On the Origin of Substrate Directing Effects in the Epoxidation of Allyl Alcohols with Peroxyformic Acid

Robert D. Bach,*,[†] Carlos M. Estévez,[†,‡] Julia E. Winter,[§] and Mikhail N. Glukhovtsev[†]

Contribution from the Department of Chemistry and Biochemistry, University of Delaware,
Newark, Delaware 19716, and Department of Chemistry, Wayne State University,
Detroit, Michigan 48202

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Abstract: The reactant cluster and transition state for epoxidation of allyl alcohol with peroxyformic acid have been located at the MP2/6-31G(d) level of theory. The free energy of activation ($\Delta G^{\ddagger}_{278}$ = 19.8 kcal/mol) predicted at the MP4//MP2/6-31G(d) level is quite comparable with experimental data for epoxidation of 3-hydroxycyclohexene ($\Delta G^{\ddagger}_{278}$ = 19.7 kcal/mol). A spiro transition state (TS) was found where the plane defined by the peroxyacid moiety is oriented at 89° to the C═C bond axis. Intrinsic reaction coordinate analysis suggests that after the barrier is crossed a 1,4-hydrogen migration of the peroxyacid hydrogen to the carbonyl oxygen takes place in concert with O−O bond cleavage affording the epoxide of allyl alcohol hydrogen bonded to the neutral formic acid leaving group. The activation parameters calculated at the B3LYP/6-311G(d,p) level are in excellent agreement with the MP4//MP2 values. The transition structure with the allyl alcohol O−C−C═C dihedral angle of 16.4° is 2.1 kcal/mol lower in energy than a transition structure with a dihedral angle of 134.3°. The directing effect of the hydroxyl group is attributed initially to a primary hydrogen bonding interaction between the relatively more acidic peroxy acid proton and the oxygen of the allyl alcohol. In both the reactant complex **1** and the transition structure (**TS-2**) for oxygen atom transfer the alcohol remains hydrogen bonded to the more basic carbonyl oxygen of the peroxyacid. The G2 proton affinities (PA_{298}) of the carbonyl oxygen and the proximal peroxo oxygen of peroxyformic acid are 177.1 and 153.3 kcal/mol, respectively.

Introduction

Control of the stereochemical aspects of the epoxidation of allyl alcohols remains an important synthetic objective.[1] In this stereoselective process, hydroxyl participation results in the delivery of the electrophilic oxygen to the sterically more congested alkene diastereoface syn to the allylic heteroatom. Both stereoelectronic effects associated with steric repulsion and attractive preassociation interactions of polar functional groups with reagents can influence both the regio- and stereochemical outcome of a reaction.[2] One of the earliest transient interactions of a substrate functional group with an incoming reagent where the directing functionality itself is not altered and remains intact in the recovered product was reported by Henbest and Wilson in 1957.[3] They observed that upon treatment with perbenzoic acid in benzene the formation of epoxides from cyclic allylic alcohols occurs on the same side as the hydroxyl group. Although 3-hydroxycyclohexene yielded mainly the cis-epoxide, 3-methoxy- and 3-acetoxycyclohexene gave predominantly the trans-epoxide but at a much slower rate. Subsequently, the concept of heteroatom directed peroxyacid epoxidation was demonstrated in a number of cyclic and acyclic systems.[2] The face selectivity observed with allyl alcohols was attributed to a hydrogen bond formed between the hydroxy group and one of the two peroxo oxygens that favors oxygen transfer to the syn face of the alkene.[3] A transition state resembling the "butterfly" mechanism of Bartlett,[4] involving the interaction of the nucleophilic alkene with the electrophilic peroxyacid, was proposed.

In 1973 Sharpless and Michaelson published a highly stereoselective method to epoxidize allylic alcohols using transition metal catalysts.[5a] Subsequently, Johnson and Kishi[6] reported a unique cooperative effect by a hydroxyl and an ether functionality in peroxyacid epoxidation. One of the key variables used in early attempts[7,8] to rationalize these stereochemical results was the O−C−C═C dihedral angle of the allyl alcohol. Optimum dihedral angles of ∼150° were suggested for stereoselective epoxidation of cyclohexenols. Sharpless[5b] used stereoelectronic arguments to arrive at the conclusion that the plane defined by the peroxyacid group is oriented at ∼60° to the C−C π-bond axis and the O−C−C═C dihedral angle was predicted to be ∼120°. Evans and co-workers[2] suggested an optimal dihedral angle of ∼140°. All of the proposed transition states invoked a backside S_N2-like attack of the alkene π-bond on the O−O β-bond of the peroxyacid[9] and a hydrogen bonding interaction between the alcohol hydroxyl group and

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[†] University of Delaware. WWW http://www.edu/chem/bach.

[‡] Present address: Departamento de Quimica Fisica. Facultade de Quimica. Universidade de Santiago de Compostela 15706 (Spain).

[§] Wayne State University.

(1) (a) Plesnicar, B. In *The Chemistry of Peroxides*; Patai, S., Ed.; John Wiley and Sons: New York, 1983; p 521. (b) Finn, M. G.; Sharpless, K. B. *Asymmetric Synth.* **1986**, *5*, 247. (c) *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. II, Chapter 5.

(2) For an excellent review on substrate-directable chemical reactions, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev. (Washington, D.C.)* **1993**, *93*, 1307.

(3) (a) Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1957**, 1958. (b) Henbest, H. B. *Proc. Chem. Soc.* **1963**, 159.

(4) Bartlett, P. D. *Rec. Chem. Prog.* **1950**, *11*, 47.

(5) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63.

(6) Johnson, M. R.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4347.

(7) Chamberlain, P.; Roberts, M. L.; Whitham, G. H. *J. Chem. Soc. (B)* **1970**, 1374.

