Mechanism of Oxygen Transfer from Oxaziridine to Ethylene: The Consequences of HOMO-HOMO Interactions on Frontier Orbital Narrowing

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Abstract: A mechanism for the the transfer of oxygen from ethylene oxide or oxaziridine to ethylene is proposed on the basis of ab initio molecular orbital calculations. The significance of the four-electron interaction between the ethylene π bond and the Walsh orbital containing the oxygen lone pair is discussed. The orbital splitting by these filled molecular orbitals decreases the energy gap between the effective HOMO (π) and LUMO (Walsh orbital), resulting in a narrowing of the energy of these frontier molecular orbitals. This repulsive interaction serves to lower the enthalpy of activation provided that it is attended by a stabilizing interaction with a higher lying empty orbital. This study on a model substrate suggests that oxygen transfer from a chiral oxaziridine to an alkene should prefer a planar transition state as a consequence of electronic constraints with the enantiomeric excess in the epoxide product resulting from steric interactions.

As our analysis of organic reaction mechanisms becomes more sophisticated, a clear division of the electrophilic and nucleophilic nature of reagents into distinct classes becomes more difficult. For example, in a recent theoretical study on nucleophilic substitution at vinylic carbon,[1a] we classified an attacking amine as the nucleophile and the carbon–carbon double bond as the "electrophilic" center. However, halogenation and epoxidation of alkenes have historically been classified as electrophilic addition reactions to the "nucleophilic" carbon–carbon double bond. This is presumably because it has generally been assumed that alkyl substituents increase the electron density of the double bond, resulting in greater reactivity of the alkene toward "electrophilic" reagents. In point of fact, the enhanced nucleophilicity of highly substituted alkenes is not due to the electron-releasing effect of alkyl groups as is commonly thought. Although the double bond may be polarized by alkyl substituents, there is little net transfer of electron density from the alkyl group through the π system to the double bond.[2] The reduction in ionization potential and the increased reactivity is due to orbital splitting achieved through a four-electron interaction of the filled π_{CH_2} orbitals of the alkyl groups with the π bond.[1b] In the present study we report on an epoxidation reaction that delineates some of the reasons for the "electrophilic" character of oxygen-transfer reagents. In particular, we will stress the importance of the HOMO-HOMO interaction between the lone pair on oxygen and the π bond of the alkene and identify the more significant molecular orbital interactions required for oxygen transfer. We will combine ab initio calculations and frontier molecular orbital (FMO) theory that utilizes a four-electron, three molecular orbital model.[1a] The principle of atomic orbital cancellation[1a] that is based upon this FMO model will be applied to the calculated molecular orbitals that evolve into the transition state on the reaction coordinate.

Among the more complex and least well understood reactions employed by organic chemists is the direct oxidation of alkenes with use of peroxy acids[3] or organic peroxides with metal catalysts.[4] The mechanism for epoxidation with peroxy acids that is generally accepted was initially suggested by Bartlett.[5] He proposed a "butterfly" mechanism involving a cyclic polar process in which

the proton is received by the carbonyl oxygen of the peracid with simultaneous attack by the double bond. Embellishment of this suggestion[6,7] has led to a transition state such as **1** where a high degree of concertedness is implied. Theoretical studies have suggested a "spiro" transition state for epoxidation as indicated in **2**[8] or an unsymmetrical attack of oxygen directly over one of the carbon atoms.[9] Sharpless[4] has recently suggested an orientation for metal-catalyzed oxygen transfer that is intermediate between spiro and planar.

"butterfly"   spiro   oxaziridine

1   **2**   **3**
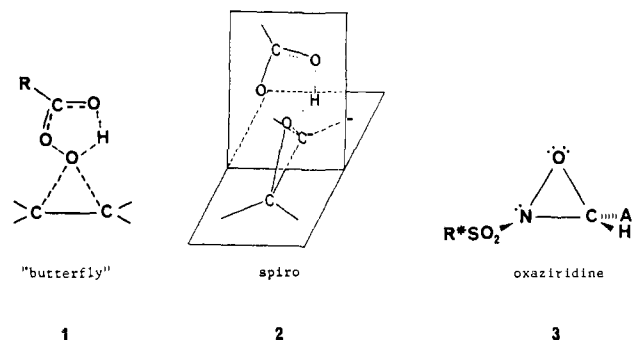
A new class of epoxidizing agents involving oxygen transfer from an oxaziridine has recently been reported by Davis.[10a] The use of chiral oxaziridines such as **3** has provided a novel method for asymmetric epoxidation of alkenes that exhibits a higher enantioselectivity than that observed with chiral peracids.[10b,c] We were intrigued by the unusual nature of this transformation involving an oxygen–nitrogen bond and its mechanistic similarity to the comparable "nucleophilic" displacement on the O–O bond in a peracid. The question of the required transition-state geometry

(1) (a) Bach, R. D.; Wolber, G. J. *J. Am. Chem. Soc.*, preceding paper in this issue. (b) Bach, R. D.; Wolber, G. J.; Pross, A. *Isr. J. Chem.* **1983**, *23*, 97.

(2) Libit, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1974**, *96*, 1370.

(3) (a) House, H. O. "Modern Synthetic Reactions"; 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; p 292. (b) Harrison, I. T.; Harrison, S. "Compendium of Organic Synthetic Methods"; Wiley-Interscience: New York, 1971; p 325; *Ibid.*, 1974; Vol. 11, p 134. (c) Swern, D. *Org. React.* **1953**, *7*, 378.

(4) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta*, **1979**, *12*, 63.

