J. Org. Chem. **1995,** *60,* 673–680 **673**

Transition Structure for the Epoxidation Mediated by Titanium(IV) Peroxide. A Density Functional Study

Yun-Dong Wu* and David K. W. Lai

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong

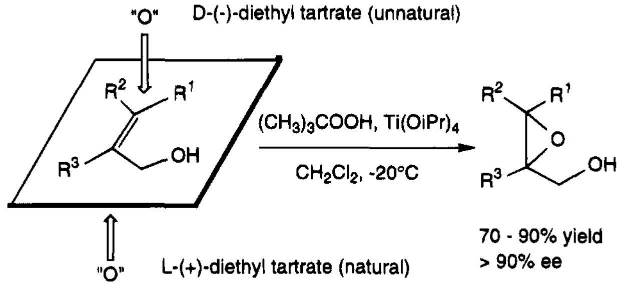
Received September 13, 1994®

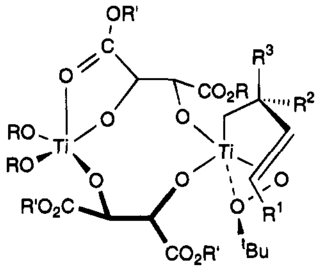
The epoxidation reaction of ethylene with trihydroxytitanium hydroperoxide has been studied by the nonlocal density functional method to model titanium catalyzed epoxidation of alkenes. Spiro and planar transition structures were optimized with the constraint of a Ti–O–O–H dihedral angle of 180°. A η^2 structure is not found in the titanium hydroperoxide reactant, but is found in the transition structure of epoxidation. The approach of ethylene is nearly anti to the breaking O–O bond. The planar structure is quite unsymmetrical and is 3.0 kcal/mol less stable than the spiro structure at the best level of calculation. The spiro preference of the transition structure is discussed based on molecular orbital theory. The monomeric mechanism of Sharpless epoxidation was also modeled. Only spiro transition structures could be located. The two C–O bonds form to similar extent in each transition structure. The allylic C–O bond is in an "inside" position with a dihedral angle of about 30–40° with respect to the C=C double bond. Each transition structure is nearly square-planar with the open site anti to the C=C bond. The activation energy is calculated to be about 10.7 kcal/mol with the BLYP/HW3 method.

Transition metal-catalyzed oxygen transfer reactions are important in both organic synthesis and biological functions.[1,2] For example, the Sharpless epoxidation[3] using titanium tartrate complexes and Jacobsen epoxidation[4] of alkenes provide powerful methods for highly enantioselective syntheses of epoxides and 1,2-dihydroxy compounds. In biological systems, metal–porphyrin-mediated oxygen atom transfer plays an important role in many processes.[5]

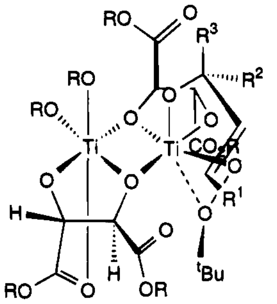
As shown in Scheme 1, the Sharpless epoxidation converts allylic alcohols into chiral epoxides with high stereoselectivity in the presence of Ti(OR)$_4$ and a tartrate ester. With very few exceptions, this reaction is effective for all types of allylic alcohols and is one of the most useful methods in asymmetric synthesis.

Scheme 1

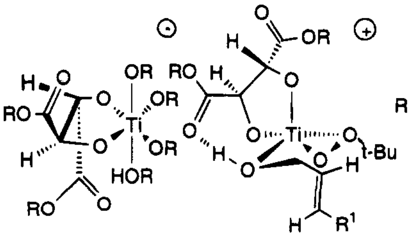




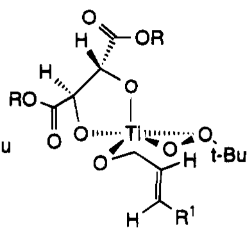
1



2



3



4

Originally, Sharpless *et al.* proposed a dimeric mechanism with a ten-membered ring pentacoordinate transition state (**1**) for asymmetric epoxidation, based on the finding of an X-ray crystal structure of the related analog complex of vanadium(IV) with tartraric acid.[6] This mechanism is further discussed recently by Potvin[7] and Erker.[8] However, X-ray crystal structures of five related Ti-tartrate complexes all exist in dimeric forms with two Ti–O–Ti bridges.[9] Consequent IR, ^{1}H, ^{13}C, and ^{17}O NMR spectrometries also suggest that the active catalyst is in

---

® Abstract published in *Advance ACS Abstracts,* January 1, 1995.

[1] (1) (a) Chong, A. O.; Sharpless, K. B. *J. Org. Chem.* **1977,** *42,* 1587. (b) Sheldon, R. A.; Kochi, J. A. In *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, **1981**. (c) Sheldon, R. A.; van Doorn, J. A. *J. Catal.* **1983,** *31,* 427, 438. (d) Sheldon, R. A. *J. Mol. Catal.* **1980,** *7,* 107.

[2] . Reddy, C. C.; Hamilton, G. A.; Madyastha, K. M. Eds. *Biological Oxidation Systems*; Academic Press: New York, 1990.

[3] (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980,** *102,* 5974. (b) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1986; Vol. 5, p 247. (c) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1986; Vol. 5, p 193.

[4] (a) Zhang, W.; Jacobsen, E. N. *J. Org. Chem.* **1991,** *56,* 2296. (b) Jacobsen, E. N.; Zhang, W.; Güler, M. *J. Am. Chem. Soc.* **1991,** *113,* 6703. (c) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Ding, L. *J. Am. Chem. Soc.* **1991,** *113,* 7063. (d) Lee, H. N.; Jacobsen, E. N. *Tetrahedron Lett.* **1991,** *32,* 6533. (e) Lee, N. H.; Muci, A. R.; Jacobsen, E. N. *Tetrahedron Lett.* **1991,** *32,* 5055. (f) Jacobsen, E. N.; Deng, L. *J. Org. Chem.* **1992,** *57,* 4320.