(8) Chautemps, P.; Pierre, J.-L. *Tetrahedron* **1976**, *32*, 549.

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one of the two peroxo oxygens. Failure to invoke hydrogen bonding to the carbonyl oxygen was based upon proposed interatomic bond distances that appeared to be too large[2,5b] and perhaps because it has been traditionally anticipated that an intramolecular 1,4-hydrogen shift of the peroxo hydrogen to the carbonyl oxygen occurred in concert with oxygen atom transfer.[4] The trajectory of the incoming oxygen with respect to the carbon−carbon double bond is another unknown variable that had not been resolved. More recently these stereoelectronic concepts have been extended to the epoxidation of allylic substrates with dioxiranes.[10]

Despite the fact that the epoxidation of alkenes was discovered nearly a century ago,[11] surprisingly little is known about the nature of the transition state for this highly efficient oxygen atom transfer reaction. Mechanistic studies on simple alkenes[12] and a series of stereochemical investigations aimed at elucidating the subtleties involved in substrate directable epoxidation[13] have defined the overall mechanism, but the transition structure has remained elusive. We now propose a mechanism for epoxidation of allyl alcohols where the initial reaction trajectory forming a prereaction complex is dominated by a strong hydrogen bonding interaction involving the more acidic peroxyacid proton and the oxygen of the allylic alcohol. The stereochemistry of the oxygen atom transfer step is a consequence of a primary hydrogen bonding interaction between the alcohol hydrogen and the carbonyl oxygen of the peroxyacid (H_2-O_3) in the transition structure (TS) and a secondary hydrogen bond between the more acidic hydroperoxide hydrogen (−OOH) and the oxygen of the alcohol (H_1-O_4).

Results and Discussion

Peroxyformic Acid. (a) Proton affinities. We initiated this study with a thorough examination of the electronic structure of peroxyformic acid.[14] For this particular study the relative basicity of the three oxygen atoms in a peroxyacid is germane to the type and magnitude of hydrogen bonding interactions it has with the allyl alcohol substrate. The peroxyacid carbonyl acts as a Lewis base and plays the role of acceptor through its interaction with the peroxyacid proton. On the basis of the G2 energy difference[15] for rotation from the hydrogen-bonded syn conformation to the planar anti form of peroxyacetic acid, the strength of the hydrogen bond for these peroxy acids is evaluated to be $\Delta H_{298} = 5.0$ kcal/mol.[16a] This intramolecular hydrogen bond is not disrupted upon complexation with either one or two molecules of water.[17] However, in methanol solvent 2-cyclopenten-1-ol is stereorandomly oxidized since in all likelihood a protic media preempts the intramolecular hydrogen bond in the peroxyacid.[2]

On the basis of the relative energies of the three isomers of protonated peroxyformic acid (**A**, **B**, and **C**; Figure 1), we calculated using G2 theory that the proton affinity of the carbonyl oxygen in peroxyformic acid ($PA_{298} = 177.1$ kcal/mol) is 23.1 kcal/mol (at 0 K) greater than its adjacent peroxo oxygen (isomer **C**) (Table 1). The nonplanar structure **C** features an elongated C−O bond and can be considered as a complex of the HCO^+ cation and hydrogen peroxide (Figure 1). This most likely reflects the fact that the O−H bond energy in the HOOH fragment is stronger than the C−O bond in peroxyformic acid. The planar C_s structure **C1**, which is 8.6 kcal/mol higher in energy than structure **C**, is a second-order saddle point rather than a minimum as determined by a frequency calculation at the MP2/6-31G(d) and B3LYP/6-31G(d,p) levels.[18] Release of the C_s symmetry constraint afforded minimum **C**. Geometry optimization of structures **A**, **B**, **C**, **B1**, and **C1** at the MP2(full)/6-31G(d,p) level made no significant change in the geometry and the stationary point type.[18b] Optimization at the B3LYP/6-31G(d,p) level led to shorter C_1-O_1 bond distances in these structures (Figure 1) though the changes in relative energy were insignificant. These data provide a clear rationale for why the dominant hydrogen bonding interaction of allyl alcohol with peroxyformic acid along the reaction coordinate involves the more basic carbonyl oxygen. Moreover, the syn-protonated isomer **A**, where the more acidic proton is hydrogen bonded to the hydroxyl oxygen, is 1.7 kcal/mol lower in energy (using G2 theory) than the anti conformer **B** that lacks any hydrogen bonding (structure **B1** is a TS for the O−OH rotation in **B**). This is particularly relevant since an intramolecular 1,4-hydrogen shift must accompany oxygen transfer to diminish the obligatory charge separation attending heterolytic O−O bond cleavage.[16c] Protonated isomer **A** is involved in the acid-catalyzed epoxidation of alkenes.[16b] The proton affinity of peroxyformic acid (177.1 kcal/mol) is almost the same as the proton affinity of formic acid (the experimental

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[9] (a) Bach, R. D.; Willis, C. L.; Domagals, J. M. *Applications of MO Theory in Organic Chemistry*; Csizmadia, I. C., Ed.; Elsevier: Scientific: Amsterdam, 1977; Vol. 2, p 221. (b) Bach, R. D.; Andrés, J. L.; Davis, F. *J. Org. Chem.* **1992**, *57*, 613.

[10] (a) Murray, R. W.; Singh, M.; Williams, B. L.; Moncrief, H. M. *J. Org. Chem.* **1996**, *61*, 1830. (b) Adam, W.; Smerz, A. K. *J. Org. Chem.* **1996**, *61*, 3506.

[11] Prileschajew, N. *Ber.* **1909**, *42*, 481.