(5) Bartlett, P. D. *Rec. Chem. Progr.* **1950**, *11*, 47.

(6) (a) Lynch, B. M.; Pausacker, K. H. *J. Chem. Soc.* **1955**, 1525. (b) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976. (c) March, J. "Advanced Organic Chemistry"; 2nd ed.; McGraw-Hill: New York, 1977; p 751. (d) Berti, G. *Top. Curr. Stereochem.* **1973**, *7*, 93.

(7) (a) Ogata, Y.; Tabushi, I. *J. Am. Chem. Soc.* **1961**, *83*, 3440, 3444. (b) Hanzlik, R. P.; Shearer, G. O. *Ibid.* **1975**, *97*, 5231.

(8) Bach, R. D.; Willis, C. L.; Domagala, J. M. In "Applications of Molecular Orbital Theory in Organic Chemistry"; Cismadia, I. G., Ed.; Elsevier: Amsterdam, 1977; pp 221–229. (b) Lang, T. J.; Wolber, G. J.; Bach, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 3275.

(9) Yonezawa, T.; Katon, H.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 307. (b) Plesnicar, B.; Taseuki, M.; Azman, A. *J. Am. Chem. Soc.* **1978**, *100*, 743.

(10) (a) Davis, F. A.; Abdul-Malik, N. F.; Awad, S. B.; Harakad, M. E. *Tetrahedron Lett.* **1981**, 917. (b) Davis, F. A.; Jenkins, R. H., Jr.; Awad, S. B.; Stringer, O. D.; Watson, W. H.; Galloy, J. *J. Am. Chem. Soc.* **1982**, *104*, 5412. (c) Davis, F. A.; Harakal, M. A.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123.
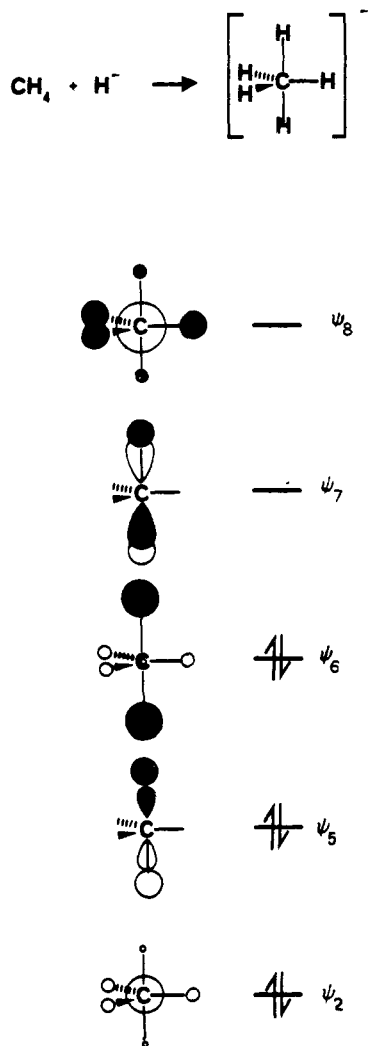
Figure 1. Frontier molecular orbitals of the transition state for hydride addition to methane (STO-3G).

for oxygen transfer is particularly relevant to our understanding of the epoxide stereochemistry observed in this and other asymmetric epoxidation reactions.[4,10c] Consequently, another objective of this study is to ascertain the energetic consequences of the orientation of approach of the reactants.

Results and Discussion

We elected to begin our study with the degenerate oxygen-transfer reaction between ethylene oxide and ethylene since the higher symmetry would simplify our analysis of the reaction pathway (eq 1). A C_2 axis bisecting the ethylene and oxirane
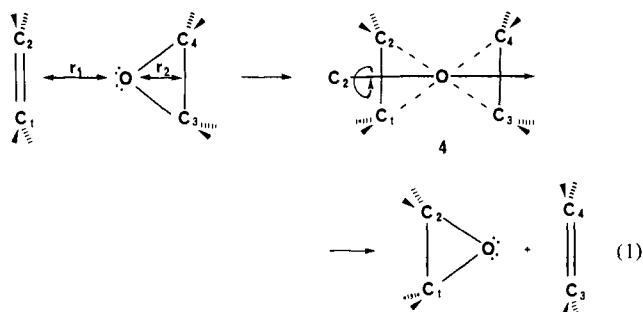
moieties was maintained throughout the reaction as shown in **4**. We assumed an S_N2 type of displacement reaction, with a "nucleophilic" ethylene displacing a second ethylene moiety from the central "electrophilic" oxygen. An understanding of the symmetry of the frontier orbitals involved in transition-state **4** is vital to our analysis of the orbital mixing involved in oxygen atom

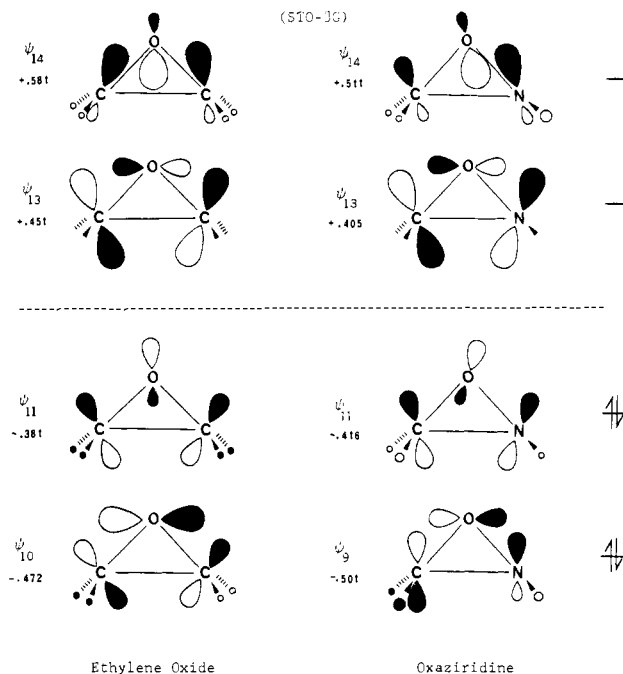Ethylene Oxide   Oxaziridine

Figure 2. Frontier Walsh orbitals in the molecular plane.

transfer. We therefore first examined a model S_N2 displacement reaction involving a transition state containing a symmetry plane.

