartrate moiety. In the case of the hydroxyl group the preferred orientation can be traced to interaction between the oxygen lone pair electrons in the hydroxyl group and the carbonyl $\pi^*$ orbital, localized on carbon in the carbonyl group of the tartrate. Calculation of the overlap population between the hydroxyl oxygen and the carbonyl carbon shows a relatively strong interaction. The preferred orientation of the methoxy group is *not* due solely to electronic interaction, as in the hydroxyl case, but here steric interactions are also very important.

The preferred orientation of the alkene at the equatorial peroxygen and the favored conformation of the hydroxyl or methoxy group in the axial position at the titanium atom leads to a transition-state model which is in accordance with the experimental results.

The spiro orientation of the alkene part of the allylic alcohol at the equatorial peroxygen is caused by electronic interactions, whereas the orientation of the oxygen–carbon bond in the allylic alcohol seems to be set by both steric and electronic factors. The asymmetric structures of the titanium–tartrates we think are due to electronic effects. Thus a mixture of electronic and steric factors is responsible for the course of this remarkable reaction.

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## Appendix I

The main part of the calculations were performed by using the extended Hückel method.[12] The orbital parameters are summarized in Table I.

For the geometries for the symmetric titanium–tartrate system we have used standard bond lengths and angles. The structure for the unsymmetric titanium–tartrate system has been taken from the crystal structure of **3**.[9] The bond length for the titanium–oxygen (in $H_2O$) bond has been chosen as 2.16 Å, which is similar to the bond length between titanium and the bridging diolate oxygen.[9] The structure of the titanium–tartrate peroxo complexes has been adjusted so it fits the peroxo part of the structure of **10**.[10] For the hydroxyl, as well as the alkoxy axial ligand calculations, the angle from the titanium–diolate plane has been chosen at 90°.

## Appendix II

Some of the calculated energy differences between alternative structures within the extended Hückel framework are small. We were concerned that preferences obtained might be due to an artifact of the calculations. We have tried to overcome this problem by applying INDO calculations[16] in some of these cases where one might be in doubt. In all the cases investigated the INDO calculations show the same trends as obtained from the extended Hückel method.

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(16) (a) Pople, J. A.; Beveridge, D. L. *Approximate Molecular Orbital Theory*; McGraw Hill: New York, 1970. (b) Bacon, A. D.; Zerner, M. C. *Theor. Chim. Acta* **1979**, *53*, 21 and references therein.