[12] (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) Vilka, M. *Bull. Soc. Chim. Fr.* **1959**, 1401. (d) Renolen, P.; Ugelstad, J. *J. Chim. Phys. Phys. Chim. Biol.* **1960**, *57*, 634. (e) House, H. O.; Ro, R. S. *J. Am. Chem. Soc.* **1958**, *80*, 2428. (f) Ogata, Y.; Tabushi, I. *J. Am. Chem. Soc.* **1961**, *83*, 3440, 3444. (g) Curci, R.; DiPrete, R. A.; Edwards, J. O.; Modena, G. *J. Org. Chem.* **1970**, *35*, 740.

[13] Berti, G. *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1973; Vol. 7, p 93.

[14] (a) Theoretical calculations were carried out with the Gaussian94 program system[14b] utilizing gradient geometry optimization. (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowki, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; González, C.; Pople, J. A. GAUSSIAN 94; Gaussian, Inc.: Pittsburgh, PA, 1995. (c) González, C.; Schlegel, H. B. *J. Chem. Phys*. **1989**, *90*, 2154. (d) González, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.

[15] For a description of the G2 level see: Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221.

[16] (a) Bach, R. D.; Ayala, P. Y.; Schlegel, H. B. *J. Am. Chem. Soc.* **1996**, *118*, 12758. (b) Bach, R. D.; Winter, J. E.; Canepa, C.; Blanchette, P. E. *J. Org. Chem.* **1997**, *62*, 5191. (c) Bach, R. D.; Owensby, A.; González, C.; Schlegel, H. B. *J. Am. Chem. Soc.* **1991**, *113*, 2338. (d) Bach, R. D.; Glukhovtsev, M. N.; Canepa, C. *J. Am. Chem. Soc.* Submitted for publication. (e) Bach, R. D.; Gonzalez, C.; Glukhovtsev, M. N.; Marquez, M.; Estévez, C. M.; Baboul, A. G.; Schlegel, H. B. *J. Phys. Chem. A* **1997**, *101*, 6092. (f) Bach, R. D.; Winter, J. E.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1995**, *117*, 8586. (g) Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C.; Estévez, C. M. Unpublished results.

[17] Complexation of a molecule of H_2O to the acidic hydrogen of HCO_3H has a stabilization energy of 9.5 kcal/mol (MP4//MP2/6-31G(d)) while ΔE_{stab} for H_2O hydrogen bonding to the carbonyl oxygen is −8.2 kcal/mol. Hydrogen bonding of a H_2O at each of the two sites results in $\Delta E_{stab} = -18.8$ kcal/mol. These data are consistent with the observation that protic solvents dramatically slow the rate of alkene epoxidations.

[18] (a) While our G2 calculations give relative energies for the isomers of protonated peroxyformic acid which are different from our earlier MP2 data,[16b] the relative stability order is the same. (b) The relative energies of structures **B1** and **C1** with respect to minima **B** and **C** are 7.1 and 8.6 (G2 theory), 8.2 and 7.5 (B3LYP/6-31G(d,p)), and 8.7 and 10.8 kcal/mol (MP2-(full)/6-31G(d,p)), respectively. The energy difference between structures **B** and **A** is 1.7 (G2), 1.9 (B3LYP/6-31G(d,p)), and 2.8 kcal/mol (MP2-(full)/6-31G(d,p)).