In a typical S_N2 displacement at a saturated carbon, it is presently thought that the attacking nucleophile transfers electron density to the σ^* orbital of a C–X bond. That same nucleophile must by symmetry also interact with the σ orbital of the C–X bond.[1a] For a simple S_N2 reaction such as hydride reacting with methane (Figure 1), both the sign and the magnitude of the two axial hydrogen (nucleophile and leaving group) atomic coefficients of the wave function (in the LCAO approximation) must reflect the molecular symmetry. As a result, the HOMO at the transition state can have no p contribution from carbon and is comprised of the antibonding combination of the four-electron interaction (H^- – σ_{C-H}) mixed in a bonding fashion with the σ^*_{C-H} bond. This mixing results (eq 2) in cancellation of the p coefficient on the central carbon atom in the HOMO. Thus, the electrophilic central atom in a symmetrical S_N2 reaction should have only a 2s contribution to the HOMO at the transition state (Figure 1). It is also a consequence of orbital symmetry that NHOMO (next highest occupied MO, ψ_5) and LUMO (ψ_7) cannot have any contribution from the atomic 2s orbital at carbon. Thus, symmetry plays a significant role in the description of the molecular orbitals for one-center-substitution reactions.

$$H^\ominus - \sigma_{C-H} \quad + \quad \sigma^*_{C-H} \quad \longrightarrow \quad HOMO_{CH_5}{}^\ominus$$
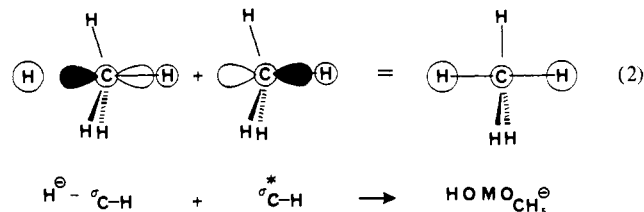
When the above symmetry principles are applied to the oxygen-transfer reaction from ethylene oxide (eq 1), correlation of the frontier molecular orbitals in the reactants with those in the transition state is greatly simplified. The pertinent frontier orbitals involved in this model reaction bear a striking resemblence to the "Walsh orbitals"[11] of cyclopropane (Figure 2). Just as an ether oxygen has two lone pairs of electrons (σ and π) that differ in

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(11) (a) Walsh, A. D. *Trans. Faraday Soc.* **1949**, *45*, 179. (b) The three filled Walsh orbitals on ethylene oxide and oxaziridine resemble those of cyclopropane. For a discussion, see: Jorgensen, W. L.; Salem, L. "The Organic Chemist's Book of Orbitals"; Academic Press: New York, 1973; p 19. (c) Reference 11b, p 160.
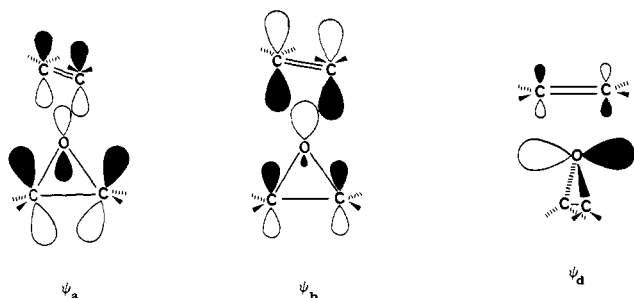
Figure 3. Frontier orbital interactions for oxygen transfer from ethylene oxide to ethylene.

Figure 4. Frontier orbital interactions for oxygen transfer.

energy by ~ 1.35 eV,[12] the two oxygen lone pairs of ethylene oxide are different in both orientation and energy. The HOMO (ψ_{12}) in ethylene oxide is the higher energy π-type (π_n) lone pair on the oxygen that is perpendicular to the plane of the ring. Although this MO has the proper symmetry to interact with the π^* orbital of ethylene in the spiro orientation (**5a**) as shown in ψ_d (Figure 3), it does not exert a large stabilizing effect on the activation energy.[13a] The initial energy gap between these orbitals is large, and the influence of the developing MO (ψ_d) is not felt until late on the reaction coordinate. This two-electron stabilizing interaction constitutes one of the subtle differences between the spiro and planar transition states. In **6a** (and **6b**) the lone pair (π_n) is perpendicular to the π^* orbital of the alkene and cannot interact by symmetry.