[5] (a) Ortiz de Montellano, P. R., Ed. *Cytochrome P-450: Reactions, Mechanism, and Biochemistry*; Plenum: New York, 1986. (b) Gunter, M. J.; Turner, P. *Coord. Chem. Rev.* **1991,** *105,* 115.

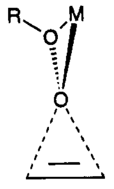
[6] Sharpless, K. B.; Woodard, S. S.; Finn, M. G. *Pure Appl. Chem.* **1983,** *55,* 1823.

[7] (a) Potvin, P. G.; Kwong, P. C. C.; Brook, M. A. *J. Chem. Soc. Chem. Commun.* **1988,** 773. (b) Potvin, P. G.; Bianchet, S. *J. Org. Chem.* **1992,** *57,* 6629.

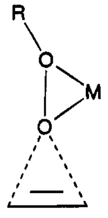
0022-3263/95/1960-0673$09.00/0

a dimeric form in solution.[10] Therefore, Sharpless *et al.* proposed a dimeric hexacoordinate transition state model (**2**) which also qualitatively explains the observed stereoselectivity. Recently, Corey proposed an ion-pair mechanism, in which the transition structure adopts a monomeric and pentacoordinated complex to explain the stereoselectivity of Sharpless epoxidation.[11] The ion-pair model (**3**) is derived from the dissociation of the dimeric hexacoordinated complex with the addition of an allylic alcohol and an alkyl hydroperoxide. In a similar manner, a monomeric mechanism via simple dissociation of the dimeric structure can also be envisaged as shown by **4**.

Detailed information about the transition structure of transition metal-catalyzed oxygen transfer reactions is important both for rationalizing experimental observations and for designing new catalysts.[12] Several theoretical considerations of metal catalysis of epoxidation have appeared. Bach *et al.* analyzed the molecular orbitals of metal hydroperoxide and explained the electrophilic nature of epoxidation and the role of metal catalysis.[13] For the model reaction of LiOOH with ethylene, they found that a spiro transition structure (**5**) is more stable than a planar (**6**) one by about 1 kcal/mol.[13] Jørgensen *et al.* reported an Extended Hückel molecular orbital study of the Sharpless epoxidation.[14] They qualitatively addressed many aspects of titanium-catalyzed epoxidation of allylic alcohols. In particular, they found a preference of about 12 kcal/mol for the spiro transition state. Jørgensen reported an *ab initio* study of the structure and reactivity of peroxo-transition metal (Ti and Ni) complexes. However, no transition structures were reported.[15]



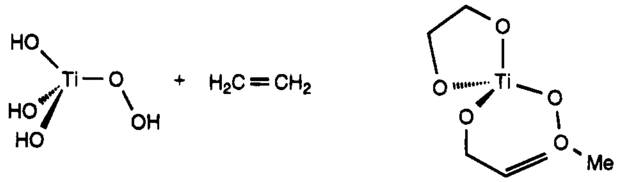
5, spiro



6, planar

Despite these studies, detailed information about the transition state of transition metal-catalyzed epoxidation is still lacking. In this paper we report a nonlocal density functional study of the transition structures of the epoxidation reaction of ethylene by trihydroxytitanium hydroperoxide and of the transition structures involved in a possible monomeric mechanism of the Sharpless epoxidation, as shown in Scheme 2. The calculations reveal some general features of transition structures of titanium-catalyzed epoxidation. The study helps elusidate the mechanism of the Sharpless epoxidation.

Scheme 2



7, acyclic model

8, cyclic model

Method of Calculation

Density functional calculations have been carried out by the Gaussian 92/DFT program,[16] using BLYP nonlocal density functional approximation, which uses Becke's 88 nonlocal exchange functional[17] and the Lee–Yang–Parr nonlocal correlation functional.[18] Such method has been shown to give quite good results for many systems,[19] including transition structures.[20] Geometric optimizations were carried out with the 3-21G basis set first.[21] Energy evaluations were done with the HW3 basis set according to Frenking,[22] which was constructed by contraction scheme [3311/2111/311] + ECP on a 10-electron core for titanium atom and the 6-31G* basis set for other atoms. In order to test the effect of the addition of polarization function on the geometries, the structures of the acyclic system were further optimized with the HW3 basis set.

Results and Discussion

1. Acyclic Model. The reactant $(HO)_3TiOOH$ (**9**), spiro transition structure **TS-10**, and planar transition structure **TS-11** were optimized with C_s symmetry as shown in Figure 1, in which the dihedral angle of Ti–O–O–H was constrained to be 180°. This is not the best conformation for the dihedral angle, which should be about −112°.[23] However, this constraint allows C_s symmetry in the calculations and it should not significantly affect the transition structures, as will be demonstrated later with the cyclic system.

In the $Ti(OH)_3OOH$ reactant, there is a roughly tetrahedral structure at the Ti center. It has been suggested that Ti–O–O might form a η^2 structure.[9] This is not found in the calculations. While one Ti–O bond is 1.875 Å, the other is 2.688 Å with the HW3 basis set. The Ti–O–O(H) angle of 105° is close to a normal O–O–R angle. These indicate that there is only weak electrostatic attraction between the Ti and O_2 atoms in the reactant.

The calculated structure is basis set-dependent. The 3-21G basis set gives shorter O–Ti bond lengths and

---

(8) (a) Erker, G.; Dehnicke, S.; Rump, M.; Krüger, C.; Werner, S.; Nolte, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1349. (b) Erker, G.; Noe, R. *J. Chem. Soc. Dalton Trans.* **1991**, 685.

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

(10) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113.

(11) Corey, E. J. *J. Org. Chem.* **1990**, *55*, 1693.

(12) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. J. *Science* **1993**, *261*, 1404, and references therein.

(13) Bach, R. D.; Wolber, G. J.; Coddens, B. A. *J. Am. Chem. Soc.* **1984**, *106*, 6098.

(14) Jørgensen, K. A.; Wheeler, R. A.; Hoffmann, R. *J. Am. Chem. Soc.* **1987**, *109*, 3240. Jørgensen, K. A. *Chem. Rev.* **1989**, *89*, 431.