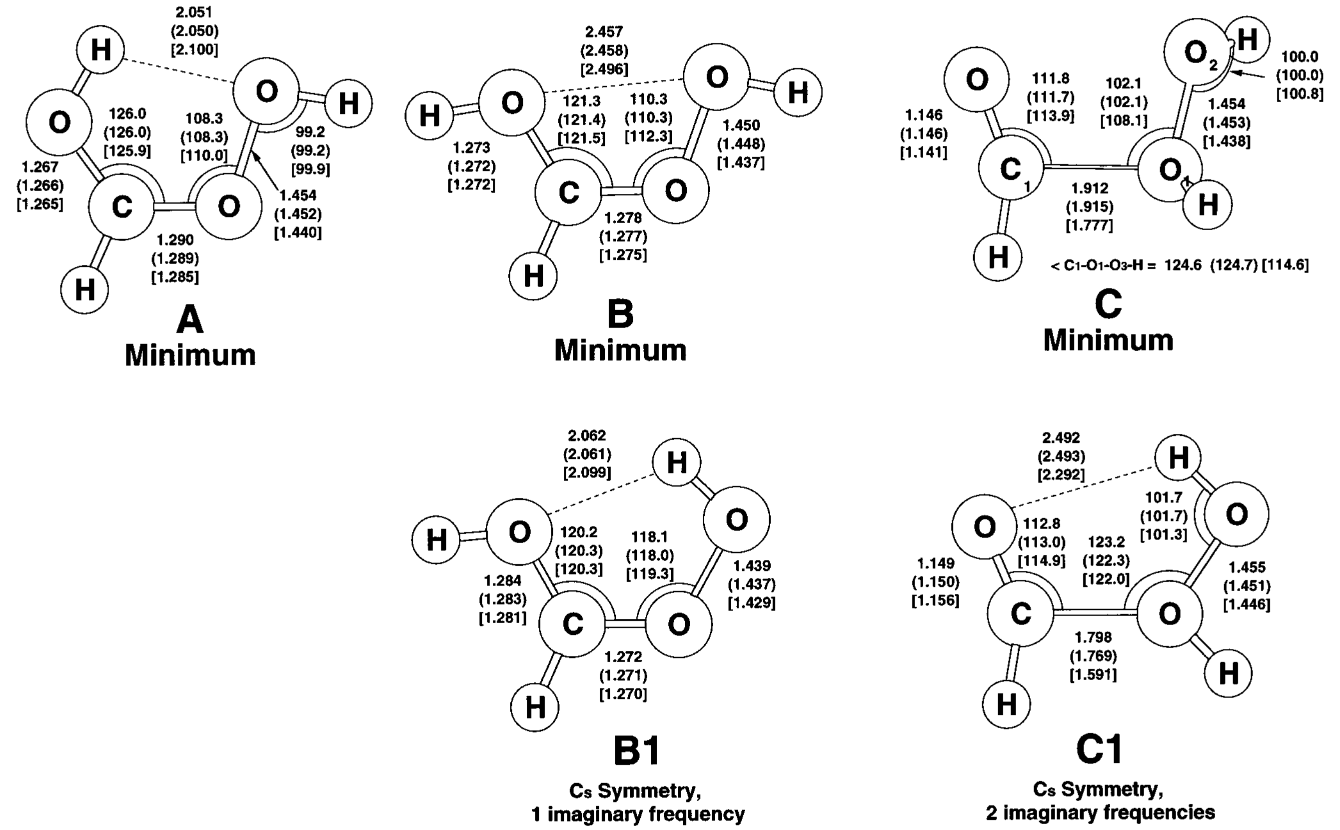

Figure 1. Structures of various isomers of protonated peroxyformic acid calculated at MP2(full)/6-31G(d), MP2(full)/6-31G(d,p) (in parentheses), and B3LYP/6-31G(d,p) [in square brackets] levels of theory. Distances are in angstroms and angles are in degrees.

Table 1. G2 Calculated Proton Affinities of Peroxyformic Acid and the Proton Affinity of Peroxyformic Anion (in kcal/mol)[a]

protonation	PA (0 K)	PA (298 K)
peroxyformic acid → structure **A**	175.8	177.1
peroxyformic acid → structure **B**	174.1	175.4
peroxyformic acid → structure **C**	152.7	153.3
peroxyformic anion → peroxyformic acid	354.2	355.5

[a] The G2 calculated energies for peroxyformic acid, its protonated structures **A**, **B**, and **C**, and for peroxyformic anion are given in Table 1S (Supporting Information).

PA_{298} = 177.3 kcal/mol,[19a] G2 calculated PA_{298} = 177.6 kcal/mol[19b]). In the gas-phase peroxyformic acid the deprotonation energy (ΔE = 355.5 kcal/mol at 298 K using G2 theory; Table 1) is slightly weaker than that for formic acid ($\Delta E = 345.3 \pm 2.3$ kcal/mol),[19a] consistent with their relative pK_a's in solution.

(b) The O−O Bond Dissociation Energies. The O−O homolytic bond dissociation energy (BDE) for peroxyformic acid calculated at the G2, G2(MP2), and MP4//MP2/6-31G(d) levels is 48.4, 49.2, and 50.7 kcal/mol, respectively.[16a] Interestingly, the BDE for peroxytrifluoroacetic acid (48.9 kcal/mol at G2(MP2)) is essentially the same as that of its parent peroxyacetic acid even though it is orders of magnitude more reactive.[21a] Another indication that the reactivity of a peroxide is not necessarily a manifestation of its O−O BDE is the observation that the epoxidation of ethylene with peroxynitrous acid (HO−ONO), which has a G2 BDE of only 22.0 kcal/mol,[16a] exhibits an activation barrier ($\Delta E^{\ddagger}$ = 18.3 QCISD(T)//QCISD/6-31G(d))[16d] comparable to that calculated for peroxyformic acid (18.8 kcal/mol)[16e] at the same level of theory.

The Epoxidation of Allyl Alcohol with Peroxyformic Acid. (a) General Features of the Transition Structure for Alkene Epoxidation with Peroxyformic Acid. The reaction trajectory for alkene epoxidation is another important issue that has only recently been resolved. Electrophilic attack of peroxyformic acid on simple nonconjugated alkenes occurs in a spiro fashion at the center of the carbon−carbon double bond.[16e,f] However, this potential energy surface is very shallow and the difference in energy between this TS and an unsymmetrical attack where the oxygen attacks directly over one carbon atom is quite small. Moreover, a planar "butterfly" structure[4] (second-order saddle point) for the epoxidation of ethylene is only 1.4 kcal/mol higher in energy than a spiro TS where the plane of the peroxyacid moiety is 90° to the C−C bond axis. The classical barrier for the epoxidation of ethylene is predicted to be 16.3 kcal/mol at the MP4//MP2/6-31G(d) level.[16e] An increase in the size of the basis set to 6-311+G(d) did not significantly affect the geometry. Optimization of this peroxyformic acid−ethylene TS at the CCSD level with and without the triples resulted in only nominal changes in the transition structure. The CCSD(T)/6-31G(d) classical barrier for ethylene epoxidation is 19.4 kcal/mol.[16e] The epoxidation of 1,3-butadiene, however, proceeds in a unsymmetrical fashion[16g] and the TS resembles a Michael-type addition in excellent agreement with kinetic isotope effects for the oxidation of a styrene derivative reported by Hanzlik.[21b]

(b) Nature of the Transition Structure for Allyl Alcohol Epoxidation. The above arguments suggest that the energetic consequences of the approach of the peroxyacid to the π-bond