The second oxygen lone pair, a σ type (σ_n), is part of the highest lying filled Walsh type[11] orbital in ethylene oxide (ψ_{11}, Figure 2). Both ψ_{11} and its antibonding complement (ψ_{14}), which also lies in the molecular plane, have the proper symmetry to interact with the alkene π bond. By analogy to the typical HOMO–LUMO interaction thought to be involved in an S_N2 displacement, the dominant orbital interaction involved in nucleophilic attack on oxygen should be the alkene π molecular orbital with the empty σ^*_{O-C} Walsh orbital ψ_{14}. However, the filled π orbital of the double bond is directed toward the oxygen lone pair in ψ_{11}, and an unavoidable four-electron interaction dominates the initial orbital interactions.
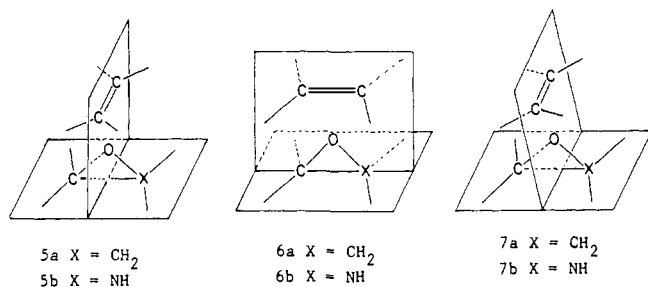

5a X = CH$_2$
5b X = NH

6a X = CH$_2$
6b X = NH

7a X = CH$_2$
7b X = NH

In principle, the interaction of two doubly occupied MO's leads to a net four-electron destabilization[14] *in the absence of higher lying orbitals of the proper symmetry to interact with the upper filled antibonding combination.*[1] As the reactants approach each other in both the planar and spiro orientations (eq 1), the π bond

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(12) (a) Sweigart, D. A.; Turner, D. W. *J. Am. Chem. Soc.* **1972**, *94*, 5599. (b) David, S.; Eisenstein, O.; Hehre, W. J.; Salem, L.; Hoffmann, R. *Ibid.* **1973**, *95*, 3806.

(13) (a) The two-electron interaction between π and π^* in the spiro transition state is much smaller than the four-electron interaction as evidenced by a difference of 0.02 kcal/mol of the π^* orbital on going to the spiro from the planar transition state (4-31G). The insignificance of this π-type interaction is a result of the long C–O bond lengths (2.1 Å) at the transition state. (b) Because of the magnitude of the initial orbital splitting, ψ_a is diminished in energy sufficiently to allow secondary four-electron interactions with the lowest lying Walsh-type orbital (ψ_8) and the σ carbon–carbon bond of ethylene, causing an increase in energy for ψ_a. The ultimate energy level of ψ_a is determined by the balance of interactions with both filled and empty orbitals of proper symmetry.

(14) For a discussin of the destabilizing influence of a four-electron interaction, see: Epiotis, N. D.; Cherry, W. R.; Shaik, S.; Yales, R. L.; Bernardi, F. "Topics in Current Chemistry"; Springer Verlag: New York, 1977; p 7.
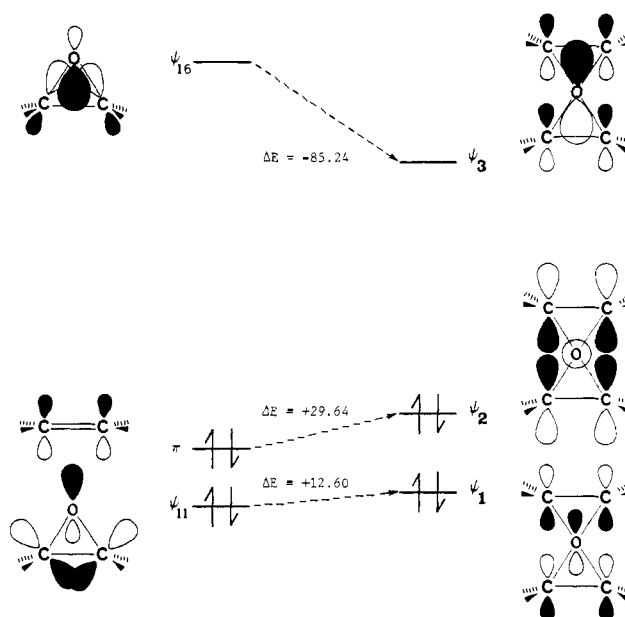
Figure 5. Orbital mixing affording symmetrical molecular orbitals at the transition state (4-31G) for oxygen transfer between ethylene oxide and ethylene.

of the alkene interacts with the *filled* Walsh orbital (ψ_{11}) containing the oxygen lone pair (σ_n) in a bonding and antibonding manner affording FMO's ψ_a and ψ_b (Figure 3). As a consequence of significant orbital splitting, the upper filled MO (ψ_b) is pushed up in energy closer to the LUMO (ψ_{14}) of ethylene oxide, facilitating the two-electron interaction (Figure 4) that accompanies the molecular collision of these two nucleophilic reactants (eq 1). The interaction of this "electrophilic orbital" (LUMO) with the developing ψ_b (Figure 3) consummates the union of atoms at the transition state. Thus, the three molecular orbital four-electron model[1a] suggests that proceeding along the reaction coordinate, ψ_b is elevated in energy by a four-electron interaction, while the bonding combination (ψ_a) is stabilized as this linear combination of fragment orbitals ultimately progresses to the transition state affording molecular orbitals ψ_1–ψ_3 (Figure 5). The repulsive nature within this molecular aggregate is evidenced as an elongation of the O–C bond (50% at the transition state) and thus is accompanied by a lowering of the energy of the antibonding Walsh orbital ψ_{14}. The expected decrease in ψ_a and other, lower orbitals, as a result of the four-electron interactions, exerts a stabilizing influence on the activation energy.[13b] The molecular reorganization induced by collision of the reactants increases the