(15) Jørgensen, K. A. *Acta Chem. Scand.* **1992**, *46*, 82.

(16) Gaussian 92/DFT Revision F.2. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Wong, M. W.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A.; Gaussian, Inc., Pittsburgh PA, 1993.

(17) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.

(18) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B 37*, **1988**, 785.

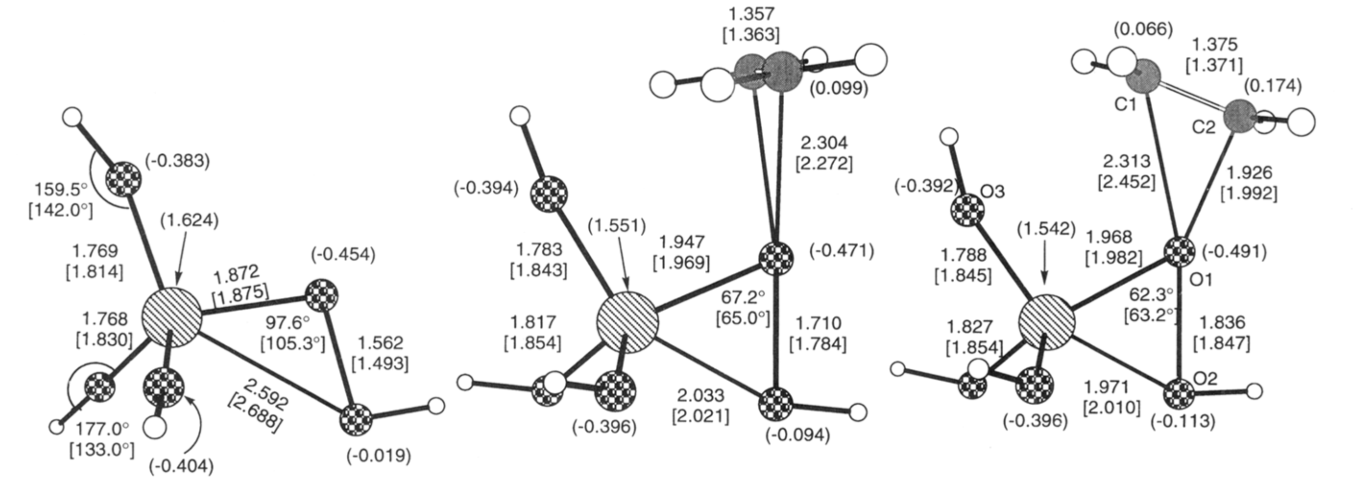
(19) Johnson, B. G.; Gill, P. M. W.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 5612.

(20) (a) Ziegler, T. *Chem. Rev.* **1991**, *91*, 651. (b) Fan, L.; Ziegler, T. *J. Am. Chem. Soc.* **1992**, *114*, 10890. (c) Stanton, R. V.; Merz, K. M., Jr. *J. Chem. Phys.* **1994**, *100*, 434.

(21) Dobbs, K. D.; Hehre, W. J. *J. Comput. Chem.* **1987**, *8*, 861.

(22) (a) Jonas, V.; Frenking, G.; Reetz, M. T. *J. Comput. Chem.* **1992**, *13*, 919. (b) Jonas, V.; Frenking, G.; Reetz, M. T. *Organometallics* **1993**, *12*, 2111. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(23) Preliminary calculation was done by the density functional program DMol, using LDA/DN on the system H_3TiOOH; the dihedral angle ∠Ti–O–O–H was found to be −112°. DMol 2.2, Biosym, Technology Inc., San Diego.



	$(HO)_3TiO_2H$, 9	**Spiro TS-10**	**Planar TS-11**
3-21G//3-21G	-1221.89376 (0.0)	-1300.00577 (-0.9)	-1299.99591 (5.3)
HW3//3-21G	-436.62683 (0.0)	-515.15162 (7.7)	-515.14850 (9.6)
HW3//HW3	-436.63661 (0.0)	-515.15913 (9.2)	-515.15430 (12.2)

Figure 1. Geometrical parameters and natural population atomic charges (at HW3 level) of the reactant $(HO)_3TiO_2H$ (**9**) and the spiro transition structure **TS-10** and planar transition structure **TS-11** for the epoxidation of **9** with ethylene with a C_s symmetry constraint. Geometries were optimized with the BLYP/3-21G and BLYP/HW3 (in parenthesis), respectively. The calculated total energies au and relative energies (kcal/mol, in parenthesis) of these structures are also shown below the structures.

much larger Ti−O−H angles. With the HW3 basis set, the Ti−O(H) bond lengths are 1.814 and 1.830 Å, respectively. The calculated Ti−O−H angels are 133° and 142°, respectively. Such large angles are also found in X-ray crystal structures of d^0 metal alkoxide systems.[9] This is often attributed to p_π−d back donation.[24] The natural population analysis supports this explanation. As shown in Figure 1, Ti(IV) has a net positive charge of 1.627 units. There is significant electron occupation in the metal 3d atomic orbitals. However, the geometrical feature can also be explained by electrostatic interactions.[25] The Ti atom is very positively charged and has attractive interaction with the hydroxy lone-pairs. The large basis set dependence of the Ti−O−H angles supports such an explanation. The calculated O−O bond length is 1.493Å, which is comparable to those determined by both high level *ab initio* calculations[26] and experiments.[27]

Several geometrical features of the transition structures are noteworthy. (1) Except for the Ti−O−H angles, the 3-21G geometry is very similar to the HW3 geometry. This indicates that the 3-21G basis set might be used for the geometry optimizations of larger systems. (2) The spiro and planar structures have quite similar Ti−O−O(H) units. (3) The Ti−O−O(H) unit is in a η^2 structure; the two Ti−O bond lengths are nearly equal, with the Ti−O(H) bond slightly longer. (4) The approach of the ethylene is nearly anti to the breaking O−O bond, similar to the transition structures of other related reactions.[28,29] (5) Geometrically, **TS-10** is an earlier transition structure than **TS-11** since it has shorter C=C and O−O bond lengths. This corresponds well with the higher activation energy for **TS-11**. (6) The spiro **TS-10** has the same forming C−O bond lengths because of the C_s symmetry constraint. As will be seen later, this symmetrical geometry holds even without symmetry constraint. On the other hand, the planar **TS-11** is quite unsymmetrical, with the outer C_2−O_1 bond being about 0.46 Å shorter than the inner C_1−O_1 bond. This might be partially caused by the steric interaction between the O_3 and C_1 centers since the O_3−C_1 distance is only 2.89 and 3.16 Å in the 3-21G and HW3 structures, respectively. As will be discussed later, electronic effects also explain this phenomenon.