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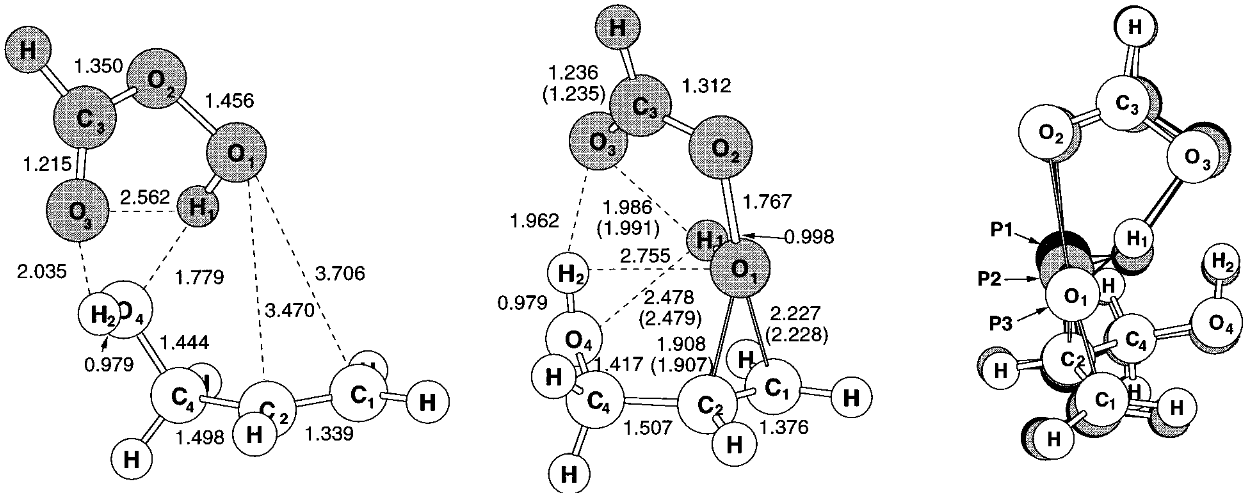
(19) (a) Hunter, E. P.; Lias, G. S. *J. Phys. Chem. Ref. Data* In press. The value was taken as cited in ref 20b. (b) East, A. L. L.; Smith, B. J.; Radom, L. *J. Am. Chem. Soc.* **1997**, *119*, 9014.

(20) (a) Calculated from the experimental enthalpies of formation given in the NIST database.[20b] (b) NIST Standard Reference Database Number 69—February 1997 Release (http://webbook.nist.gov/chemistry).

(21) (a) Hart, H. *Acc. Chem. Res* **1971**, *4*, 337. (b) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *106*, 1401. (c) Miertus, S.; Scrocco, E.; Tomasi, J. *J. Chem. Phys.***1981**, *55*, 117.



1

∠O2-C3-O3=128.06
∠C3-O2-O1=111.98
∠O2-O1-H1=101.83
∠O4-C4-C2=111.91
∠C4-C2-C1=123.02
∠C1-C2-C4-O4=107.12
∠O1-C2-C4-O4=23.09
∠C2-C1-O1-H1=43.74
∠C2-C1-O2-C3=-24.21
∠O3-C3-O2-O1=8.35

$E_{MP2/6\text{-}31G(d)}$ = -456.67015 a. u.
$\Delta E_{stabilization(MP2/6\text{-}31G(d))}$ = -9.80 kcal/mol
$E_{MP4/6\text{-}31G(d)//MP2/6\text{-}31G(d)}$ = -456.76462 a. u.
$\Delta E_{stabilization(MP4/6\text{-}31G(d)//MP2/6\text{-}31G(d))}$ =
-10.69 kcal/mol

TS-2

∠O2-C3-O3=127.98 (128.05)
∠C3-O2-O1=105.28 (105.29)
∠O2-O1-H1=91.67 (91.76)
∠O4-C4-C2=112.49 (112.48)
∠C4-C2-C1=122.32 (122.30)
∠C1-C2-C4-O4=25.46 (25.64)
∠O1-C2-C4-O4=-65.02 (-65.01)
∠C2-C1-O1-H1=110.81 (110.99)
∠C2-C1-O2-C3=89.01 (88.91)
∠O3-C3-O2-O1=4.69 (4.70)

$E_{MP2/6\text{-}31G(d)}$ = -456.63892 a. u.
$\Delta E^{\ddagger}_{(MP2/6\text{-}31G(d))}$ = 8.55 kcal/mol
$E_{MP4/6\text{-}31G(d)//MP2\text{-}6\text{-}31G(d)}$ = -456.68920 a. u.
$\Delta E^{\ddagger}_{(MP4/6\text{-}31G(d)//MP2/6\text{-}31G(d))}$ = 7.71 kcal/mol

IRC

	P1	P2	P3
Reaction coord.	0.000	-1.49	-4.48
Relative energy	0.000	-5.19	-40.94
Distances:			
O1-O2	1.767	1.952	2.339
O1-C1	2.755	2.017	1.561
O1-C2	1.908	1.666	1.478
O1-H1	0.988	1.015	1.201
H1-O3	1.986	1.840	1.519
H1-O4	2.478	2.406	2.418
O4-H2	0.979	0.985	0.984
H2-O3	1.962	1.936	1.879
O3-C3	1.236	1.262	1.307
C3-O2	1.312	1.280	1.238

Figure 2. Reactant cluster, **1**, transition state, **TS-2**, and the IRC path study of the epoxidation of allyl alcohol with peroxyformic acid showing the movement of atoms from the transition state (dark, **P1**) toward the products (light, **P3**) with an intermediate structure, **P2**. The calculation was done at the MP2/6-31G(d) level. The reaction coordinate is in units of amu bohr, the relative energies are in kcal/mol, and the distances are in Å. Geometric parameters in parentheses are at the MP2/6-31G(d,(p)) (see text) level of theory.

should be less important than the directing effects of hydrogen bonding. The initial calculations for this study were at the MP2/6-31G(d) level of theory. At the MP4/6-31G(d)//MP2/6-31G(d) level gas-phase reactant cluster **1** is stabilized by 10.7 kcal/mol (Figure 2) as a consequence of a relatively strong hydrogen bond between the more acidic peroxyacid hydrogen (pK_a = 7.1) and the oxygen of allyl alcohol ($r_{H_1-O_4}$ = 1.78 Å). A weaker hydrogen bonding action between the alcohol (pK_a ~18) and the carbonyl oxygen ($r_{H_2-O_3}$ = 2.04 Å) is responsible for keeping the electrophilic oxygen (O_1) poised above the nucleophilic π-bond ($O_4-C_4-C_2{=}C_1$ dihedral angle = 107.1°). However, as a consequence of a relatively high entropy (in absolute value) of formation for the pre-reaction complex ($\Delta S = -31.65$ cal/mol K), the free energy of formation of **1** is only slightly negative ($\Delta G_{278} = -0.2$ kcal/mol), suggesting that at least in the gas phase the directing effect of the hydroxyl substituent is principally a transition state phenomenon.