Transfer from Oxaziridine to Ethylene

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Table I. Energetics (kcal/mol) and the Oxygen-Ethylene Bond Distance (Å) for the Degenerate Oxygen Transfer between Ethylene Oxide and Ethylene

basis set	planar			spiro		
	ΔE_{tot}	$r_1 = r_2$	$\Delta E_{HOMO}{}^a$	ΔE_{tot}	$r_1 = r_2$	$\Delta E_{HOMO}{}^a$
STO-3G	+101.9	1.835	+59.38	+100.1	1.784	+48.98
STO-3G + CI[b]//STO-3G	+115.9	1.835		+111.1	1.784	
STO-3G + CI[b,c]	+114.8	1.782				
4-31G//STO-3G	+60.5	1.835	+54.74	+64.0	1.784	+63.62
4-31G	+55.0	2.053	+29.64	+55.0	2.051	+30.10
6-31G*	+87.8	1.996		+87.7	1.988	

[a] Relative increase in HOMO (ψ_b, Figure 3) at the transition state. [b] See ref 16a. [c] Minimization of $r_1 = r_2$ only.

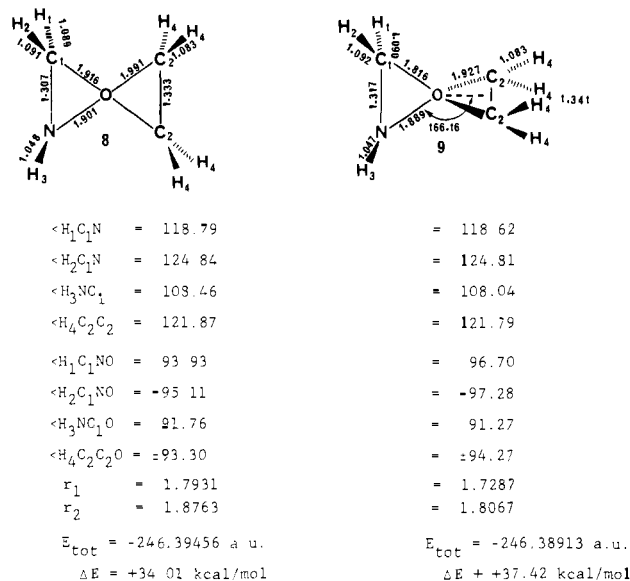|			
$<H_1C_1N$	= 118.79	=	118 62
$<H_2C_1N$	= 124 84	=	124.81
$<H_3NC_1$	= 108.46	=	108.04
$<H_4C_2C_2$	= 121.87	=	121.79
$<H_1C_1NO$	= 93 93	=	96.70
$<H_2C_1NO$	= -95 11	=	-97.28
$<H_3NC_1O$	= 91.76	=	91.27
$<H_4C_2C_2O$	= ±93.30	=	±94.27
r_1	= 1.7931	=	1.7287
r_2	= 1.8763	=	1.8067
E_{tot}	= -246.39456 a.u.	E_{tot}	= -246.38913 a.u.
ΔE	= +34 01 kcal/mol	ΔE	+ +37.42 kcal/mol

**Figure 6.** Planar and spiro transition states for oxygen transfer from oxaziridine (STO-3G) with energies (4-31G).

potential energy of the overall system contributing to the activation energy. We conclude that *orbital splitting by filled MO's brings HOMO (π) and the effective LUMO (ψ_{14}) closer together, resulting in a narrowing of the energy gap of these FMO's on the reaction pathway for oxygen transfer.*

Frontier orbital narrowing, however, is neither a necessary nor a sufficient condition for a chemical reaction to take place. The differences in frontier orbital energies of the reactants can actually *increase* as the transition state is approached.[1a] This is a consequence of the fact that as the frontier orbitals of the reactants evolve into the molecular orbitals of the transition state ($\psi_1-\psi_3$, Figure 4) the energy of the orbital comprising HOMO of the "nucleophile" (ψ_2) will tend to seek an energy level that is approximately intermediate between ψ_1 and ψ_3 (Figure 4). Thus, the energy level and nodal characteristics (Figure 5) of ψ_2 at the transition state will depend upon the relative extent of the two- and four-electron interactions. Frontier orbital narrowing will be maximized when the reaction coordinate is HOMO–HOMO dominant[1a] as in this case where ψ_2 experiences a marked increase in energy (29.6 kcal/mol) while LUMO (ψ_{16})[15] drops 85.2 kcal/mol upon its evolution into molecular orbital ψ_3 (LUMO at the transition state). The ultimate energy level of ψ_3 will result from a balance between its initial increase in energy due to any contribution from a stabilizing two-electron interaction upon mixing with the filled MO ψ_b and the stabilization of the developing antibonding MO as a result of bond elongation as the transition state is approached. It should be recognized that the energy of ψ_3 may also be influenced by its mixing with higher lying empty orbitals.