The natural atomic charges (with hydrogens summed into heavy atoms) calculated by natural population analysis[30] are given in Figure 1. There are about 0.2 units of charge transfer from the ethylene to the TiOOH complex in the spiro structure **TS-10**. The charge transfer is increased to 0.24 units in the planar structure **TS-11**. As expected, the negative charge from the ethylene mainly is accepted by the leaving hydroxy group of the peroxide, which in turn, partially donates to the titanium atom through p−d back donation.

The spiro transition structure **TS-10** is calculated to be more stable than the planar transition structure **TS-11** with each level of calculation. While this preference is about 6.2 kcal/mol at the 3-21G level, it is reduced to 3.0 kcal/mol at the HW3 level. The 3-21G basis set gives

---

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

[25] Reed, A. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1991**, *112*, 7363.

[26] O−O: 1.469 Å. Bach, R. D.; Owensby, A. L.; Gorizalez, C.; Schlegel, H. B.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1991**, *113*, 6001.

[27] (a) Schaefer, H. F., III. *Acc. Chem. Res.* **1979**, *12*, 288. O−O (expt): 1.475Å. (b) Jorgensen, K. A.; Swanstrom, P. *Acta Chem. Scand.* **1992**, *46*, 82. O−O (expt): 1.46 Å.

[28] Bach, R. D.; Owensby, A. L.; Gonzalez, C.; Schlegel, H. B.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1991**, *113*, 2338.

[29] (a) Bach, R. D.; Coddens, B. A.; McDouall, J. J. W.; Schleyel, H. B.; Davis, F. A. *J. Org. Chem.* **1990**, *55*, 3325. (b) Back, R. D.; Wolber, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 1410.

[30] NBO version 3.1: Glendening, E. D.; Reed, A. E.; Garpenter, J. E.; Weinhold, F. University of Wisconsin, Madison.

quite low activation energies for both **TS-10** and **TS-11** with respect to the reactants. The HW3 basis set significantly increases the activation energy. The HW3 optimization gives an activation energy of 9 kcal/mol with **TS-10**.

There is general interest in the preferred conformation of the epoxidation transition state. Davis *et al.* used a planar transition structure to explain the stereochemistry of epoxidation of prochiral olefins with chiral oxazidines.[31] Rebek *et al.* also suggested a preference for the planar transition structure to rationalize the unprecedentedly high rates of epoxidation of cis alkenes relative to trans and 1,1-disubstituted alkenes by conformationally constrained peroxy acids.[32] By emphasizing the importance of the overlap of an oxygen sp^3 lone-pair with the olefin π^* orbital, Sharpless *et al.* proposed an intermediate orientation between spiro and planar structures which also explain the above experimental observations.[33] Recently, Bach *et al.* found a 8.7 kcal/mol preference for a spiro transition structure over a planar transition structure for the reaction of performic acid with ethylene,[34] but both spiro and planar transition structures have similar energies for oxygen transfer from oxazirine to alkene and sulfoxide.[29] Cremer *et al.* also found almost identical preference for the planar and spiro transition structures of epoxidation of ethylene with carbonyl oxide.[35]

Our calculated significant preference for the spiro transition structure is in agreement with the earlier calculations by Bach *et al.* on the reaction of LiOOH with ethylene[13] and by Jørgensen *et al.* on the Sharpless epoxidation.[14] A spiro transition structure has also been proposed to rationalize the reactivity of epoxidation mediated by metal oxides.[36]

According to the frontier molecular orbital theory,[37] the major stabilization of the transition state involves the highest occupied molecular orbital (HOMO) of the $(HO)_3TiOOH$ and the lowest unoccupied molecular orbital (LUMO) of ethylene (π^*) and the LUMO of the $(HO)_3TiOOH$ and the π orbital of the ethylene. The HOMO and LUMO of the $(HO)_3TiOOH$ are schematically shown by **12** and **13**, respectively, based on calculations. The HOMO of $(HO)_3TiOOH$ is mainly the π^* of the peroxygens resulting from the negative combination of the two p_z type lone pairs on the two oxygens. The LUMO is a combination of the σ^* of O−O with the $d_{x^2-y^2}$ orbital of the titanium atom.

As shown in Figure 2, the energy gap between the HOMO of C_2H_4 and the LUMO of TiOOH is 3.57 eV. This energy gap is 1.35 eV smaller than that between the HOMO of TiOOH and the LUMO of C_2H_4. Thus, the former should be the dominant interaction in the transition structures. This is reflected by the electrophilic addition characteristics of the reaction and the nearly antiperiplanar approach of the C=C to the O−O in the transition structures.

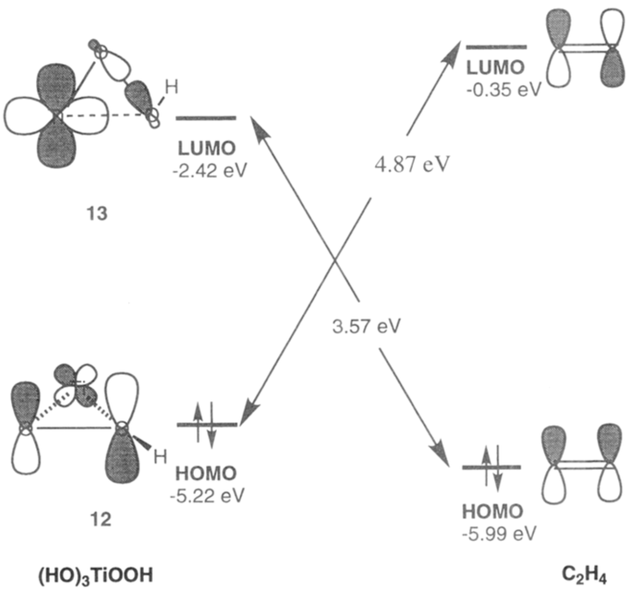
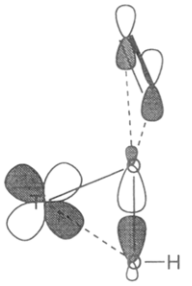
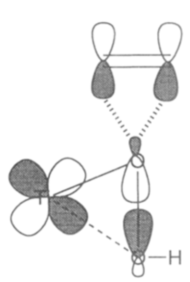


Figure 2. The frontier molecular orbitals of the $(HO)_3TiOOH$ and the ethylene. The calculations were carried out with the BLYP/HW3 method.