The transition state for oxygen atom transfer (**TS-2**) provides a much clearer picture of the hydroxyl directing effect. The S_N2-like backside attack of the π-bond on the O−O bond ($\angle(C_1-C_2)-O-O = 172°$) is directed by the hydroxyl group to the syn-face of the double bond ($r_{H_2-O_3}$ = 1.96 Å) albeit with a relatively small $O_4-C_4-C_2{=}C_1$ dihedral angle of only 25.6°. The more acidic peroxyacid hydrogen is bonded to both the hydroxyl oxygen ($r_{H_1-O_4}$ = 2.48 Å) and the carbonyl oxygen. The plane of the peroxyacid functionality in spiro **TS-2** is 89.0° with respect to the C_2-C_1 bond axis.

Animation of the vectors of the single imaginary frequency (MP2/6-31G(d), 436 *i* cm^{-1}) shows principally O−O bond elongation in concert with rotation about the C_2-C_4 bond such that the out-of-plane deformation of C_2 shortens the C_2-O_1 bond distance. Little motion of C_1 and C_4 or the developing carboxylate moiety ($O_2-C_3-O_3$) was in evidence. The hydrogen bonding interaction with the carbonyl oxygen (H_3-O_2) showed little if any motion. Intrinsic reaction coordinate (IRC) following[14d] suggests that the net nuclear event in **TS-2** is the formal transfer of HO^+ to the carbon−carbon double bond. A 1,4-hydrogen transfer of the peroxyacid hydrogen to the carbonyl oxygen occurs in concert with oxirane C−O bond formation *after the barrier is crossed* (Figure 2). The C_3-O_2 bond is seen to shorten and the C_3-O_3 bond lengthen as the carboxylic acid forms and the O−O bond ruptures along the reaction coordinate. The dominant O_3-H_2 hydrogen bond is maintained throughout the oxygen transfer process.

(c) Activation Barriers for Allyl Alcohol Epoxidation. We predict a classical barrier height ($\Delta E^{\ddagger}$) for epoxidation of allyl alcohol of 7.7 kcal/mol (MP4//MP2/6-31G(d)) relative to isolated reactants and a $\Delta G^{\ddagger}_{278}$ of 19.6 kcal/mol ($\Delta H^{\ddagger}_{278}$ = 7.98 kcal/mol, $\Delta S^{\ddagger}_{278} = -41.76$ cal/mol K). When polarization functions (6-31G(d,(p)) were added to the two acidic hydrogens involved in hydrogen bonding (H_1, H_2) the geometry of **TS-2** was not altered in any significant manner (Figure 2).[22] To avoid the inaccuracy that can potentially arise from an unbalanced basis set and to estimate the influence of polarization p functions on the energetics of reaction, we performed MP4 single point

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[22] A cautionary note is in order since the potential energy surface at the MP2/3-21G level was distinctly different from that observed at MP2/6-31G(d). An IRC showed that the acidic peroxyformic acid hydrogen migrated to the alcohol oxygen instead of the anticipated intramolecular migration to the carbonyl oxygen.

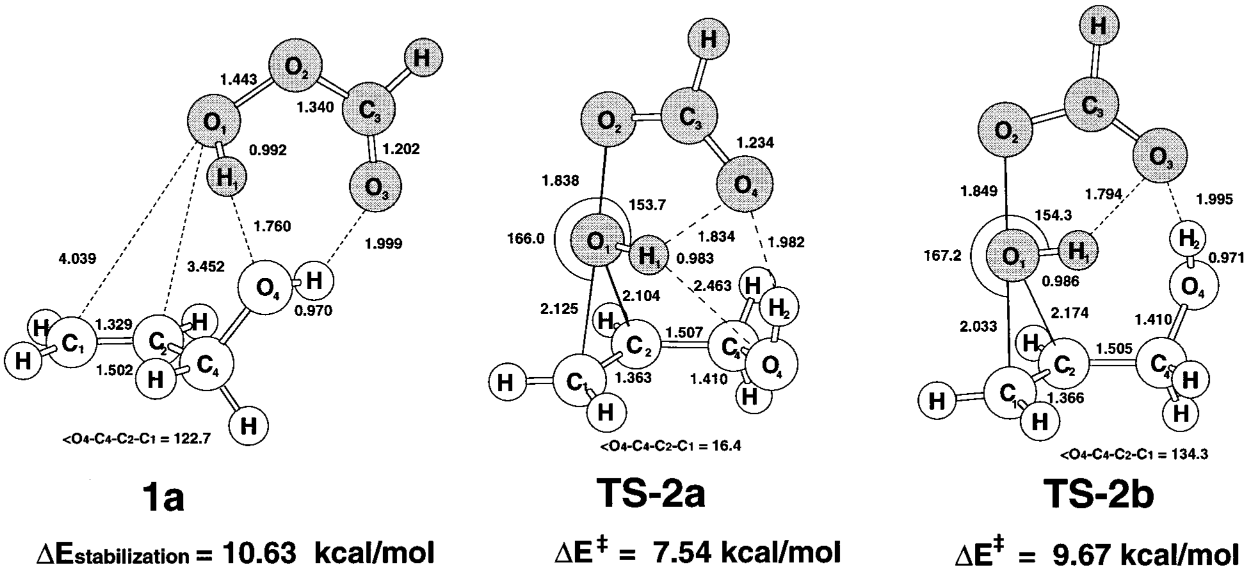

Figure 3. Reactant cluster **1a** and transition states **TS-2a** and **TS-2b** for the epoxidation of allyl alcohol with peroxyformic acid calculated at the B3LYP/6-311G(d,p) level of theory. Distances are in angstroms and angles in degrees. Relative energies are with respect to isolated reactants.