The above orbital mixing is also consistent with the symmetry requirements of an S_N2-type displacement reaction (eq 1), where
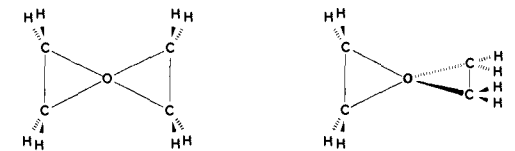
prior to the transition state the alkene is antibonding to the oxygen. At that null point where the incoming nucleophile has changed from net antibonding to bonding with the central oxygen, symmetry precludes mixing of s and p orbitals on the central atom, as the molecular orbitals must be symmetrically disposed on either side of the symmetry plane. Obviously *any contribution* from an oxygen p orbital along the axis of the reaction would destroy the plane of symmetry in HOMO (ψ_2, Figure 5). Consequently, the HOMO at the transition state for oxygen transfer contains a pure s orbital on oxygen antibonding to two ethylene fragments. This HOMO orbital may be derived (eq 3) from a linear combination of fragment orbitals, $\pi - \psi_{11}$ and ψ_{14}, as suggested above. The p coefficients on oxygen cancel in a manner analogous to that given in eq 2 and a symmetrical molecular orbital results. With the attending change in p orbital phase on the reaction surface, a net bonding interaction between the oxygen and alkene carbons and an antibonding interaction with the departing ethylene develops at or immediately after the transition state. Since the dominant interaction in eq 3 is invariant to the C_2 rotational axis in **4**, we should not anticipate a marked geometric preference for a spiro vs. a planar transition state.

$$\tag{3}$$
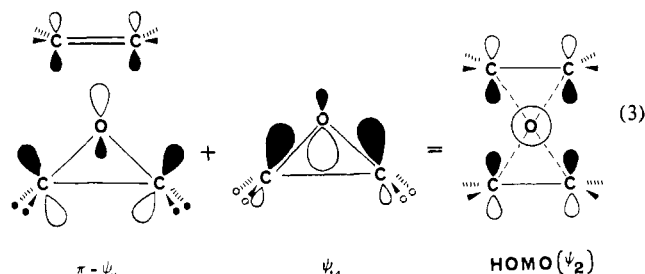
Having completed our FMO analysis of oxygen transfer (eq 1), we examined the energetics of the reaction pathway with the aid of ab initio molecular orbital calculations.[16] With an STO-3G basis set, the calculated activation energies for the (assumed) symmetrical spiro (**5a**) and planar transition states (**6a**) differed by only 1.8 kcal/mol (Table I). Less symmetrical systems (eg., **7a**) were in all cases higher in energy. Upon removal of the rotational constraint about the C_2 axis in **4**, the planar transition state collapsed to the spiro geometry. Since this reaction surface involves the repulsive interaction of the ethylene π bond with the

(15) This antibonding Walsh orbital is ψ_{14} with an STO-3G basis set but is elevated to ψ_{16} with the 4-31G basis set.

(16) (a) All calculations were run with use of the GAUSSIAN 80 series of programs. Minimization of the ethylene or ethylene oxide moieties was always constrained to be symmetrical with all carbons or hydrogens assumed identical. This constraint was not used in minimization of the formimine or oxaziridine moieties. (b) Binkley, J. S.; Whiteside, R. A.; Krishnan, R.; Seeger, R.; DeFrees, D. J.; Schlegel, H. B.; Topiol, S.; Kahn, L. R.; Pople, J. A. *QCPE* **1981**, *13*, 406. (c) Configuration interaction calculations included four filled and two empty orbitals with all single and double excitations. The energy of the starting materials was calculated by performing an STO-3G plus CI calculation on the STO-3G optimized structures of ethylene and ethylene oxide held 5.0 Å apart. This energy was the same as that obtained by performing separate CI calculations on the optimized ethylene and ethylene oxide molecules. (d) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214. (e) The geometry and STO-3G minimized total energy of formimine has been previously reported (4-31G E_{tot} = -93.87933 au).[8b] The geometry and energy of oxaziridine follow: r_{NO} = 1.447 Å, r_{OC} = 1.426 Å, r_{CN} = 1.471 Å, r_{NH} = 1.054 Å, $r_{CH_{cis}}$ = 1.091 Å, $r_{CH_{trans}}$ = 1.090 Å, $\angle$HNO = 104.50°, $\angle$H$_c$CO = 116.98°, $\angle$H$_t$CO = 117.47°, $\angle$HNOC = 100.37°, $\angle$H$_c$CON = 110.19°, $\angle$H$_t$CON = 106.55°, E_{tot} = -166.64625 au, 4-31G E_{tot} = -168.52661 au.

Table II. The Transition-State Geometries (Å and deg) and Energies (au) for Oxygen Transfer between Ethylene Oxide and Ethylene

	r_{C-O}	r_{C-C}	r_{C-H}	∠HCC	∠HCCO	E_{tot}
ethylene STO-3G		1.306	1.082	122.17		−77.07395
4-31G		1.316	1.073	121.99		−77.92216
6-31G*		1.317	1.076	121.81		−78.03172
ethylene oxide	1.432	1.483	1.088	119.47	105.04	−150.92850
	1.459	1.460	1.069	119.79	106.18	−152.62676
	1.401	1.453	1.077	119.88	103.07	−152.86736
spiro transition state	1.907	1.343	1.082	121.77	94.81	−227.84279
	2.157	1.333	1.070	121.77	91.10	−230.46122
	2.097	1.335	1.073	121.59	91.52	−230.75930
planar transition state	1.953	1.337	1.082	121.83	93.96	−227.83983
	2.159	1.333	1.070	121.75	91.10	−230.46126
	2.105	1.334	1.073	121.57	91.49	−230.75917

oxygen σ lone pair (ψ_{11}), the energy level of HOMO is increased, while LUMO (ψ_{14}) is decreased due to this large four-electron interaction.[1a] At the transition state, the HOMO–LUMO gap has diminished appreciably, and the inclusion of higher energy (excited state) configurations could become important. We therefore deemed it advisable to examine the effect of configuration interaction (CI) on the activation energy. Maintaining the above geometry (r_1 = 1.835 Å) an STO-3G plus CI calculation[16c] resulted in an increase in activation energy of 11 and 14 kcal/mol for **5a** and **6a**, respectively (Table I). Optimization of r_1 (STO-3G+CI, assuming a parabolic function) did not change the energy appreciably, although r_1 did contract to 1.78 Å. This suggests that excited-state configurations do not contribute significantly to the overall pathway, at least at this level of approximation.