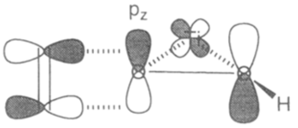
We first analyze the interaction between the HOMO of ethylene and the LUMO of the $(HO)_3TiOOH$, since this is the most important interaction for the reaction. When the ethylene approaches the $(HO)_3TiOOH$ in the spiro fashion, the best overlap can be achieved with ethylene nearly antiperiplanar to the O−O bond, in a symmetrical arrangement, as shown by **14**. When ethylene approaches the $(HO)_3TiOOH$ in the planar fashion (see **15**), a symmetrical arrangement between the transferring oxygen and ethylene and an ideal antiperiplanar approach of ethylene to the O−O bond would not be favorable because of the involvement of the d orbital from the titanium atom. There is a negative overlap between the ethylene HOMO with the d orbital of titanium. This explains why the inner O−C bond is formed to a smaller extent than the outer C−O bond in the planar transition structure. Also because of the d orbital interaction, the overlap in the planar transition structure is not as good as in the spiro transition structure.



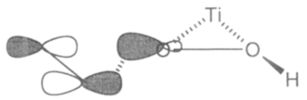
14 Spiro
π + LUMO



15 Planar
π + LUMO



16 Spiro
π^* + HOMO



17 Planar
π^* + SHOMO

Most of the discussions in the literature about the preference of alkene orientation of the transition struc-

---

[31] Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123.

[32] Rebek, J., Jr.; Marshall, L.; Wolak, R.; McManis, J. *J. Am. Chem.* Soc. **1984**, *106,* 1170. Rebek, J., Jr.; Marshall, L.; McManis, J.; Wolak, R. *J. Org. Chem.* **1986**, *51*, 1649.

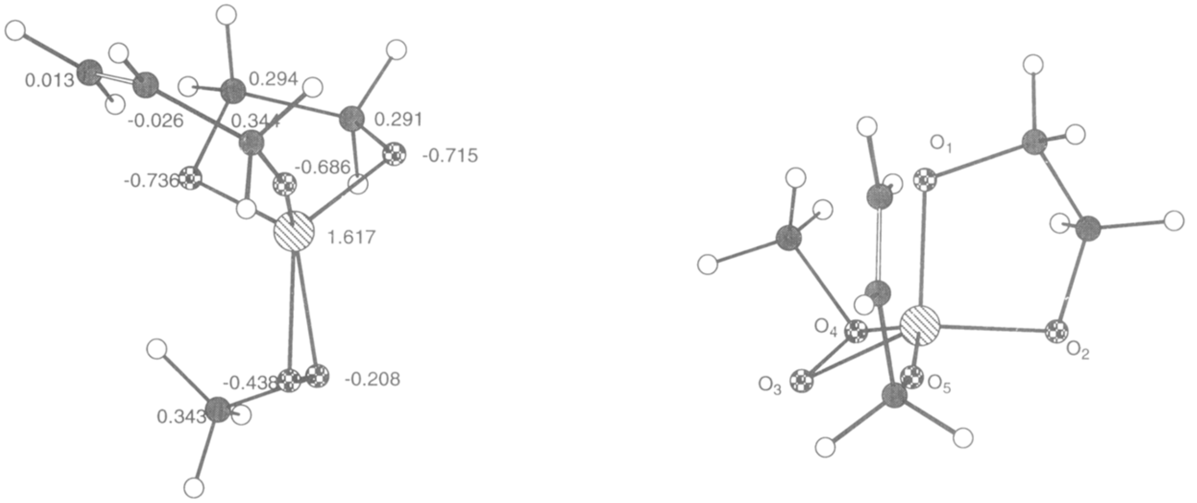
[33] Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta*, **1979**, *12*, 63.

[34] (a) Bach, R. D.; McDouall, J. J. W.; Owensby, A. L.; Schlegel, H. B. *J. Am. Chem. Soc.* **1990**, 112, 7065. (b) Plesnicar, B.; Tasevski, M. Azman, A. *J. Am. Chem. Soc.* **1978**, *100*, 744.

[35] Cremer, D.; Bock, C. W. *J. Am. Chem. Soc.* **1986**, *108*, 3375.

[36] Groves, J. T.; Nemo, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 5786.

[37] Fukui, K. *Acc. Chem. Res.* **1971**, *4*, 57.



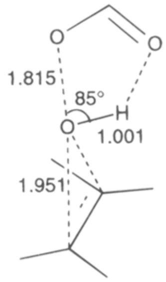
21

Figure 3. Two views of the optimized structure of the reactant of the cyclic model with the BLYP/3-21G method. Natural population atomic charges (HW3, with H atoms summed in) are also give.

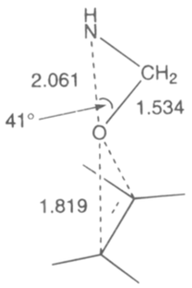
ture are based on the interaction between the out-of-plane lone pair of peroxy oxygen which is the HOMO of TiOOH in the current case and the LUMO of the alkene.[13,14] This interaction can be achieved only in the spiro transition structure, as shown in **16**. For the planar transition structure, the LUMO of ethylene has to interact with the in-plane lone pair, as shown in **17**, which is the SHOMO. Since the in-plane lone pair is much lower in energy than the out-of-plane one,[38] the spiro transition structure enjoys a larger stabilizing interaction than the planar transition structure and should be more favorable. It also explains why the planar transition structure should be unsymmetrical.