calculations using the 6-31G(d,p) basis set (with polarization functions added to all hydrogens). The classical barrier ($\Delta E^{\ddagger}$) is 6.9 kcal/mol with respect to isolated reactants and 19.0 kcal/mol relative to the cluster, pointing out that the effect of the polarization functions is small and does not affect the global discussion. This theoretical barrier is remarkably close to the enthalpy ($\Delta H^{\ddagger} = 8.35$ kcal/mol) and entropy ($\Delta S^{\ddagger} = -41.0$ cal/(mol K)) reported for epoxidation of 3-hydroxycyclohexene with peroxybenzoic acid in benzene solvent (5 °C).[3b] We have shown previously[16f] that $\Delta S^{\ddagger}$ values calculated relative to isolated reactants are in better agreement with experiment than entropies of activation computed from a prereaction complex.[16f] In the more polar protic solvent acetic acid, the $E_a = 18.3$ kcal/mol ($\Delta S^{\ddagger} = -16.1$ cal/mol K) for epoxidation of allyl alcohol with peroxyacetic acid.[23a] These observations are consistent with experiment since the relative rate of epoxidation is more a function of the number of alkyl group substitutents on the double bond than the actual structure of the alkene.[24] It is also well established that protic solvents decrease the rate of epoxidation by disrupting the intramolecular hydrogen bond in the peroxyacid thereby impeding the 1,4-hydrogen shift that accompanies oxygen atom transfer and produces a neutral carboxylic acid leaving group.[23]

When the free energy of activation is computed relative to reactant cluster **1**, $\Delta G^{\ddagger}_{278} = 19.8$ kcal/mol ($\Delta H^{\ddagger}_{278} = 17.0$ kcal/mol, $\Delta S^{\ddagger}_{278} = -9.93$ cal/(mol K)). An SCRF[21c] correction for benzene solvent ($\epsilon = 2.28$) has only a minor effect and reduces this classical barrier from 19.6 to 19.3 kcal/mol. The barrier heights ($\Delta E^{\ddagger}$) for **TS-2** at the QCISD(T)//MP2/6-31G(d) level are predicted to be 11.4 relative to isolated reactants and 21.8 kcal/mol relative to cluster **1**, respectively. At the QCISD(T)//QCISD/6-31G(d) level the classical barrier for the epoxidation of propene is 16.0 kcal/mol (Table 2). The $\Delta H^{\ddagger}$ for epoxidation of allyl alcohol computed relative to reactant cluster **1** is close to the $E_a = 18.3$ measured in acetic acid solvent.[23a]

Table 2. Activation Barriers Relative to Isolated Reactants (in kcal/mol) for the Epoxidation of Ethylene, Propene, and Allyl Alcohol with Peroxyformic Acid Calculated at Various Computational Levels

	$\Delta E^{\ddagger}$			
substrate	MP4SDTQ//MP2	QCISD(T)//QCISD	B3LYP//B3LYP	QCISD(T)//B3LYP
ethylene	16.3[a]	18.8[a]	14.1[a]	18.7[a]
propene		16.0[a]	12.0[a]	15.9[a]
allyl alcohol	7.7[a]	(11.4)[a,b]	7.5[c]	11.4[c]

[a] The 6-31G(d) basis set was used for both single point energy calculations and optimizations. [b] QCISD(T)/6-31G(d)//MP2/6-31G(d) calculation; the same value was obtained for the QCISD(T)6-311G(d,p)//B3LYP/6-311G(d,p) barrier. [c] The 6-311G(d,p) basis set was used for both single point energy calculations and optimizations.

(d) Calculations at the B3LYP/6-311G(d,p) Level of Theory. We have recently found as part of a related study on the nature of the transition structure for a series of alkene epoxidation reactions with peroxyformic acid that the transition structures for oxidation of ethylene and propene calculated at the B3YLP level, as well as at the QCISD and CCSD levels, are symmetrical with a spiro orientation of the electrophilic oxygen, whereas the MP2 calculations favor an unsymmetrical approach of the peroxyacid over one of the carbon atoms of the double bond.[16e] The recent study by Yamabe[25a] at the MP2 level suggested that the unsymmetrical nature of these transition structures was supported by kinetic isotope effects (KIE) reported by Hanzlic.[21b] However, our earlier report concluded that the asymmetric approach of the peroxyformic acid in the TS was an artifact of the MP2 method.[16f] Singleton et al.[25b] have recently reported experimental KIE and B3LYP calculations that also support a symmetrical TS for the epoxidation of propene. Although the predicted MP2 activation barriers appear to be quite reliable, the different C−O bond distances in **TS-2** (1.907, 2.228 Å) prompted us to also examine this oxidative

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(23) (a) Dryuk, V. G. *Russ. Chem. Rev.* **1985**, *54*, 986. (b) DiFuria, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853. (c) Swern, D. *Organic Peroxides*; Wiley-Interscience: New York, 1971; Vol. II, pp 73−74 6. (d) For a discussion of solvent assisted proton transfer in alkyl hydrogen peroxides, see: Dankleff, M. A. P.; Ruggero, C.; Edwards, J. O.; Pyun, H. Y. *J. Am. Chem. Soc.* **1968**, *90*, 3209. (e) Curci, R.; DiPrete, R. A.; Edwards, J. O.; Modena, G. *J. Org. Chem.* **1970**, *35*, 740.

(24) (a) Swern, D. *J. Am. Chem. Soc.* **1947**, *69*, 1692. (b) The relative rates of epoxidation of ethene, propene, styrene, isobutene, and 2-butene with peracetic acid are 1, 22, 59, 484, and 489, respectively.