A 4–31G calculation on this transition state (r_1 = 1.835 Å, 4–31G//STO-3G) suggested that the planar orientation was preferred by 3.5 kcal/mol. However, full geometry optimization of the transition state for this symmetrical oxygen transfer at this level of approximation failed to show any discernible energy difference between the two transition states (Table I). The optimized planar transition-state **6a**, which has all five heavy atoms occupying a common plane, was calculated to be 55.0 kcal/mol (4-31G) above the energy of the reactants when $r_1 = r_2 = 2.053$ Å. The activation energy for oxygen transfer in the symmetrical ($r_1 = r_2 = 2.051$ Å) spiro orientation, where the C–C bond axes are at right angles, was found to be essentially identical. Thus, a split valence basis set resulted in a much looser transition state, while an STO-3G basis with CI afforded a shorter C–O bond (Table II). Further optimization with a 6-31G* basis set afforded a more compact transition state, where there is again no significant geometrical preference (Table I).

The initial HOMO (π) − LUMO (ψ_{14}) energy separation was 0.666 au (418 kcal/mol (4-31G)). These two FMO's approach each other in energy as the transition state is achieved but yet must avoid an orbital crossing. The "avoided crossing"[17] of the reactant and excited-state surfaces is a consequence of this orbital energy narrowing. In the planar orientation ψ_b, the out-of-phase combination (π − ψ_{11}) that evolves into HOMO (ψ_2) at the transition state is elevated in energy by 29.6 kcal/mol (Figure 5) as a result of the four-electron orbital splitting. The LUMO orbital (ψ_{14})[15] has decreased 85.2 kcal/mol at the transition state largely as a result of C–O bond elongation. We note that, in principle, early on the reaction coordinate an opposing orbital energy increase in LUMO (ψ_c) may be operating due to the two-electron stabilizing influence of the interaction of the developing HOMO (ψ_2, Figure 4) with LUMO. The increase in

the lower level bonding FMO (ψ_{11}, NHOMO) is due to secondary orbital interactions.[13b]

We wish to point out that in an initial cursory examination (STO-3G) of this oxygen-transfer reaction (eq 1), we altered r_1 in decrements of 0.015 Å while minimizing r_2 until we arrived at that point where displacement of the ethylene moiety of ethylene oxide was exothermic without a barrier. With all other geometric variables optimized while maintaining C_2 symmetry, we found that this energy maximum for a planar orientation was unsymmetrical with r_1 = 1.675 Å and r_2 = 1.415 Å (STO-3G). This point on the reaction surface was 11.2 kcal/mol (STO-3G) above the symmetrical planar transition state that is required by the principal of microscopic reversability.

In similar fashion, we found the unsymmetrical (r_1 = 1.660 Å, r_2 = 1.409 Å) spiro energy maximum to be 6.4 kcal/mol (STO-3G) above the transition state. Thus, from the above discussion, it is obvious that both r_1 and r_2 must be varied simultaneously on the reaction coordinate and that significant C–O bond elongation (62.5%) is required to achieve a symmetrical transition state for oxygen transfer. A simple picture of one reagent "displacing" the other does not provide an adequate description of the reaction surface.

As anticipated, the transfer of oxygen from oxaziridine to ethylene was calculated to be an exothermic process (ΔE = 34.5 kcal/mol, 4-31G//STO-3G) that proved to be remarkably similar to the comparable reaction in eq 1. Employing the same logic as above that assumed an S_N2 type of displacement, we found the "displacement point" for a planar orientation **6b** (r_1 = 1.720 Å, r_2 = 1.409 Å) to be 79.0 kcal/mol (4-31G//STO-3G) above the ground state of the reactants. The energy required for formimine displacement in a spiro mode was 76.7 kcal/mol with the ethylene approaching along the O–N bond axis as in **7b** (r_1 = 1.675 Å, r_2 = 1.400 Å). Using the above structures as an initial guess, we fully optimized (STO-3G) the transition structures for oxygen transfer using energy gradients.[16d] The planar **8** and spiro **9** transition structures were 34.01 and 37.42 kcal/mol above reactants with an energy difference of only 3.41 kcal/mol (4-31G//STO-3G, Figure 6).[16e] Thus, the calculated (4-31G//STO-3G) activation barriers for oxygen transfer from an oxaziridine are 26.5 and 26.6 kcal/mol less than that for the comparable reaction with ethylene oxide (Table I).

Examination of the experimental evidence of Davis[10] unquestionably established the necessity for a preferred planar orientation in this reaction in order to afford the observed stereochemistry of the resultant chiral epoxide. Our model structures, which are essentially void of steric interactions, do show a slight preference for the planar orientation for epoxidation with an oxaziridine when the reagents are close together at the transition state ($r_1 \leq 1.8$ Å). Inclusion of configuration interaction was shown earlier to

(17) Fukui, K. "Theory of Orientation and Stereoselection"; Springer-Verlag: New York, 1975; p 107.
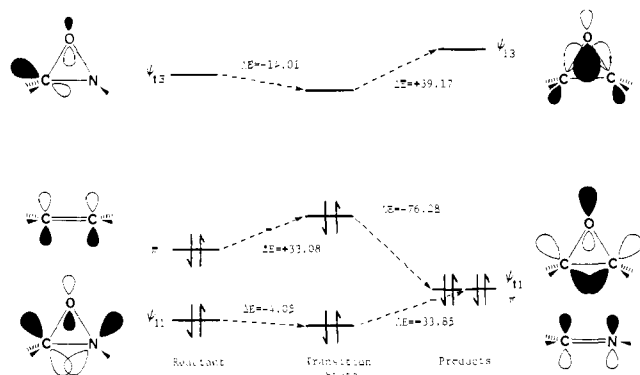
Figure 7. Orbital mixing from the starting materials to the transition state and products for oxygen transfer from oxaziridine to ethylene.

cause a further contraction of r_1 with ethylene oxide.