Both interactions must contribute to the spiro preference. However, we felt that the first interaction might be more important for the following reasons: (1) The energy gap between the HOMO of TiOOH and the LUMO of C_2H_4 is much larger, and the interaction should be less effective. Accordingly, the mixing between the two orbitals is quite small in the transition structures. (2) If the second interaction is important, a preference for the spiro transition structure would be expected for other epoxidations as well. However, Bach *et al.* recently reported that the spiro preference disappears in the reaction of oxazirine with ethylene and sulfoxide.[29] (3) While Bach *et al.* reported a 8.7 kcal/mol preference for the spiro transition structure of the reaction of performic acid with ethylene,[34] in a more recent paper, they mentioned that they found an unsymmetrical spiro transition structure which is more stable than the symmetrical spiro transition structure they reported before.[39] This also suggests that the second interaction may not be important.

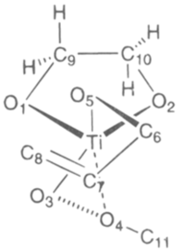
According to the first explanation, the planar transition structure is destabilized only when there is significant interaction between the $\pi_{C=C}$ orbital and the metal d orbital. This interaction is equivalent to the closed shell $\pi_{C=C}/\sigma_{M-O}$ four-electron repulsive interaction. The magnitude of this interaction is largely dependent upon the angle of O−O−M. A large O−O−M angle should result in a large destabilization for the planar transition structure. In our current case, this angle is 65° in the spiro transition structure **TS-10** and becomes slightly smaller in the planar transition structure. The preference for the spiro transition structure is about 3 kcal/mol. The O−O−H angle in the spiro transition structure of the reaction of ethylene with performic acid is 85° (**18**), and a preference of 8.7 kcal/mol for the spiro transition structure over the planar transition structure was obtained.[13] The N−O−C angle in the spiro transition structure of the reaction of ethylene with oxazirine is only 41° (**19**), and little repulsive interaction in the planar transition structure is expected.[29] This explains why the spiro and planar transition structures are nearly identical in energy.



18



19



20

2. Cyclic Model. In the acyclic model just presented, a C_s symmetry constraint was imposed. To check the effect of this constraint on the geometry of epoxidation transition structure, we further studied a cyclic system, **8**, with full geometric optimization. This also serves as a simplest model for the monomeric mechanism of Sharpless epoxidation where tartrate ester groups are not included.

First of all, the reactant was fully optimized. This structure **21** serves as a reference for the calculation of the activation energy for the reaction. Two views of the optimized structure with natural atomic charges are shown in Figure 3. Selected geometric parameters are given in Table 1 (see **20** for numbering scheme). It should be pointed out that no vigorous search for the most stable conformation was performed, but it is unlikely that

---

[38] In the current case, the difference is 1.75 eV. or about 40 kcal/mol. The in-plane lone-pair is the SHOMO of the $(HO)_3TiOOH$ unit.

[39] Bach, R. D.; Andres, J. L.; David, F. A. *J. Org. Chem.* **1992**, *57*, 613.

Table 1. Selected Bond Lengths (Å), Bond Angles (deg) and Dihedral Angles (deg) for Pentacoordinate Complex 21 and Transition Structures 22–25 at BLYP/3-21G Level

	21	22	23	24	25
Bond Lengths					
Ti–O_1	1.854	1.852	1.828	1.851	1.861
Ti–O_2	1.844	1.856	1.865	1.830	1.836
Ti–O_3	1.888	1.959	1.960	1.972	1.967
Ti–O_4	2.312	2.015	2.039	2.032	2.021
Ti–O_5	1.775	1.832	1.838	1.846	1.839
O_3–O_4	1.568	1.766	1.772	1.791	1.773
C_7–C_8	1.339	1.367	1.369	1.372	1.370
C_7–O_3	4.968	2.226	2.205	2.192	2.175
C_8–O_3	4.910	2.210	2.170	2.100	2.176
Angles					
O_1–Ti–O_2	89.6	85.9	90.6	91.8	89.5
O_1–Ti–O_3	112.4	100.5	117.0	130.7	145.6
O_2–Ti–O_3	125.9	155.0	137.7	127.8	112.3
O_1–Ti–O_4	90.7	109.0	105.6	93.0	95.7
O_2–Ti–O_4	91.8	102.4	91.0	104.9	109.7
O_3–Ti–O_4	83.4	65.2	66.0	65.2	65.2
O_5–Ti–O_1	113.5	112.8	114.4	106.5	108.0
O_5–Ti–O_2	109.6	108.3	106.7	107.4	109.4
O_5–Ti–O_3	105.3	91.5	91.0	89.9	90.0
O_4–Ti–O_5	146.9	129.0	135.6	141.3	133.9
Ti–O_3–O_4	54.2	62.0	61.4	61.7	62.0
Dihedral Angles					
C_6–O_5–Ti–O_1	25.6	105.9	133.2	103.3	132.2
C_8–C_7–C_6–O_5	−0.6	−31.7	−35.5	34.2	31.5
O_3–Ti–O_5–C_6	97.8	3.8	12.7	−29.5	−18.0
O_1–C_9–C_{10}–O_2	43.2	40.3	43.3	43.4	40.8
C_{11}–O_4–O_3–Ti	−108.6	−113.0	105.0	−111.0	111.7

a much more stable conformation will be found. This structure leads to transition structure **22**, as shown in Figure 4, upon approach of the C=C double bond to the peroxy oxygen without other significant conformational changes.

The allylic moiety is in an extended conformation so that the C=C double bond has no interaction with the electrophilic oxygen and the metal center. The allylic C–O bond is nearly eclipsed with the C=C double bond with an about 1° dihedral angle. This is in accord with the preferred conformation of allylic alcohol determined by experiments.[40] The five-membered diolate ring is in an expected half-chair conformation with two C–H bonds nearly axial (∠H–C–C–H = 167°) and the other two C–H bonds nearly equatorial (∠H–C–C–H = 77°). The Ti–O–O–Me dihedral angle is about 109°.