(25) (a) Yamabe, S.; Kondou, C.; Minato, T. *J. Org. Chem.* **1996**, *61*, 616. (b) Singleton, D. A.; Merrigan, S. R.; Liu, J.; Houk, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 3385.

process at the B3LYP/6-311G(d,p) level.[26] As anticipated based upon our earlier DFT calculations, the C−O bonds of the developing epoxide in allyl alcohol computed at the B3LYP/6-311G(d,p) level are almost equal (2.104, 2.125 Å, **TS-2a** in Figure 3). The O−O bond in **TS-2a** is slightly longer (1.838 Å) and the two dominant hydrogen bonds (H_1-O_3 and H_2-O_3) are somewhat longer (1.834, 1.982 Å). The pertinent $O_4-C_4-C_2=C_1$ dihedral angle in **TS-2a** (16.4°) is also quite close to that found at the MP2 level (25.6°). We have also located a first-order saddle point for the oxidation of allyl alcohol (**TS-2b**) where C −C bond rotation in the allyl alcohol has occurred ($\angle C_4-O_4-C_2=C_1 = 134.3°$). This TS that was suggested by earlier workers and invoked a hydrogen bonding interaction of the allyl alcohol with the peroxo oxygen is 2.1 kcal/mol higher in energy than **TS-2a** at this level of theory. A $\Delta\Delta E^{\ddagger}$ of this magnitude suggests that **TS-2a** is on the dominant pathway of the potential energy surface for the epoxidation reaction. The dihedral angles between the peroxo functionality and the axis of the C=C bond in these nearly spiro TS are 85.6 and 110.1, respectively. The energetics of the reaction are remarkably close to the MP4//MP2 barriers for **TS-2** (Figure 2) with a classical barrier relative to reactants of 7.5 kcal/mol and an energy of stabilization of the reactant complex **1** of 10.6 kcal/mol.[27] This close agreement may well be fortuitous since in general activation barriers for peroxyacid epoxidation of alkenes at the B3LYP/6-31G(d) and B3LYP/6-31+G(d) levels are systematically lower (up to 5−6 kcal/mol) than the barrier heights calculated at such higher correlated levels as QCISD.[16e] The QCISD(T)//B3LYP/6-311G(d,p) calculated barrier (11.4 kcal/mol) has the same predicted value as the QCISD(T) barrier on the MP2 geometry, suggesting that these two TS are indeed quite comparable in structure.

In general, the enthalpy of activation for epoxidation of an alkene in the condensed phase is about 2 kcal/mol *lower* that that of its corresponding allyl alcohol.[2,3] This has generally been attributed to an inductive effect of the hydroxyl group reducing the nucleophilicity of the carbon−carbon double bond. However, the more negative entropy of activation associated with complexation of the incoming peroxyacid with the alcohol hydroxyl group affords a slightly higher observed $\Delta G^{\ddagger}_{278}$ for the latter. As noted above, these activation parameters are highly solvent dependent.[23d,e] Interestingly, the QCISD(T) single point barriers calculated on the QCISD/6-31G(d) and B3LYP/6-31G(d) geometries for epoxidation of propene are 16.0 and 15.9 kcal/mol, respectively.[16e] This represents a reduction in $\Delta E^{\ddagger}$ due to the hydroxyl substituent in allyl alcohol at both levels of theory of about 4.5 kcal/mol relative to the oxidation of propene. Thus, in contrast to their relative reactivity in solution, the intrinsic gas-phase reactivity of an allyl alcohol is considerably *greater* than that of its corresponding alkene. It is likely that the discrepancy between theory and experiment is a consequence of the hydrogen bonded pre-reaction complex and ground state solvation of the allyl alcohol. The observed rate constant in solution is proportional to the equilibrium concentration of the complex. At least in the gas phase this equilibrium constant is small. Such complexation has a major influence on reducing the entropy requirements for what is otherwise a bimolecular process with a relatively high negative entropy.

Conclusions

We conclude from these data that an intricate hydrogen bonding network involving *both the peroxyacid and the alcohol hydrogens* is responsible for the directing effect in the epoxidation of allyl alcohols. The dominant interaction in both the ground and transitions states involves hydrogen bonding of the allyl alcohol to the more basic carbonyl oxygen of the peroxy acid. The trajectory of the approaching electrophilic oxygen atom to the carbon−carbon double bond is of secondary importance relative to the hydrogen bonding interaction with the carbonyl oxygen (H_2-O_3).

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Supporting Information Available: G2 total energies (at 0 and 298 K) of peroxyformic acid, its anion, and structures **A**, **B**, **C**, **B1**, and **C1** of protonated peroxyformic acid (1 page). See any current masthead page for ordering and Internet access instructions.

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(26) (a) The DFT calculations were carried out with the three-parameter hybrid method of Becke.[26b−d] The exchange functional is a combination of Local Spin Density, Hartree−Fock, and Becke 1988.[26b] The correlation functional is a combination of the Lee−Yang−Parr[26e] gradient corrected correlation functional and Vosko−Wilk−Nusair[26f] local correlation functional. (b) Becke, A. D. *Phys. Rev.* A **1988**, *37*, 785. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (d) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *80*, 11623. (e) Lee, C.; Yang, W.; Parr, R. G.; Frisch, M. J. *Phys. Rev.* **1988**, *B41*, 785. (f) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200.

(27) The stabilization energy for complex **1** computed at the B3LYP/6-311G(d,p) level is 10.6 kcal/mol and single point calculations at the QCISD(T) and MP4 level gave energies of 11.1 and 11.4 kcal/mol below that of isolated reactants. The three barrier heights for the oxygen transfer computed relative to these reactant clusters are 18.2, 22.5, and 19.3 kcal/mol, respectively.