Analysis of the energy changes of the ground-state molecular orbitals on going to the transition state was rendered more difficult by the loss of symmetry due to the nitrogen atom.[18] However, the similarity to our model displacement with ethylene oxide was evident. The four-electron orbital splitting was comparable in magnitude to that noted with ethylene oxide. The HOMO orbital very closely resembled that in Figure 5, with a minute contribution of an oxygen atomic p orbital as a result of the loss of symmetry.

Correlation of the reactant orbitals with those in the products is also consistent with the suggested orbital mixing in the transition state. The nucleophilic Walsh orbital ψ_{11} in oxaziridine is transformed into the C=N π bond (Figure 7) as the oxygen with its σ_n "lone pair" is transferred to ethylene affording ψ_{11} of ethylene oxide. The π_n lone pair in the spiro orientation mixes with π^* and affords ψ_{10} of the product ethylene oxide.

In summary, oxygen transfer is mediated by a four-electron orbital splitting that serves to elevate the energy of a filled orbital, the "effective HOMO" (ψ_b) on the reaction coordinate, with an energy-compensating decrease in the level of ψ_a. This repulsive interaction serves to lower the $\Delta H^{\ddagger}$ of the reaction provided it is attended by a stabilizing two-electron interaction of ψ_b with a higher lying empty orbital (ψ_{14}).[15] Thus, in many such "electrophilic" reactions with alkenes the early part of the reaction trajectory is dominated by an inescapable four-electron interaction involving the nucleophilic alkene π bond and a lone pair on the heteroatom undergoing nucleophilic displacement. The electrophilic nature of such a reagent may be attributed to the fact that the reagent has an empty antibonding orbital that initially decreases dramatically in energy as one proceeds along the reaction coordinate. It is the interaction of the developing filled central orbital ψ_b with this empty "electrophilic orbital" that is responsible for the facility of electrophilic addition reactions to alkenes. It

is the four-electron orbital splitting early on the reaction coordinate that serves to elevate ψ_b, the effective HOMO which interacts with an unoccupied orbital, and causes an increase in the energy of the LUMO orbital as illustrated in Figure 4. The net result of this combined interaction is to reduce the activation energy at the expense of an *empty orbital that increases in* energy. This is not a new concept since it is this type of orbital mixing that provides the "conjugation energy" in the allyl anion, amides,[19] and butadiene.[20a] It has also been recognized[20b] that HOMO–HOMO orbitals are closer in energy and their orbital splittings are typically larger in magnitude than the corresponding HOMO–LUMO orbital splitting.[21] Consideration of HOMO–LUMO stabilizing interactions, pioneered by Fukui,[17,22a] Hoffmann,[2] Salem,[22b] Houk,[22c] and others,[22d] has provided a valuable tool for predicting reactivity trends and regiochemistry.

Four-electron interactions markedly influence the energetics of reactions. This initial orbital destabilization and accompanying stretching of the weak N–O (or O–O) bond with the subsequent decrease in the effective LUMO is responsible for the electrophilic character of epoxidation reagents. This should be particularly true with peroxy acids and halogen molecules where an unusually weak bond is present. Such electrophilic reagents that contain a weak σ bond often possess a relatively *high* σ^* orbital that can be readily induced to decrease dramatically in energy upon perturbation by an alkene. It is in this latter case where one should anticipate a narrowing of the frontier orbital energies when the LUMO decreases in energy as a result of bond elongation. This four-electron, three molecular orbital model when combined with a cognizance of atomic orbital cancellation provides valuable information about the energetics of chemical reactions and the origin of the molecular orbitals that comprise the transition state. Application of these basic concepts to the E_2 elimination and the Diels–Alder reactions is in progress.

(18) The oxygen π_n lone pair is interacting with the adjacent nitrogen lone pair with a lower bonding combination at –0.522 au (ψ_{10}) and the higher lying filled π^* combination (ψ_{12}) at –0.437 au.

(19) Bach, R. D.; Braden, M. L.; Wolber, G. J. *J. Org. Chem.* **1983**, *48*, 1439.

(20) (a) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; John Wiley & Sons: New York, 1976; p 18. (b) Reference 20a, p 26.

(21) It is recognized that the four-electron destabilization is proportional to the median energy of the two filled orbitals while the magnitude of the orbital splitting is a function of the energy difference just as the stabilizing 2-electron interaction is.[1a]

(22) (a) Fukui, K. *Science* **1982**, *218*, 747. (b) Salem, L. *J. Am. Chem. Soc.* **1968**, *90*, 543, 553. Houk, K. N. *Top. Curr. Chem.* **1979**, *79*, 1. (d) Herndon, W. C. *Chem. Rev.* **1972**, *72*, 157; Hudson, R. F. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 36; Klopman, G. "Chemical Reactivity and Reaction Paths"; John Wiley & Sons: New York, 1974.