The Ti–O bond lengths are comparable to those in the acyclic trihydroxy Ti^{IV} hydroperoxide model. The two Ti–O bonds in the five-membered ring are 1.844 and 1.854 Å. The Ti center is more like tetrahedral, with O–OMe behaves as one ligand. The Ti–peroxo bond (1.888 Å) is longer than the other distal oxygen bond (2.312Å). As we mentioned before, the geometry is quite basis set-dependent. Without geometrical constraint, the angle ∠C–O–Ti between the allylic alcohol moiety and the Ti atom is very large (166.5°), and this is primarily due to the lack of polarization function in the 3-21G basis set. *The other two Ti–O–C angles are quite close to* tetrahedral because they are constrained in the five-membered ring.

Four transition structures (**22**–**25**) have been located with full geometric optimization with the BLYP/3-21G method. Each structure was optimized with the requirement of one negative eigenvalue. Two stereoviews of these structures are shown in Figure 4. Structure **23** is different from structure **22** in the orientation of the OMe group. Structure **24** and **25** have the C=C bond approach the peroxide on the opposite face from structures **22** and **23**, respectively. The energies of these structures were further calculated with the BLYP/HW3 method. The calculated total energies and relative energies with respect to the complex **21** are given in Table 2. Selected bond lengths, bond angles, and dihedral angles of these structures are collected in Table 1.

The transition structures are similar to the spiro structure of the acyclic system discussed in the previous section. This is indicated by the near 90° dihedral angle of C_8=C_7–O_3–Ti. The C=C double bond approaches the O–O unit with about 150–160° dihedral angle. The small deviation from an ideal antiperiplanar attack is due to the constraint of the formation of the five-membered ring. We were unable to locate any planar transition structure. This supports the spiro preference discussed before. There is staggering about the allylic center. The allylic C_6–O_5 bond is in an "inside" position according to Houk's definition.[41] The C_8–C_7–C_6–O_5 dihedral angle ranges 32–36°. These angles are close to that derived qualitatively by Sharpless which is about 50°.[3b] The Ti–O–O unit forms a nice η^2 structure, with the Ti–O_4 being about 0.06 Å longer than the Ti–O_3 bond. The Ti–O_3–O_4–Me dihedral angle is similar to that in the reactant.

The two forming C–O bonds are formed to very similar extents. The external C_8–O_3 bond is slightly shorter than the C_7–O_3 bond. This nearly symmetrical transition structure is in agreement with the experimental observation by Sharpless *et al.* that the secondary deuterium isotope effect at the C_2 and C_3 of allylic alcohol are very similar. They also reached the conclusion that the external C–O bond is formed to a slightly larger extent.[10]

The geometry of the diolate moiety changes little from the reactant to the transition structure. The O_1–Ti–O_2 angle ranges from 86–92°. The O_1–C–C–O_2 dihedral angle is 40–43°. These are similar to those observed in the X-ray crystal structures of titanium tartrate complexes.[9]

Each transition structure is close to a square-pyramidal geometry. The axial open site is indicated by the arrow in Figure 4. It is clear that the axial open site is related to the orientation of the allyl moiety. Thus, in structures **22** and **23**, the peroxide approaches the C=C double bond from the *si* face, and the open site is anti to the Ti–O_1 bond while in structures **24** and **25**, the peroxide approaches the C=C double bond from the *re* face, and the open site is anti to the Ti–O_2 bond. Such a relationship is probably caused by torsional effect of the formation of the five-membered ring (Ti–O_3–C_7–C_6–O_5) and the requirement of an antiperiplanar relationship between the C_7=C_8 and the O_3–O_4 bond. The dihedral angle of O_3–Ti–O_5–C_6 is quite small in structure **22**, but is about 30° in structure **24**.

It is interesting that structures **22** and **24** have the same stability with the HW3 basis set. These structures have opposite orientations for the allyl moiety, but the same orientation for the peroxy methoxy group. Structures **23** and **25** are somewhat higher in energy. Since steric interaction with the methoxy group is not serious,

---

(40) (a) Murty, A. N.; Curl, R. F., Jr. *J. Chem. Phys.* **1967**, *46*, 4176. (b) Brown, R. S.; Marcinko, R. W. *J. Am. Chem. Soc.* **1978**, *100*, 5721. (c) Silvi, B.; Froment, F.; Corset, J.; Perchard, J. P. *Chem. Phys. Lett.* **1973**, *18*, 561.

(41) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jager, B.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.

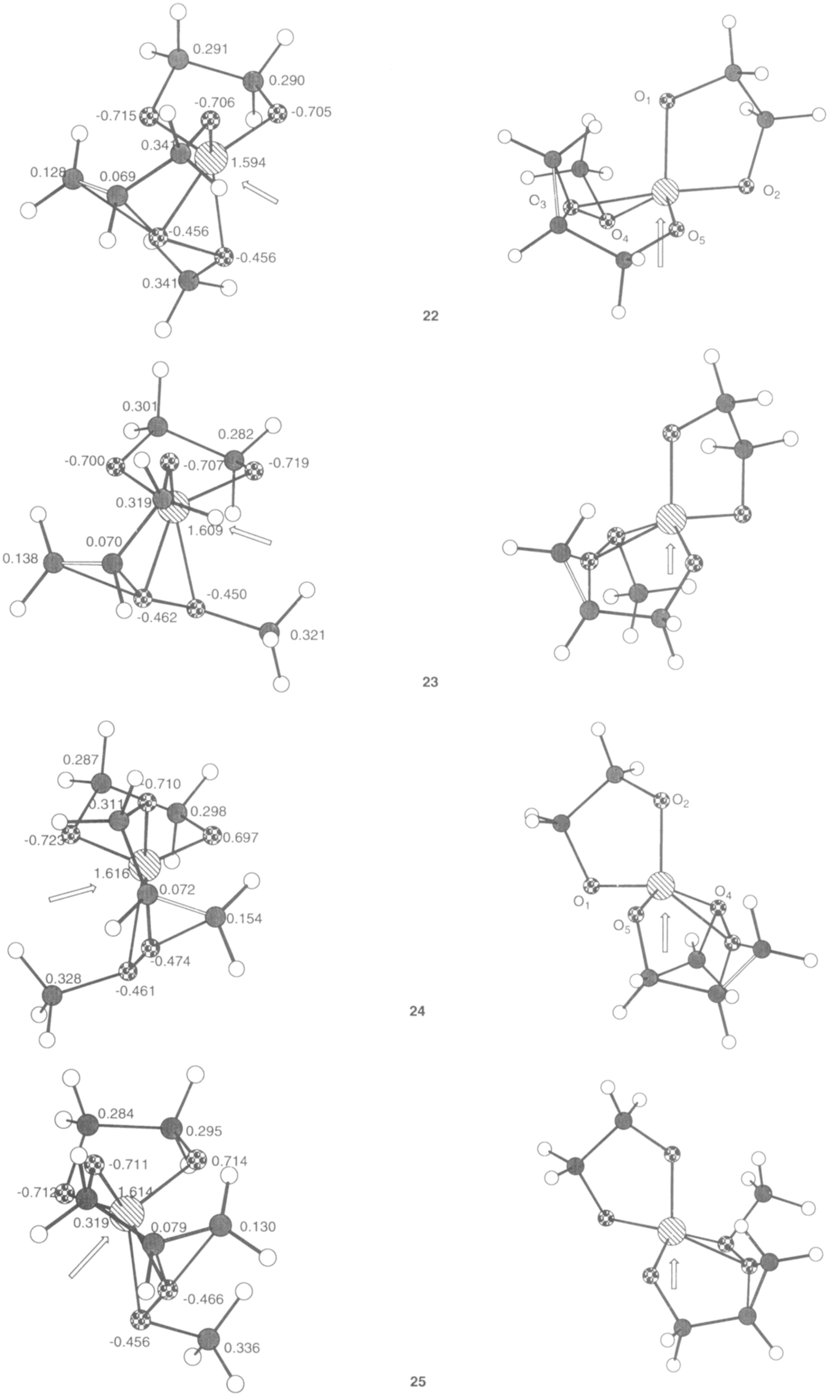


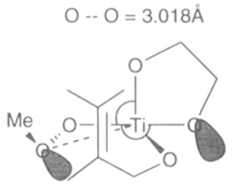
Figure 4. Two views of the transition structures (**22**–**25**) of the cyclic model optimized with the BLYP/3-21G method. Natural population atomic charges (HW3, with H atoms summed in) are also given.

this conformational preference for the methoxy group is attributed to the avoidance of the lone pair-lone pair repulsion between the distal oxygen atom of the alkyl peroxide and the diolate oxygen atom of the five-

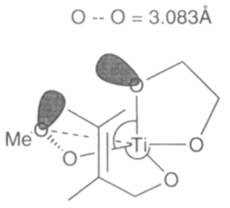
Table 2. Calculated Total Energies (au) and the Activation Energies E_a (kcal/mol) of the Pentacoordinate Structures

	21	22	23	25	25
3-21G//3-21G	−1453.94296	−1453.92705	−1453.92419	−1453.92356	−1453.92510
E_a (kcal/mol)	–	10.0	11.8	12.2	11.2
HW3//3-21G	−669.91522	−669.89823	−669.89619	−669.89823	−669.89739
E_a (kcal/mol)	–	10.7	11.9	10.7	11.2

membered ring. As illustrated by **26** and **27**, which represent structures **22** and **23**, respectively, the lone pair of the distal oxygen in **26** does not point directly to the equatorial diolate oxygen, whereas the lone pairs shown in **27** point toward each other. Therefore, structure **27** suffers from severe electrostatic repulsive interaction between the lone pairs as shown.



26



27

The calculated activation energy with the most stable structure **22** is 10.7 kcal/mol with the HW3 basis set (Table 2). This is quite similar to that calculated for the acyclic model which is 9.2 kcal/mol with the Sprito **TS-10** (Figure 1). We have also located transition structures of a hexacoordinate model with the addition of a sixth ligand (H_2O) to the current cyclic model. The calculated activation energy with the best structure is 12.6 kcal/mol. This indicates that a sixth ligand does not have significant effect on the activation energy. These results along with a detailed analysis of the stereocontrol with the dimeric mechanism proposed by Sharples *et al.*[3b] will be presented in a future publication.[42]

Conclusion

We have used nonlocal density functional method to model titanium-catalyzed epoxidation of alkenes. It has been demonstrated that the transition structures can be calculated satisfactorily by the BLYP/3-21G method. Several conclusions can be reached:

(1) There is a significant preference for a spiro transition structure over a planar transition structure. This conformational preference is rationalized by a more favorable interaction between the HOMO of the alkene (π orbital) and the LUMO of TiOOR (combination of d_{Ti} and σ^*_{O-O}) in the spiro transition structure over the planar transition structure.

(2) The spiro transition structure for the epoxidation is nearly symmetrical with the two C−O bonds forming to a similar extent. The planar transition structure, on the other hand, have the outer C−O bond form to much larger extent then the inner C−O bond.

(3) There is a η^2 structure for the Ti−O−O unit in the transition structure. The nature of electrophilic addition of the reaction is indicated by a small energy gap between the HOMO of alkene and the LUMO of the TiOOR and by a negative charge transfer of about 0.2 units from the C=C unit to the TiOOR in the transition structures.

(4) The transition structure for a possible monomeric mechanism of Sharpless epoxidation favors a square-pyramidal geometry. The open site is in the opposite direction of C=C bond orientation. This is different from the geometry in Corey's ion-pair model.

Acknowledgment. We are grateful to Professor K. N. Houk (University of California, Los Angeles) for very helpful discussions. The Hong Kong Government provided financial support for the project. We also thank the Center of Computing Services and Telecommunications at HKUST for providing valuable computing facilities.

JO941584O

---

[42] Wu, Y.-D.; Lai, D. K. W. Manuscript in preparation.